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and subjects see pages 2767-2770*

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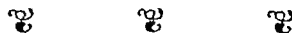


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CASE REPORT

Electrocardiographic Evidence of Myocardial Degeneration in an American Prisoner
of War Following Undue Physical Stress and Other Factors, *M D Mieras, Capt ,*
(MC), AUS, and R L Zimmerman, First Lt , (MC), AUS

(Continued on page 1412)

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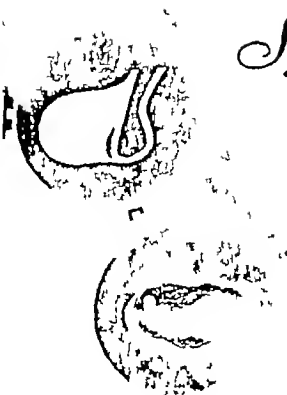
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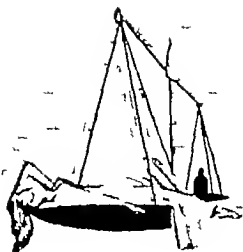
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[See pages 1416 and 1418 for additional Society Officers]

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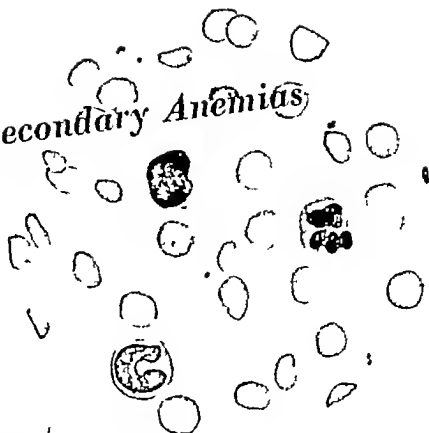
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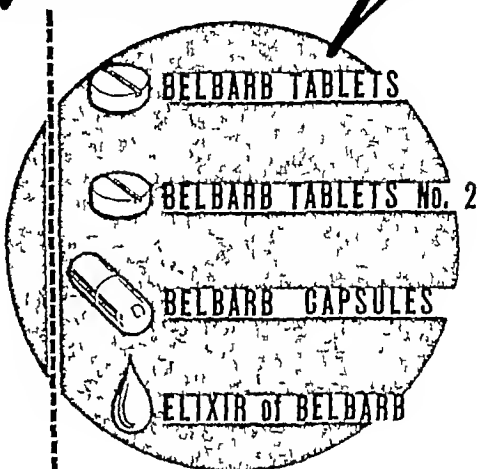
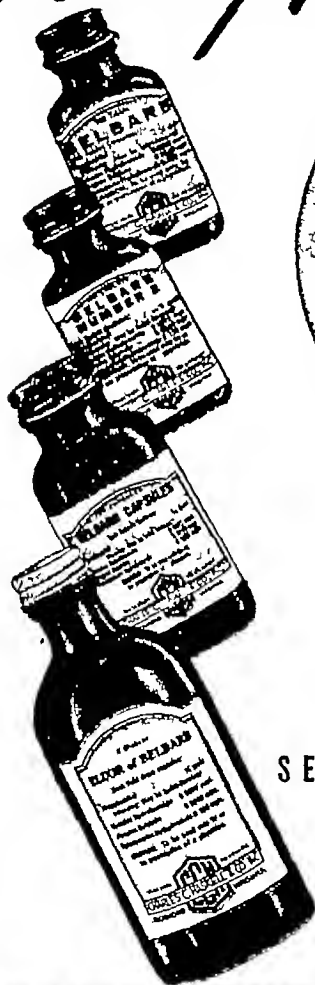
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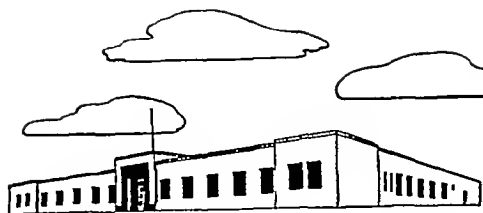
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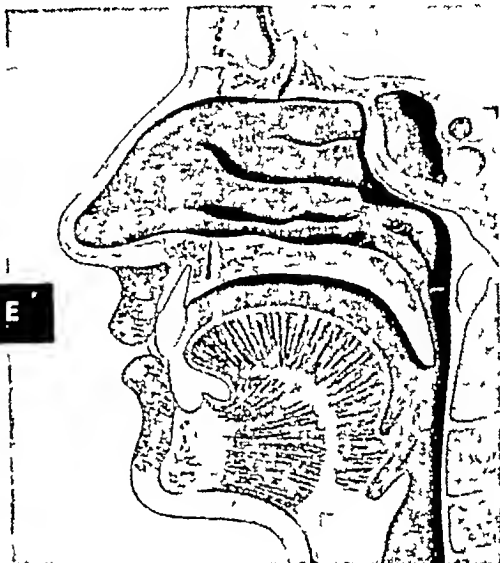
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When the physician uses ARGYROL he knows that he is contributing most to recovery through support of nature's own First Line of Defense

The cleansing, demulcent, bacteriostatic action of ARGYROL is attained by its three-fold action



Three-Fold Action of ARGYROL

- 1 ARGYROL is decongestive, without irritation to the membrane, and without ciliary injury
- 2 ARGYROL is powerfully bacteriostatic, yet is non-toxic to tissue
- 3 ARGYROL stimulates secretion and cleanses, thereby enhancing Nature's own first line of defense

Three-Fold Approach to Para-nasal Therapy

- 1 The nasal meatus by 20 per cent ARGYROL instillations through the nasolacrimal duct
- 2 The nasal passages with 10 per cent ARGYROL solution in drops
- 3 The nasal cavities with 10 per cent ARGYROL by nasal tamponage

ARGYROL *the Physiologic*
Anti-infective with broad, sustained action



Made only by the **A C BARNES COMPANY, NEW BRUNSWICK, N J**
 ARGYROL is a registered trade mark, the property of A C Barnes Company

FACTS ARE STUBBORN THINGS...

| A Comparison of Food Values in Leading Infant Cereals | | | | | | |
|---|---|---------------------------|--------------------------------------|----------------------------------|------------------------------------|----------------------------------|
| Precooked Cereal | Natural Food Sources | Protein ¹ % | Carbohydrate ² g/100 g | Calories ² Per Oz. | Thiamine ² Mg/100 G. | Niacin ² Mg/100 G. |
| CEREVIM | Whole wheat meal, natural, non-fat milk solids, wheat germ, corn meal, brewer's yeast, barley, malt. | 19.4 | 65.2 | 108 | 2.1 | 3.3 |
| A | Wheat meal, natural, wheat germ, corn meal, powdered beef bone, little leaf, brewer's yeast. | 15.0 | 69.9 | 106 | 1.20 | 0.55 |
| B | Cornmeal, milk syrup, powdered beef bone, powdered yeast. | 14.0 | 69.8 | 100 | * | * |
| C | Branflakes, whole wheat flour, corn meal, wheat germ, milk syrup, brewer's yeast. | 15.5 | 71.1 | 107 | 1.50 | 0.37 |
| D | Whole wheat meal, corn meal, wheat germ, milk, non-fat milk solids, brewer's yeast. | 15.0 | 73.1 | 102 | 1.03 | 0.36 |
| E | Old fashioned, yellow corn meal, wheat, durum middlings, non-fat milk solids, brown sugar, defatted wheat germ, brewer's yeast. | 14.74 | 68.81 | 104 | * | * |
| F | Whole wheat meal, corn meal, wheat germ, milk syrup, dried papaya fruit, non-fat milk solids, brewer's yeast. | 15.5 | 71.35 | 102 | * | * |

(1) FROM LABEL STATEMENTS OF COMPOSITION ON REGULAR PACKAGES PURCHASED TO MAY 9, 1946.
(2) REPORT OF THE COUNCIL ON FOODS AND NUTRITION, J. A. M. A., 126:102, 1944; J. A. M. A. 123:402, 1943.
NOT REPRINTED IN REFERENCE (2)

AND SHOULD BE STUDIED CAREFULLY
WHEN SELECTING A FIRST SOLID FOOD



This compilation of facts from reports by the Council on Foods and Nutrition and from label statements of composition of better-known precooked cereals, show that

CEREVIM

IS TRULY

a first among first foods

CEREVIM is highest in protein—amino acid content, thiamine and riboflavin and unsurpassed in niacin. CEREVIM supplies the greatest caloric value with a minimum of carbohydrate. CEREVIM is rich in iron, copper, calcium and phosphorus. Prepared from eight natural food sources, CEREVIM offers a nutritionally well-balanced infant cereal.

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Hay fever sufferers are finding prolonged symptomatic relief with minimal dosage—only three drops—of Privine, Ciba's potent vasoconstrictor.

Privine Hydrochloride acts quickly on the nasal mucosa without retarding ciliary activity. Its solution is buffered to a pH of 6.2, closely simulating normal nasal secretions.

Physicians will find that by advising their patients to use no more than the recommended three drops in each nostril, no oftener than three times daily, gratifying and prolonged relief will be experienced.

PRIVINE is available in two solutions: 1 per cent and 0.05 per cent, packaged in 1 ounce bottle with dropper designed to dispense but three drops—the recommended dose. Also available in bottles of 16 fluid ounces.

PRIVINE NASAL JELLY—Tubes of $\frac{1}{2}$ oz., containing 0.05% Privine Hydrochloride.

*Privine—Trade Mark Registered in U. S. Pat. Off.
Brand of Naphazoline Hydrochloride*

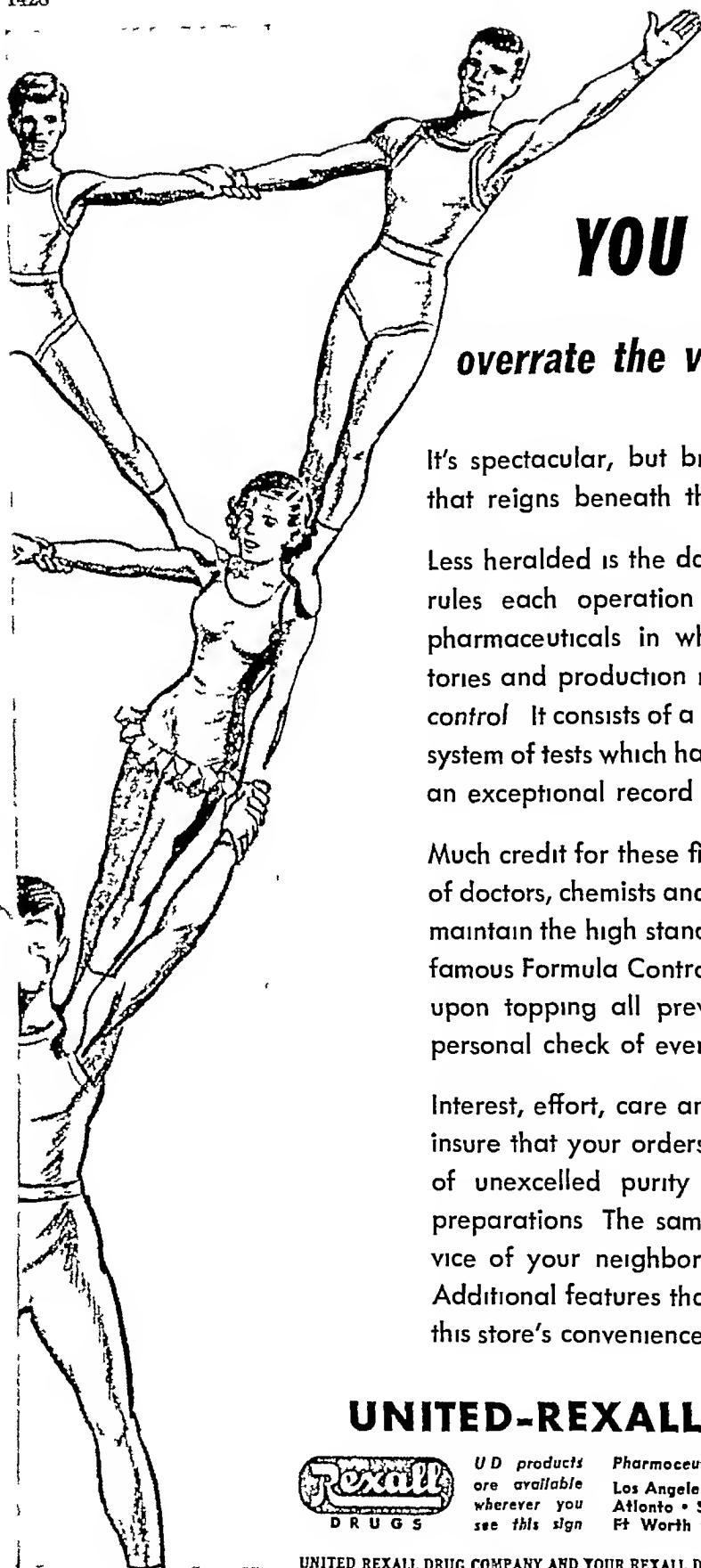


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In Canada: Ciba Company Limited, Montreal



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Interest, effort, care and experience combine to insure that your orders are filled with materials of unexcelled purity when you specify U.D. preparations The same qualities mark the service of your neighborhood Rexall Drug Store Additional features that patients appreciate are this store's convenience and economy.

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At first the infant,
Mewling and puking in the nurse's arms*



ZYMONOL has long been recognized by obstetricians and pediatricians as an ideal bowel management therapy

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Soft, comfortable, regular evacuation is assured without catharsis or colloidal bulkage. Because Zymenol is agreeably palatable, sugar free, and the only emulsion effective in *teaspoon* doses, patient control is seldom a problem.

For patient-acceptable bowel management in a age group—specify Zymenol.
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**Glidden processed brewers' yeast assures zymolytic factors and natural vitamin B complex without live yeast cells.



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Effective in

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The Common Denominator of Reducing Diets

Whether weight reduction is to be brought about gradually, at the rate of a pound or two per week, or drastically at the rate of a pound per day, all reducing diets must recognize one cardinal requirement: the need for protein of the right quality in the right amount

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Lean meat may well be called the common denominator of reducing diets. Its protein content is notably high, and the protein it supplies is of high biologic quality, adequate for every protein need

The Seal of Acceptance denotes that the nutritional statements made in this advertisement are acceptable to the Council on Foods and Nutrition of the American Medical Association



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MAIN OFFICE, CHICAGO ... MEMBERS THROUGHOUT THE UNITED STATES



healing sleep is one of the most effective therapeutic agents. But when clinical conditions alter sleep habits, adequate rest may be most difficult to secure.

When sleep patterns of your patients are altered, 'DELVINAL' sodium vinbarbital will provide a night of restful sleep in the majority of instances with relative freedom from unpleasant side-effects of excitation or 'hangover'. 'DELVINAL' sodium vinbarbital is a mild sedative that has a relatively short induction period and a moderate duration of action.

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Business
Opportunities

Pages 1513 and 1515

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BACTERIAL ENDOCARDITIS

A detailed line drawing of two hands. The right hand holds a syringe with a needle, and the left hand holds a small vial labeled 'PENICILLIN SCHENLEY'. The background is filled with a dense, stippled texture.

No 1 in Schenley

Laboratories' continuing
summary of
Penicillin Therapy

BEFORE YOU DECIDE ON THE PENICILLIN OF YOUR CHOICE

For many years, Schenley has been among the world's largest users of research on mycology and fermentation processes. In addition Schenley Laboratories manufactures a complete line of superior penicillin products—products thoroughly tested for potency and quality. These two important facts mean you may give your patients the full benefits of complete penicillin therapy.

SCHENLEY PENICILLIN PRODUCTS

Penicillin Ophthalmic Ointment Schenley
Penicillin Troches Schenley
Penicillin Tablets Schenley
Penicillin Ointment Schenley
Penicillin Schenley

Penicillin is the best agent available for the treatment of subacute bacterial endocarditis. Daily administration of 200,000 to 300,000 units or, in infections with resistant organisms, much more, in divided doses (every 3 hours) is required. Intramuscular injections are usually the route of choice, however, in certain instances, it may appear desirable to employ continuous drip. Therapy should be continued for a minimum of 3 weeks and must be continued until the blood cultures are consistently negative. Penicillin alone is as effective as penicillin and heparin combined.

Final determination of cure depends upon long term observation, but if the patient remains asymptomatic and bacteriologically free for a period of 4 weeks after cessation of penicillin therapy, the prognosis for complete cure is excellent. However, it must be remembered that valvular damage and renal lesions are not favorably influenced

DAWSON, M. H., AND HUNTER, T. H.: *The Treatment of Subacute Bacterial Endocarditis with Penicillin. Results in Twenty Cases* J.A.M.A. 127:129 (Jan. 20) 1945. FAYOUR, C. B., JANEWAY, C. A., GIBSON, J. G., II AND LEVINE, S. A.: *Progress in the Treatment of Subacute Bacterial Endocarditis*, New England J. Med. 234:71 (Jan. 17) 1946.

SCHENLEY LABORATORIES, INC Executive Offices 350 Fifth Avenue N Y C

For National Rehabilitation



Yes, it's a fact

In addition to its refreshing quality and its flavor, ice cream contains many important health giving food elements. It contains the following nutrients:

Vitamins Ice Cream is a good source of Vitamin A and Riboflavin (Vitamin G) and contains other vitamins found in milk.

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All of these nutrients promote health and well being.

And remember, the particular combination of nutrients found in Ice Cream is unusual. This is one reason why Ice Cream is accorded such an important role in our national rehabilitation program.

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In Age and in Youth.

MANDELAMINE

Reg. U. S. Pat. Off.
(Methenamine Mandelate)

IS AN ESPECIALLY EFFECTIVE URINARY ANTISEPTIC

Safety, ease of administration and characteristically prompt action combine to make Mandelamine an especially efficient agent in the treatment of urinary infections in children and in elderly patients.

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Uncomplicated oral administration of Mandelamine requires no supplementary acidification, restriction of fluid intake, dietary control, or other special measures. Only in those infections due to urea-splitting organisms, may accessory acidification be necessary.

Early control of common urinary infections is the characteristic response to Mandelamine therapy. Disturbing urinary symptoms are usually alleviated rapidly and, in the absence of obstruction, the urine is promptly cleared of organisms in a high percentage of cases.

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Please send me literature, and a
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mine.

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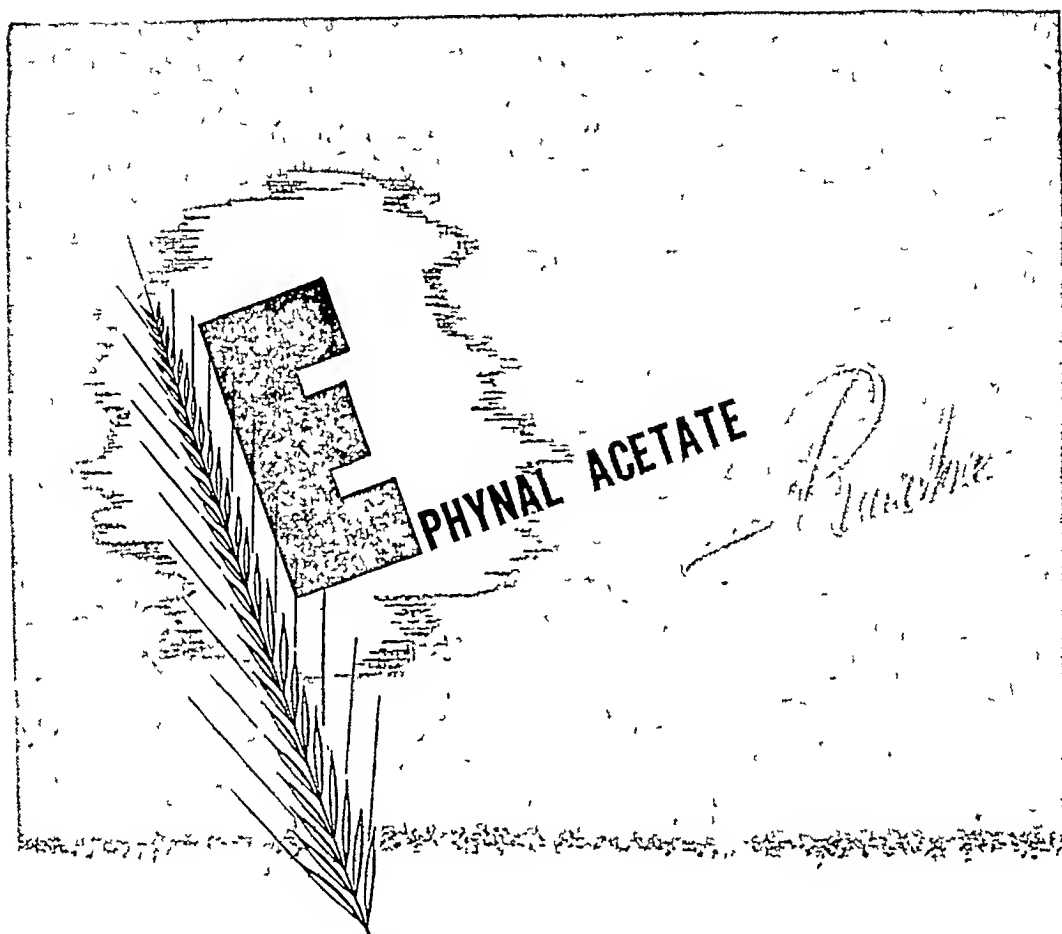
State

NEPERA CHEMICAL CO. INC.

Manufacturing Chemists



Yonkers 2, New York



FOR THREATENED AND HABITUAL ABORTION

In the treatment of habitual abortion, "vitamin E should be used because it appears to offer great hope in salvaging pregnancies that would otherwise habitually abort." * Ephynal Acetate—the Roche vitamin E preparation (α tocopherol acetate)—is particularly suitable for the treatment of habitual and threatened abortion because it is stable, of unvarying potency and purity, and well tolerated even in large doses and over long periods of time. Its freedom from side reactions is of signal value in all disorders amenable to vitamin E therapy. Available in tablets of 3, 10, and 25 mg.

HOFFMANN-LA ROCHE, INC., Roche Park, Nutley 10, New Jersey

*A. T. Herrig & R. G. Livingstone. *New England J. Med.* 230:798 1944



Announcing

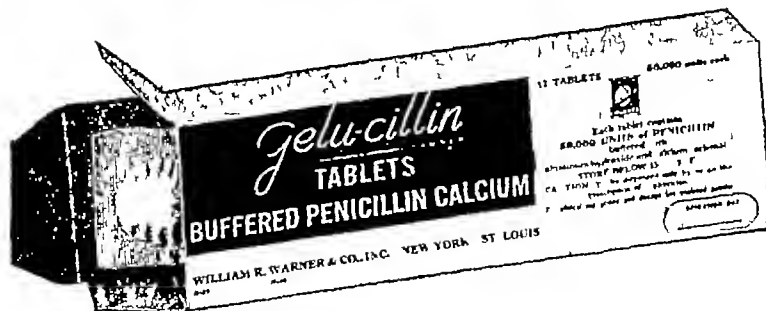
Gelu-cillin 'WARNER'
50,000 units of penicillin per tablet

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Buffered against destructive action
of gastric acid

Gelu-cillin 'WARNER'
Convenient to administer . scored
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Gelu-cillin 'WARNER'
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of 12 3 strips of 4 tablets

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113 WEST 18th STREET • NEW YORK 11, N Y



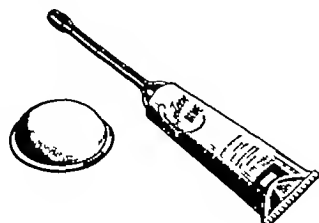


COLOR TESTS with the accurate aid of this Nessler apparatus help control the quantity of ingredients in the various Lanteen products. Control of the efficacy of all its products, by the latest scientific means, is the constant aim of Lanteen Medical Laboratories. Lanteen Lilac (Mensinga-type diaphragm) is available only on the prescription of a physician.

Since patients are not mechanically minded, simplicity and ease of handling are prime requisites for continued use. Lanteen Lilac flat spring diaphragm is extremely simple to place—it is collapsible in one plane only. No inserter required.

L A N T E E N

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to combat
the depression of

chronic organic disease Many patients with chronic organic disease—arthritis or asthma, for example—sink into a persistent depression characterized by discouragement, or even despair. Unless effectively combated, this depression may handicap management of the basic disorder and intensify its symptoms.

By restoring optimism and interest in useful living, Benzedrine Sulfate frequently helps to overcome prolonged depression accompanying chronic illness. Obviously, in such cases careful observation of the patient is desirable and the physician will distinguish between the casual case of low spirits and a true mental depression.

benzedrine sulfate (*racemic amphetamine sulfate, S.K.F.*) Tablets and Elixir



Smith, Kline & French Laboratories, Philadelphia, Pa.



IN POISON IVY



IN SUN RASHES



FOR INSECT BITES

PRESCRIBE *Enzo-Cal* for ITCHING

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Laboratories

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- Prompt antipruritic action.
- Protects and aids healing.
- Cleaner and more convenient to use; patients prefer it.
- Soft, greaseless cream combining semi-colloidal calamine and zinc oxide with benzocaine.

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Gerilac

A NEW DIETARY SUPPLEMENT FOR THE AGED

Gerilac has a milk-nature most perfect food—modified to provide a high protein and low fat content with the addition of other dietary factors considered essential in geriatric nutrition so that

Gerilac supplies in one reliquified pint at least one-third of the protein, a full allowance of each of the vitamins and minerals, and about one-tenth of the calories recommended for daily intake by the Food and Nutrition Board National Research Council

Gerilac offers these nutritional values in a palatable easily consumed and readily digestible form (suitable for use as a fever age or in Special Diets). It also lends itself ideally for the nutrition of convalescents and of pre- and postoperative cases.

Borden's

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Gerilac

STERILIZED MILK FOR SPECIAL DIETS

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RAY-FORMOSIL

FOR THE TREATMENT OF

ARTHRITIS and RHEUMATISM

70% EFFECTIVE
 Waugh (British Medical Journal, 1, 1945 873) has treated over 1200 cases of arthritis by intra articular injection of acid and has observed that 70% of cases of all types have been rendered free from pain, with sufficient restoration of function to allow return to normal occupation

● Ray-Formosil for intramuscular injection is a clinically proved, effective treatment in most cases of Arthritis and Rheumatism. It is a non-toxic and sterile, buffered solution containing in each cc the equivalent of:

Formic Acid 5 mg.

Hydrated Silicic Acid. . . . 2 25 mg.

A descriptive folder will be furnished upon request.



RAYMER PHARMACAL COMPANY

PHARMACEUTICAL MANUFACTURERS, PHILADELPHIA 34, PA.

The So-Called Physiological Anemia of Infants—

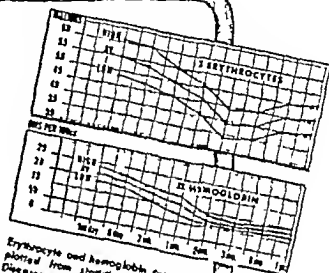
MOST infants experience a mild hypochromic anemia, due to iron deficiency in the dietary beginning at about the fourth month of life. This well known fact has for long been so lightly regarded that it is often referred to as the "physiological anemia" of infancy. That this is a misnomer is indicated by the work of Mackay* who following thorough and controlled studies, showed that (1) the anemia was preventable by iron medication (2) the anemia, though slight, lowered markedly the resistance of the child to infectious disease, and (3) growth was retarded by iron deficiency. Mackay's investigation showed that in babies given iron the incidence of infection was lower and its duration considerably shorter and that babies given iron averaged one pound heavier than those in the control group.

The conclusion was:

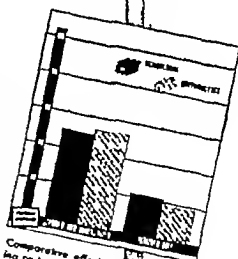
NO ANEMIA, EVEN OF SLIGHT DEGREE, IS INSIGNIFICANT because it is too important a factor in predisposing to infection.

It has been shown that homogenized iron-containing foods yield considerably more utilisable iron than similar foods which have been strained only. The texture of homogenized baby foods is so fine that they may be fed—mixed in the milk formula—through a nipple opening of ordinary size. Supplemental feeding of homogenized baby foods may be started as early as the fifth week of life, before the prenatal stores of iron are exhausted and before the usual anemia of infancy has set in. Only Libby's Baby Foods are homogenized as well as strained.

*See: Kracker Roy H. Diseases of the Blood, Philadelphia, Pa., J. B. Lippincott Co., 1941 ed. 2 p. 332.



Erythrocyte and hemoglobin curves of first year of life plotted from statistics of Holt and McIntosh. Holt's Diseases of Infancy and Childhood, New York, N. Y. D. Appleton-Century Co. 1940 11th ed., p. 613.



Comparative effects of strained feeding on hemoglobin and erythrocytes of celiac animals. Left: strained and homogenized; right: strained, but not homogenized.



Libby, McNeill & Libby
Chicago 9, Illinois

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MEDICAL
ASSOCIATION

TESTOSTERONE PROPIONATE

Obtainable from your usual source of supply in 1 cc ampules, 5 mg, 10 mg, and 25 mg, in boxes of 3, 6, and 50

Approved literature describing the use of this preparation in recognized indications will be forwarded to physicians on request

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HARRISON, N. J.

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RARE CHEMICALS

West Coast Distributors: GALEN COMPANY, Berkeley 2, California

in **NAUSEA** and
VOMITING OF PREGNANCY



Of the appetite stimulating B vitamins, the specific factors provided by Pyrrithiad most rapidly relieve the hyperemesis of pregnancy. This dangerous gastrointestinal disturbance which restricts absorption at a time of increased vitamin requirement, in many cases is promptly alleviated by injections of Pyrrithiad. Unless so relieved, nausea and vomiting of pregnancy may lead to polyneuritis, a symptom of profound thiamine deficiency. Pyridoxine hydrochloride and thiamine hydrochloride, as contained in Pyrrithiad act promptly and apparently with specificity in this condition. Pyrrithiad is supplied as a solution for intravenous or intramuscular injection and as tablets for oral use.

LAKESIDE LABORATORIES Milwaukee 1 Wisconsin

On request. Complete literature including a reprint of the report of Hart and coworkers *Am. J. Obst. and Gynec.* 48:251, 1944.

Pyrrithiad **LAKESIDE**

Effective Against CHIGGERS

(RED BUGS)



SULFUR FOAM APPLICATORS

Convenient Cloth Applicators
Impregnated with Sulfur and Soap

DURING THE COMING SEASON this timely prescription product will bring relief and grateful thanks from patients suffering from chiggers

Sulfur Foam Applicators are indicated whenever sulfur is to be used externally

They have the advantage of

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PROPHYLAXIS
SULFUR FOAM APPLICATORS



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NEW YORK STATE JOURNAL OF MEDICINE

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VOLUME 46

JULY 1 1946

NUMBER 13

Editorial

The Annual Meeting

The State Society held its 1946 annual meeting, the first general sessions since the close of the Great War, at the Hotel Pennsylvania in New York City from April 29 to May 3, 1946. The registered attendance of doctors, nurses, and students was 4,561. As of May 1, 1946, the total membership of the Medical Society of the State of New York was 19,940. Apparently, about one quarter of the members seems to have attended.

This is heartening both for the chairman of the sections who work long and hard to prepare their respective programs, for the exhibitors, who by their rental of exhibit space make the financing possible, and, likewise, for the Convention Committee of the State Society. The scientific exhibits this year were of more than usual interest and diversity. The availability of good photographic materials is to be noted, now that the war is over, and it is to be hoped that color photography will be developed more widely and used more freely than in the past.

The extended session of the House of Dele-

gates permitted more time for the work of the reference committees in the consideration of the annual reports of officers and of resolutions introduced by members. The account of these proceedings will be published in this issue and subsequent issues of the JOURNAL and deserves careful reading by the members of the society. The constituent county societies were each represented by full delegations and a thorough and complete discussion of all the business on hand prevailed. The Speaker of the House, Dr. Louis H. Bauer, conducted the meetings with his usual skill and competency and this was his final appearance in this capacity, for now he is the President-Elect.

An unusual feature of the meeting was the award of a prize, a well-behaved puppy, and several additional book prizes, for essays by school children on the use of animals for scientific experimental work. This marks the first time awards have been given outside the membership of the society itself, the presentations being made during the course of the final session and witnessed by the par-

ents of the winners and representatives of the New York City Public Schools

Among the important business matters transacted by the delegates were the final steps taken to establish a corporation by the society, authorized to enter into contractual agreement with the Veterans Administration to implement, for the entire State, local medical service for veterans with service-connected disabilities. It is hoped that a fair uniform fee schedule can shortly be instituted for the State as a whole and that

claims for services rendered in this program can be expedited as rapidly and satisfactorily as possible. The proposed arrangement should prove of mutual advantage to all concerned.

In this issue of the JOURNAL are contained the addresses made by guest speakers at the Annual Banquet, which merit the careful attention of our readers. The scientific papers presented at the Section Meetings will appear in subsequent issues, as well as the detailed proceedings.

Dr. Simon Flexner

Another great figure in American medicine passed away on May 2 at the advanced age of eighty-three. A renowned investigator in the field of infectious diseases in his own right, Dr. Flexner was the organizer and first director of the Rockefeller Institute for Medical Research, from which he retired in 1935 with the rank of director emeritus.

There were other distinctions. Among his achievements were the production of a curative serum for cerebrospinal meningitis, in cooperation with the late William H. Park and others, as well as his researches on poliomyelitis and the filterable viruses. In the first World War he developed our knowledge of the acute dysenteries while serving in the Philippines and was finally commissioned a lieutenant colonel.

Dr. Flexner's university connections were numerous and prominent and he was awarded many honorary degrees. He made many outstanding contributions to medical

literature. For many years he was a member of the State Society until his retirement. One of his signal contributions to the profession was his unfailing support of the efforts to curb the activities of the antivivisectionists. Year after year with a group of others interested in the subject, he appeared at the legislative hearings where his eminence as an investigator constituted a convincing argument in itself. One of the last acts of his long life was to lend his aid in the campaign against the recent antianimal experimentation bills, by his participation in the organizing committee of the Friends of Medical Research, which made a successful fight against these restrictive measures.

Simon Flexner had a long, eventful and successful career, as an investigator, a teacher, and an administrator. His noteworthy achievements in medicine mark him as an outstanding member of the profession, worthy of the many encomiums with which he has been honored.

Medical Publicity

Does good medicine get *good* publicity? Does it get *enough* good publicity? The answer to the first question is *no*. The answer to the second question is *no*. There is no doubt that good publicity men are to be had. There is also no doubt that here and there organized medicine has availed itself of their services, but as yet merely a small beginning has been made.

In the main, publicity is the art of bringing to the public consciousness items of

news relating to advancements in the science or the art of medicine, or of some event in which the practice of medicine is concerned.

Doctors more often than not have very little conception of the art of creating publicity. They have shunned it for themselves and have carried a distaste for it into their relationship with organized medicine. This has been a natural carryover and is quite understandable.

News paper editors and editors of periodicals which are popularly circulated are engaged in the job of publishing items concerning current events which, in their opinion, will interest and inform the public so that the public in turn will read their papers. They do not make the news, but they decide what is news and the emphasis and "slant" with which it is to be presented, making the effort with the better journals to be as objective as their opinions will allow them to be. Even so, the very function of selection and emphasis makes their judgments necessarily discriminating, depending on the conception each editor may have of his reader's threshold of acceptance.

Under the circumstances, it will be seen that for organized medicine to obtain publicity it must first select an idea or situation which can be presented to editors by a publicity man who knows how to do it interestingly, and finally, the editors will have to be convinced from the news release that the material is news which the readers of their periodicals or journals will wish to read. Because doctors are interested in an aspect of medicine, it does not follow that all of the public or even any considerable portion of the public is interested in the same aspect. The reader's chief interest is based on what the material may mean to him, now or in the future. The art of the publicity man's contribution is to find the least common denominator between the medical content and the reader's capacity to understand. The factual material must be oversimplified. The special skill required is to perform this feat without outraging the verities of the factual content, thus remaining on good terms with the medical man, while presenting to the public a partial, but not distorted, interpretation that the editor and reader will accept as having present or prospective effects on themselves, their families, or their friends.

A correspondent writes us to the effect that "Conscientious members of the medical profession today are pained because good medicine does not get good publicity. They read what the proponents of the Wagner-Murray-Dingell Bill have to say about the benefits that the people are about to receive, but they find little mention of what the medical profession has already done for them.

"There is now open at Number 30, Rockefeller Plaza an Exhibit of Naval Research and Inventions. Those who visit it are given a fifteen-page booklet. In it are shown diagrams of Atoms, demonstrations of Radar, Jet Propulsion and Guided Missiles. One-third of one page is devoted to the Exhibit of the Bureau of Medicine. The proportion is forty-four parts of destruction to the one of conservation. The forty-four parts are completely mysterious to the average observer. The one part is comprehensible to almost anyone. Yet forty-four to one is about the average ratio of news coverage accorded to the good deeds of medicine."

To answer our correspondent, we can only say that good medicine like good people, at least in this country, seldom is front-page news. Bad medicine, on the other hand, like crime, is newsworthy because it is exceptional and the more exceptional it is the more likely to make the front page.

Our correspondent continues, "The development of penicillin, the use of blood and blood substitutes in the treatment of shock, the reduction of the death rate of the wounded in World War II to 45 per cent from 820 per cent in World War I, three cases of tetanus among the immunized personnel in the Army, one case of tetanus among the battle casualties, these are astounding developments." They are. They are the result of superior research, superior applications of medical techniques. Many of these items have made the front page during the war, even under restrictions of censorship. But, having made the news in the original instance, they have no continuing newsworthiness except when new facts of usefulness are found and announced. What the doctor forgets, but the publicity man remembers every moment is that the word "news" is the plural of "new." The next thing forgotten by the one and remembered by the other is that news is based on *happenings* of today, not last week or last month. There must be an *event* to which the probative material in the release is tied. Early in the Committee hearings on the Wagner-Murray-Dingell Bill, the case on behalf of the bill was presented. Unless some member of the Committee, or the witnesses out of their own mouths made statements derog-

atory of the bill, and could be *quoted as so doing*, there was nothing for the news columns to the advantage of organized medicine in the events which occurred. When the other side—our side—is presented, the case should be different, provided there is somebody on hand to get the material to the newspapers in releases easy to read and ready to print.

Another thing which the publicity man bears constantly in mind is that statements for or against proposed legislation may be repeated in substance time after time, if uttered by some person, especially one whose title commands attention, at different public meetings, or on different occasions. The meeting is the basic *event* recounted in the press, the statements are a part of the event. Every publicity man knows this, and part of his job is to arrange occasions for public statements to be made, and it is his function to see that medical spokesmen make them with clearness, strength, brevity, and discretion. At times this may call for the combined capacities of a Chesterfield and a Machiavelli, for it is not always easy to get a doctor to say what he means, within the compass of what a newspaper will quote, and to omit what may harm his cause more than it helps. In a word, the doctor is an expert on the content, the publicity man is an expert in expressing the content effectively with the public. If, additionally to that, he is able to bring his clients to the point where they think always in terms of what their words will mean to the public (not merely to their own colleagues), and grant

the right of the public to have opinions, wrong or right as they may be, then the publicity man has grown into the exercise of a public relations function.

We think that our correspondent and many other physicians who are pained or discouraged in the matter of medical publicity might revise their views if they would take the time to study the mechanism of publicity and consider whether doctors are competent to handle it. We believe they are not, and we further believe that the more medicine employs competent public relations counsel, the better will be the impression made upon the public. True, they cost money. In the complicated civilization of today an idea is not self-propelled from the point of origin to its destination. If the idea is to be disseminated to large numbers of people, it will not run like wild fire among them without cost, as did the news of the Lincoln-Douglas debates, or even the McKinley-Bryan campaign speeches. The radio, the newspapers, the magazines, the movies, and the automobile subject the citizen to a continuous bombardment of impressions.

The idea that we wish every citizen to know must force its way among these distractions. The bill for the freight must be paid, made up of items for expert personnel, postage, mimeographing, printing. Skill and money are required if we are to be heard above the welter of confusing voices, shouting on every hand various ideas that are to somebody's advantage to impress upon the public consciousness.

Current Editorial Comment

Relationship of Industrial Physician
 "What," asks *Medical Economics*,¹ "of the relationship of the industrial physician and the employee? Industry should recognize that while the physician usually works for management and is paid by management his professional responsibility is primarily to the employee. His relationship with the employee should be the same confidential one which exists between the private practitioner and his patient."

It continues

When a plant health service is instituted, employees are frequently suspicious. They fear that management is trying to put something over, that it may be planning to use the service for its own ends, perhaps get rid of trouble-makers or men whose condition may increase

their compensation risks. Because of this suspicion, some employee groups have been slow to support industrial health service, and sometimes, though I think not often, with reason.

It is only as the integrity of the physician's position is completely demonstrated that suspicion can be removed. The plant physician must not permit his services to be used in the interest of management against employees, or in the interest of the employee against management.

The industrial physician usually does not practice curative medicine in the plant, except for minor ailments and in cases of emergency. After emergency treatment, the employee is referred to his family physician for treatment. This procedure must be clearly understood in the beginning. The physician must not overstep the line.

¹ Vol. 23, No. 7, April, 1948, p. 148.

MORAL AND PSYCHOLOGIC ASPECTS OF THE CONTROL OF VENEREAL DISEASE

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A PSYCHIATRIST cannot hope to give to a group of workers in the field of social hygiene any new knowledge. At best he can only try to contribute some new perspective and arouse some new lines of thought.

Those of us who work with the problems of people, either individually or as a group, often become discouraged. Progress seems slow in comparison with the effort made, and even in the vigorous reports from the field of social hygiene, a faint note of despair creeps in. Actually, one of the best ways to find courage is to look backward, not to yesterday but some 200 years to the middle of the eighteenth century. Anyone who reads the literature of that day must acknowledge that conditions have changed for the better. The gross self-indulgence, the gross disregard for human suffering, the self-complacency of the privileged few, the harsh repression of the unprivileged majority were then accepted as a normal way of life.

It was a long road from there to the present social conscience and our vast network of welfare work. The dramatic, though often sentimental, social-consciousness of the Victorian novelist, the doctrine of evolution and steady change that inspired the great scientists, the growing practicality of the economists and philosophers, all made the world aware that conditions were worse than they need be. In one field after another people were inspired to try to correct the evils and their efforts have been strikingly effective.

The possibility of eradicating venereal disease could hardly have been conceived of two hundred years ago. Much groundwork had first to be laid and, even now, the social hygienist struggles against tremendous obstacles. Perhaps the greatest of these is human nature itself. In a problem so intimately linked with the social and moral habits of a people, it is perhaps inevitable that progress should be slow. Not only the source of the infection but the actual occurrence of an infection is hidden away by the guilt of the patient. Other diseases may inspire horror and people may fear to acknowledge them but no others carry the same implication of delinquency and fear of punishment. The guilty patient only too often fears less the suf-

fering from the disease than the shame of confession. Each generation is born with the same deep instinctive needs, the same selfish egotism, the same greed to satisfy self before society. Faced with guilt, the average man thinks of protecting himself rather than the community. And to the average man, venereal disease is an unpleasant reality about which he has done his utmost by escaping from getting it himself. The external world has changed, one may truthfully say, for the better, we are perhaps learning how to prepare the young more adequately for the world as it is, but the essential nature of man remains.

One of the basic factors that we have to reckon with is the extent to which, in the vast complexity and growing efficiency of our civilization, we have developed the pattern of specialization. More and more we, as individuals, devote our energies to a narrow field and depend on others to supply the needs which once were the concern of every man. Even the farmer who has remained closest to our earlier self-sufficiency has forgotten many of his earlier skills. What city dweller could competently feed, clothe, or shelter himself, let alone protect himself against the inroads of disease? Our physical comforts, our security against human or animal enemies, our very lives depend upon the skills of professional specialists. We have gained much from this concentration of effort but we have also learned to lean on others, to pay with money for our ignorance and sloth, and to put so much responsibility upon the specialist to protect us that we as individuals are doing less than our share. We scatter paper or worse in the street, trusting to the sanitation department to clean it up. We pay social workers to care for the poor rather than caring directly ourselves for them. We try to get our sons back home before the war job is finished, trusting that the Government will manage somehow if we merely pay our taxes. And we leave it to the health authorities to eliminate disease, not wanting to be bothered with contributing anything more than money to the work. Although we have gained a social conscience, and recognize the need to deal with the ills of society, we have grown slack about giving toward their correction more of ourselves than our money, or a little of our time toward raising it. Having done that, we retreat into our own self-indulgence, leaving the real work to the paid

specialist We walk through life expecting protection from others and abandoning the effort to protect ourselves And in so unpleasant a field as that of venereal disease, it is even more convenient to leave the responsibility to others

It is hard to see how or why anyone could actually oppose a campaign to eliminate venereal disease from society The pain and disgust arising from a gonorrheal or chancroid infection, the discomfort and anxiety created by the later stages of syphilis must arouse a desire to avoid them in even the least intelligent person Information about these diseases has certainly been widely spread so that few people today are completely ignorant One rarely hears, now, the once popular statement among boys that they could best prove their manhood by acquiring gonorrhea

There are a few people whose sense of guilt about sex creates in them so strong a need for self-punishment that they may unconsciously seek infection On the whole, however, such people are few If venereal disease persists, it is not because of widespread neurotic compulsion nor because of ignorance

The treatment of the venereal diseases has had the attention of scientists who have found means of rendering the victims noncontagious within a short time, often with complete cure One of the difficult features of eliminating tuberculosis is that the disease once acquired is merely arrested and may again become an active source of contagion at any time This is not true of venereal disease, since it can be completely cured and so treatment actually eliminates the patient as the source of the disease And yet we know that some completely cured persons do acquire a new infection, proving that even personal experience has not deterred them It is conceivable that the effectiveness of treatment may have robbed the diseases somewhat of their terror, and so people are less fearful of getting them Even so, it is obvious that a large number of those infected do not seek treatment voluntarily It is no doubt true that public clinics are still far from ideal in the attention they give to the emotional reactions of their patients Not only the fear of unsympathetic handling but the association with undesirable characters and the chance of publicity may keep some from going for treatment There may, in fact, be a need for more and better facilities for therapy Still, during the war when more people than ever had money to pay to a private practitioner, the known venereal rate rose, which implied that many were going untreated It is really scarcely probable that either improvement in treatment or lack of suitable facilities has contributed appreciably to the spread of the diseases

It has been recognized that professional prostitution is a fertile source of infection The authorities and the protective agencies have waged a vigorous campaign against it The life of a prostitute is certainly not a pleasant one and economic conditions here and now rarely drive a girl into this life in order to live, as has been true in the past We have come to recognize that the prostitute is often driven by neurotic compulsion into this life Denied this form of expressing her neurosis, she may develop other symptoms It may be that the failure to check prostitution by repressive measures is due in part to failure to recognize that we are dealing with mental illness rather than with crime Still, the actual number of sufferers from this neurotic compulsion hardly accounts for the persistence of the practice Prostitutes would not exist if they were not used by men They may stimulate the interest of men but the desire must first be there And even without prostitution, promiscuous sex activity goes on

To all of these factors, the social hygienists have given much attention—to the spread of information, to the repression of prostitution, and to the providing and improving of therapy But there must still be something lacking in the program if the disease has not been eliminated but increases One is forced to stop and consider whether there may be more basic causes for the evil than have been recognized and dealt with Certainly few people wish to become diseased or wish to spread the infection, and yet the disease persists The readiness of the public to leave all effort and responsibility to the specialized authorities is certainly a large factor in the problem But it is evident that a more positive element than this passivity must be opposing their efforts

The real problem, of course, arises from the sex drive of men and women both One cannot attribute the cause to either of the sexes alone since more and more women are adopting the aspects, the attitudes, the appetites, and the habits of men If there were no sex activity at all, venereal disease, of course, would quickly disappear Or, even if all sex activity were confined to marriage partners who had been passed as uninfected, there would, in a short time, be no problem The fact that the disease persists rests upon the fact that sex contact exists outside of these certified marriages The problem before the social hygienist then is really reduced to one of social morality

But what is a young man, strong and vigorous as our good food and healthful living have made him, to do when the deep urge toward sex expression arises? The ideal held up by the churches and by the moralists is complete con-

tinence before marriage and subsequent strict fidelity. The assumption seems to be that the physical pressure can be relieved by emission dreams and the emotional by sublimation in sports or intellectual or creative pursuits. I have no doubt that for some young men this is possible but in reality their number is few.

Our society may uphold in theory the necessity for confining sex activity to marriage but actually marriage today is increasingly difficult to achieve. Our standard of living is such that the ability to earn enough to support a family is slow in coming. There are many years between the onset of puberty and the time when the average young man can start to maintain a family. As a matter of fact, we have even set up a barrier to early marriage by requiring the consent of parents for a boy under 21 to marry. For at least seven years, at a time when the sex urge is very strong and self-control imperfect, we deny him the outlet which we hold up as the only suitable one. We have raised the age at which a boy can leave school and start earning a living, thus delaying his progress toward the point of being able to support a family. All of these measures may be good in themselves but they add to the difficulty of the problem that the social hygienist is trying to deal with.

If we assume that complete continence is possible and desirable, we should logically try to lessen the stimulation toward activity. Actually, we are not a people who take self-denial easily. Even during the war with the arousal of patriotism, the rationing system was far from effective. We Americans had been brought up on the principle of abundance, of the possibility of getting whatever we want, and we do not take easily to prohibitions. Our method of bringing up children is an extremely indulgent one and parents find it hard to deny any of their children's wishes for fear of losing their love. There is even an attitude in education that children must not learn failure but must be promoted in school, whether or not they have earned the promotion by attending to their studies. All of this is a poor preparation for a boy or a girl to deny himself the satisfaction of his sexual appetite. Moreover, we have made something of a cult of love and leading one's own life regardless of consequences. Directly or indirectly, this attitude is presented in the current moving pictures, stories, and radio programs. The sexually stimulating pictures of pin-up girls were considered almost a necessity for the boys in service. The fashions of dress, the dances, even the advertisements in the subways are sexually suggestive. With little capacity for self-denial and with stimulating surroundings, is it likely that young people will develop self-control and be continent?

In all other respects our society encourages achievement at any cost, and without delay. Naturally, this carries over to the field of sex. One might expect fear to serve as a deterrent. However, the influence of the old religion with ideas of eternal punishment has dwindled away. It has been replaced commonly by a casual attitude that one lives only once and has a right to enjoy life. We have developed such confidence in the scientist who can miraculously save us from the consequences of our neglect that we have lost the fear of punishment by nature as well as by God. In such a general situation the old ideal of continence before marriage lingers on in but few places. To tell a young man that the solution of his sex problem before marriage is complete suppression of his desire is to mark oneself as out of step with the times.

For the idealistic young man with inadequate self-control, autoeroticism still plays a role. Rarely does one find a boy now who really believes that he injures himself by masturbation. The old type of literature which foretold dire consequences has largely disappeared. It has been replaced by statements that auto-eroticism is a normal stage in the development of a boy which even has the value of making him accept sex into his life. However, solitary enjoyment loses its value to the average boy who sees others more adventurous and who is reaching out toward reality rather than fantasy. It is even possible that the boy who spends years in fantasizing sex relations may be handicapped in a successful heterosexual adjustment, finding reality less satisfying than fantasy. It is true that by confining his sex activity to himself he is escaping the possibility of venereal disease but again one can question which is the greater evil. Can we conscientiously encourage masturbation as a solution?

With the elimination of prostitution, it is probably more common for boys today to express their sex desires with a girl of their own class and age, even to the extent of having a "steady girl friend." This type of pseudomarrriage, which provides the privileges without the responsibilities of marriage, certainly is a threat to family formation. It is true that the former attitude of concern about the virginity of a bride has practically disappeared and many of these relationships lead to legal marriage, especially if pregnancy occurs. However, a girl so easily acquired does not always have great value and with the comparative ease of divorce this custom perhaps contributes to the growing instability of marriages. Moreover, it is certainly true that venereal disease is spread through this custom, although perhaps the official reports can never be as accurate as those about prostitutes whom the boy has no

need to protect It seems very doubtful that society would favor this solution for the problem of young men

Another practice which is becoming more prevalent than perhaps society in general recognizes is homosexuality This may commonly start as a casual adventure rather than as a deep emotional attachment but the freedom from consequences and the increasing opportunities make it a growing competitor with casual heterosexuality Certainly this is as great a potential source of the spread of venereal disease as relations between men and women Unfortunately, there is still so much social disapproval of the practice, however, that the man who acquires the disease in this way is unlikely to acknowledge it, and honestly report the man who is spreading the disease

Prostitution has been widely banned and even though it still exists, it has lost in popularity It still furnishes an outlet for some of the cruder young men and those who want to divorce their sex life from emotion Actually, the need to go to a prostitute has almost the connotation of failure to achieve a girl without pay Moreover, there is in all men a strong desire for conquest and a sense of competition which make prostitution less attractive than a personal relationship Even without repressive measures, prostitution might gradually disappear

I realize that I am giving a rather pessimistic picture of the present attitude of young people toward sex If, however, we wish to deal effectively with a sex problem, we cannot blind ourselves to reality Boys and girls, men and women with strong, normal sex drives, with little experience in self-denial, with lessening fear of the consequences of venereal disease because of its treatability, with little religious fear of punishment for sin, with marriage hard to achieve and no longer a real sacrament, with a cynical opinion of the stability of family life, with constant stimulation from their surroundings—such young people are going to continue to risk getting venereal disease despite having information, despite eradication of prostitution, and despite improvement of treatment facilities Any effective campaign must be adjusted to the basic facts

In the face of such obstacles, it is not easy to think of additions to the social hygiene program that might be effective If we take it for granted that premarital and extramarital sex relations are for the present widespread, it would seem desirable to face openly this fact and to think in

terms of improving physical protection against disease, of making prophylaxis more effective and more easily available It is true that prophylactic stations for men in military service were not always used and there might be the same resistance to using them that shows in the use of public clinics It is conceivable, however, that ways could be worked out to make the use of prophylactics more acceptable and more widespread If this were done, one would have to recognize that it is making extramarital sex activity even more free from consequences and perhaps more common The evils of this would have to be weighed against the possibility of eliminating venereal disease And any such program could not be rightly started upon without serious thought

Although it would be difficult to accomplish, it is conceivable that there might be some lessening of the constant external stimulation toward sex excitement Some efforts have been made to censor the moving pictures but, as one observes them, it is evident that the basic attitude toward sex has only been more subtly presented rather than changed Certainly it has been difficult to raise public opinion against prostitution and it might be even more so to try to suppress the erotic literature and pictures which we come across everywhere Nevertheless, I believe that there is more stimulation from this source now than from prostitution and it might well merit the attention of the social hygienist

Going even further afield, the social hygiene program might involve increasing attention to the study of the factors that make early marriages difficult to achieve and to sustain More stress upon the responsibility of each individual rather than upon the specialist, with its relation to the total picture of the need for accepting responsibility in a free society, might, in the long run, yield some results

In general, however, no program can be effective that disregards these deeper basic drives in people The essential tendency toward self-indulgence in human nature and the fact that generations succeed each other so rapidly, force us to recognize that no program can remain static but must be constantly adjusted to changing social attitudes But until the general public is willing to protect the community before indulging themselves, the problem of venereal disease will persist

14 Washington Square

SAFETY FIRST

Doctor "We're trying to check the epidemic in the village Are you taking precautionary measures to prevent the spread of contagion?"

Housewife "Oh yes indeed, doctor We've even bought a sanitary cup, and we all drink from it"—*Canadian Doctor, Sept., 1945*

THE HEMORRHOIDAL-PROSTATIC-IMPOTENCE SYNDROME

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IN THIS brief paper it will be my purpose to present 3 typical cases, in a total series of 37, demonstrating an apparent relationship between sexual impotence, prostatic hypertrophy, and internal hemorrhoids. No definite conclusions should be drawn from so small a series of cases, and none will be advanced. Certain inferences, however, might reasonably be in evidence, and on the basis of inference, an anatomicopathologic theory will be offered as a tentative and probable explanation of the facts.

One of the cases to be presented was referred for the injection treatment of hemorrhoids, the effect upon a coexisting impotence being purely incidental to treatment of the hemorrhoids. The second case was referred by the first patient, peculiarly enough, for impotence. This patient asked to be treated for his impotence by the same rectal injections used for his friend! The third case was complicated by a rectal adenoma but revealed the same hemorrhoidal prostatic-impotence syndrome.

Case Reports

Case 1—M. J., a contractor 45 years of age, twice-married, presented himself with chief complaints of rectal bleeding while straining at stool, and constipation, the former of six months' duration, and the latter "all his life." Further history revealed nocturia, four times each night; mild difficulty of micturition, especially in starting the stream, and moderate frequency. No mention was made of sexual impotence at this time.

Physical examination revealed a well-developed, well-nourished male. The only relevant positive findings were a complete ring of internal hemorrhoids, none pedunculated, and all of moderate size, none of which prolapsed on straining. The prostate was moderately enlarged, slightly tender, and soft throughout.

Therapy consisted of ten weekly treatments with quinine and urea hydrochloride, injecting two quadrants each week, according to the technique outlined in previous writings.¹ Rectal bleeding ceased quickly and the patient was discharged with instructions to return in two months.

At the time of return the patient jubilantly announced that not only had rectal bleeding ceased but also the nocturia and difficulty of micturition. He further volunteered that for the past month there had been a definite improvement both in libido and in the quality of erections. As he phrased it, "I have become five years younger sexually." Rectal examination revealed the prostate to be the same size as at the initial examination and slightly

tender, as before, but it seemed less soft in its consistency. No further hemorrhoidal injections were indicated. A further recheck in six months revealed a maintenance of this status.

Case 2—R. L., an engineer 47 years of age (an employee of M. J., above) presented himself with a chief complaint of impotence and requested "the same rectal injections used for his friend." The impotence was of two years' duration and had never been investigated. He attributed it to his over-indulgence in alcohol, two to three pints of whiskey a day on many occasions. Nocturia, frequency, and burning on urination were noted.

On physical examination, I found a well-developed, well-nourished man of huge bulk and stature—weight 203 pounds, height 6 feet 4 inches. There was no evidence of cirrhosis of the liver. The prostate gland was found to be definitely enlarged and boggy. The secretion obtained on massage contained few pus cells. Although there were no rectal symptoms, several moderate-sized internal hemorrhoids, and one combined anorectal hemorrhoid were found.

I informed the patient of these findings and advised operation rather than injection treatment. I warned him that treatment of the hemorrhoids by injections would probably have little or no effect upon his sexual condition. However, he insisted upon the gamble, and six weekly injections of quinine and urea hydrochloride were given. Urinary antiseptics were also prescribed.

Upon re-examination, two months later, subsequent to the completion of treatments, the prostate was found to be slightly decreased in size, although still soft, and the combined anorectal hemorrhoid required further injection. The nocturia, frequency, and dysuria had ceased almost completely, but the sexual status was unchanged. The four-month recheck revealed an identical rectal status, but a surprisingly changed sexual status. Sexual desire, sturdy erections and ejaculations were elaborately described in great detail, with both the mathematic precision and picturesque language of an engineer.

Case 3—W. P., a garage mechanic, 52 years of age, gave a history of increasing rectal bleeding, constipation and straining at stool with protrusion of a "rounded mass" from the rectum easily replaced by the fingers, all of six months' duration.

Also noted were a history of one acute episode of urinary retention two years previously, subsequent nocturia and dysuria, several episodes requiring introduction of a catheter, and present difficulty in completely emptying the bladder. Sexual power and desire had rapidly declined since the first acute episode. The patient presented himself for treatment of the proctologic conditions.

Physical examination was irrelevant aside from the proctoscopic and rectal digital investigations. The prostate was markedly protuberant, tender, and

¹ Cantor, Alfred J. Ambulatory Proctology. New York City: Paul B. Hoeber Inc. 1946, p. 172.

boggy Rectal prolapse, which carried down a sessile rectal adenoma situated on the posterior rectal wall, was demonstrated. Several small internal hemorrhoids were noted.

Treatment consisted of surgical excision of the adenoma, followed by fulguration of its base. Two weeks later the internal hemorrhoids were injected with quinine and urea hydrochloride, and one month thereafter injections of the same solution were introduced in the treatment of the prolapsus recti.

At the present time, four months later, rectal symptoms have entirely ceased, rectal prolapse has not recurred, the prostate is definitely smaller and firmer, urinary symptoms are slight, and, most remarkable of all, sexual power and desire have greatly increased.

Comment

To draw definite conclusions from a small series of 37 cases would be unwise and unwarranted. However, to overlook the inferences of these cases would be equally unwise. In each case there was evident an apparent relationship between hemorrhoids, prostatic hypertrophy, and sexual impotence. At least we may say that subsequent to treatment of the hemorrhoids there resulted an apparently consequential decrease in size of a previously enlarged prostate, and an improvement in a previously diminished sexual vigor.

It is difficult to account for the changes on an anatomic and physiologic basis. We may assume, however, that the close relationship of the blood supply of the prostate gland and of the rectum is an important factor. It would seem that with the obliteration of the rectal varices a previously passively congested prostate gland is relieved of its congestion.

It is well known that the pudendal plexus of veins constitutes the anterior part of the prostatic

plexus. The venae comites of the internal pudendal artery arise in the plexus, and these venae comites, before proceeding on to become a single internal pudendal vein, receive veins from the inferior hemorrhoidal. The inferior hemorrhoidal veins are intimately connected with the internal hemorrhoidal plexus, through the terminal veins of the columnae rectales. This plexus, in turn, leads into the middle hemorrhoidal vein, which empties into the hypogastric vein. The inferior hemorrhoidal and internal pudendal veins are also tributaries of the hypogastric vein.

There must be an equally close lymphatic interrelationship between the prostate gland and the rectal wall.

It would seem reasonable to conjecture the possibility of passive vascular congestion (and perhaps associated lymphatic congestion of the prostate gland), due to the varicose reservoir supplied by hemorrhoids. If this is so, then it is equally reasonable to suppose that with removal of this varicose reservoir a cessation of passive vascular prostatic congestion might result. This may explain the improved prostatic condition observed in the above cases on re-examination, after hemorrhoidal injections. The improved sexual status may reflexly, directly, or psychically (or in all three manners combined) be the next link in the hypothetic chain. Similar results have been observed in 23 surgically treated cases. Further observations, and analyses of the follow-up course of both injection and surgical cases will aid in evaluation of the hemorrhoidal-prostatic-impotence syndrome.

No conclusions are offered. I merely submit for consideration the probability of a hemorrhoidal-prostatic-impotence syndrome.

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VETERANS' RIGHTS

"Each physician should have a major hospital—that is, one to which he wishes to attach himself more intimately and do most of his work."

"A properly organized medical staff will not give advantages to any individual or group of physicians, or discriminate against the young physician properly qualified and competent, but will insure desirable supervision of all clinical work done in the institution."

The above excerpts from the Manual of Hospital Standardization, published by the American College of Surgeons, plainly lays down the principles that every physician should have a hospital to work in and the privilege of doing any procedure of which he is capable.

These principles are vital at the present time as they affect our returned veterans, especially the younger men who did not have an opportunity to

make a hospital affiliation before they went into service.

These veterans will return to find that when they do have hospital cases, vacant beds are at a premium and that unless they were previously members of some hospital staff, staff positions are frozen for the duration. In addition, many of them have been in no position to show their ability as most of their experience will have been in the armed services.

Every hospital staff should immediately consider this problem so that we who stayed behind may show our appreciation to those who went, with something besides empty words and a pat on the back. Let us work to see to it that every physician, especially the returned veteran, has a place to work and the privilege of working.—W B Harm, M D, *Detroit Medical News*, Nov 12, 1945

ELECTROCARDIOGRAPHIC EVIDENCE OF MYOCARDIAL DEGENERATION IN AN AMERICAN PRISONER OF WAR FOLLOWING UNDUE PHYSICAL STRESS AND OTHER FACTORS

M D MIERAS, Capt., (MC), AUS, and R L ZIMMERMAN, First Lt., (MC) AUS

(From the Station Hospital Fort Totten, New York)

This patient was a 24-year-old AAF gunner who went overseas in May, 1943, parachuted down in February, 1944 over Germany unharmed except for the loss of a few teeth, remaining a prisoner of war for fifteen months until he was liberated by the Russians in May 1945. During his internment he was subjected on several occasions to severe exertion (at one time he was forced to run with full equipment for several miles at bayonet point and on another occasion was forced to march about 750 miles in six weeks). The food was always inadequate. Red Cross packages reaching him only at infrequent intervals. His dietary intake averaged about one fourth of one Red Cross parcel content per week plus a daily intake of one seventh of a loaf of German black war bread 50 Gm of horse dog or ox meat, three medium-sized potatoes, carrots, sauerkraut and cabbage irregularly. On this regime he lost a total of 45 pounds.

Following liberation, the patient drank heavily for a few days. When he arrived in the United States he went on a "drinking bout" which lasted for fifty days of his furlough time, during which he averaged about one quart of liquor daily.

Five days prior to admission, on August 6, 1945 the patient was seized with a sharp, nonradiating, subternal pain, occurring at rest. His civilian doctor took an electrocardiogram and told him he had a "nervous condition." The pain lasted two days and disappeared spontaneously without medication. On August 11, 1945, he was hospitalized at Station Hospital, Fort Totten, New York where a review of his previous electrocardiogram revealed inversion of T₁ and T₂ and diphasic T₃. His civilian doctor had not given him digitalis.

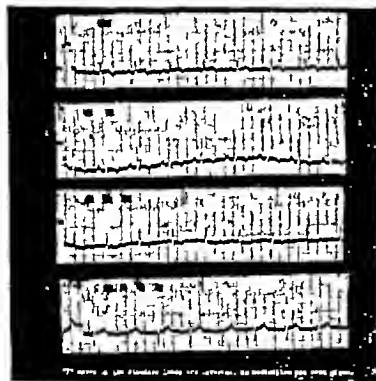


Fig 1

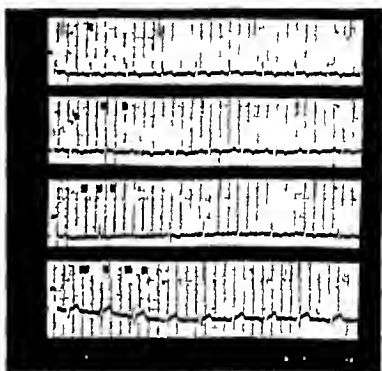


Fig 2

Upon admission here he had no complaints but gave the history of the pain described above which had occurred five days before and lasted for two days. He had never had rheumatic fever. In fact, his past history was free of any serious illness except for an attack of "yellow jaundice" in 1943 from which he recovered after fifteen days of hospitalization.

Physical examination revealed a well-nourished man having no enlargement of the heart clinically or roentgenologically. There were no murmurs or arrhythmias and the heart sounds were of good quality. The lungs were clear, liver was not palpable. There was no edema. The remainder of the examination was negative and there was no clinical evidence of avitaminosis. The patient did not show weight loss described in the history above, having been on normal rations since his liberation.

Laboratory findings on admission were as follows: white blood count, 5,000, 60 per cent polymorphonuclears, sedimentation rate, 5 mm, urine normal. One week after admission the white blood count was 10,400, with 72 per cent polymorphonuclears, and the sedimentation rate was 14 mm. Kahn test was negative. Electrocardiogram taken on August 11, 1945, revealed inversion of T waves in leads I and 2, diphasic T in lead 3, and was identical with the electrocardiogram taken by his civilian doctor, a copy of which was brought to Fort Totten for comparison (Fig 1). A second electrocardiogram on August 14, 1945, revealed more inversion of the T wave in lead 3 (Fig 2).

Starting August 20, 1945, the patient was given a high vitamin diet, 100 mg of thiamine chloride intravenously and six multivitamin capsules daily. No other medication was given. The patient was ambulatory but stayed most of the time in his ward.

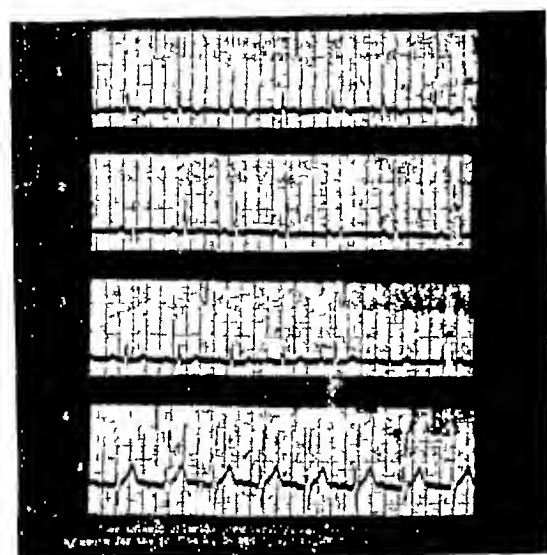


FIG 3

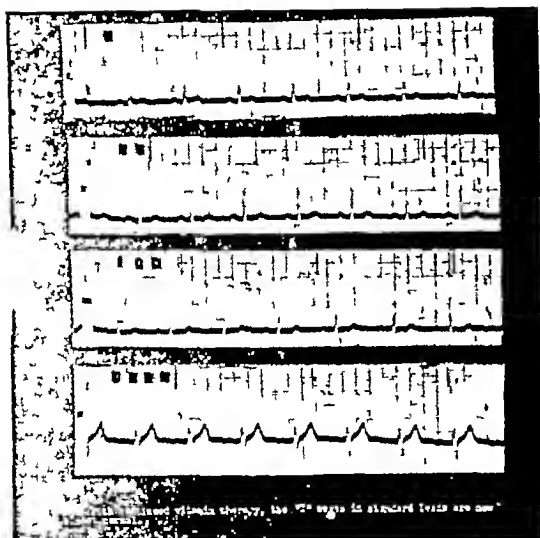


FIG 4

He had had no alcoholic beverages since his admission to the hospital.

After seven days of this therapy, the third electrocardiogram, taken on August 27, 1945, demonstrated that T_2 and T_3 were beginning to lose their negativity (Fig 3). The same regimen of thiamine chloride intravenously and multivitamin capsules by mouth was maintained and the electrocardiogram taken on September 4, 1945, showed T waves in the standard leads almost normal (Fig 4). The last electrocardiogram, on September 18, 1945, revealed a normal tracing (Fig 5).



FIG 5

Comment

This case is being presented to demonstrate electrocardiographic evidence of myocardial degeneration in a soldier who had been a prisoner of war in Germany subjected to undue physical hardship, marked malnutrition, along with heavy ingestion of alcohol following his liberation. With no treatment other than rest, high vitamin diet, thiamine chloride intravenously, and vitamins by mouth, there was brought about a complete reversal of the negativity of the T waves in the standard leads in a period of thirty days.

We were unable to demonstrate evidence of rheumatic heart disease or other conditions which might have produced these electrocardiographic changes. Even though he complained of substernal pain, clinically, and electrocardiographically, the patient did not present the clinical entity of a coronary lesion.

We are presenting this case on the presumption that the conditions under which this prisoner of war lived while in Germany may have produced some myocardial changes which remained unchanged until high vitamin regimen was instituted, and that the combination of avitaminosis, physical stress, and ingestion of large amounts of alcohol produced the myocardial degeneration.

It is felt that many returnees who have been prisoners of war and may have been subjected to similar experiences can be observed for possible latent myocardial degeneration similar to that described above.

Man alone has the gift of reason, yet he alone behaves in a manner that seems illogical and irrational.—*Clinical Medicine*, March, 1946

MEDICAL SERVICES AND THE VETERANS ADMINISTRATION*

EDMUND EASTWOOD, M.D.

(Director, Outpatient Service, Department of Medicine and Surgery, Veterans Administration)

WHEN General Hawley took over the Medical Service of the Veterans Administration last August, he established as his long-range objective, "A Medical Service Second to None"

An easy thing to say, "a medical service second to none," but what does it mean? It means a many-faceted goal, difficult to attain

In terms of medicine and surgery, it means that in all of the special branches of its science and art, the Veterans Administration will provide a service that meets the highest standards set for each

In terms of physical equipment, it means hospital beds, outpatient clinics, modern, up-to-date scientific equipment

In terms of personnel, it means that adequate staffs of qualified personnel in all of the professional, subprofessional, and nonprofessional categories will be in those hospitals and outpatient clinics to serve the veteran

In terms of professional cooperation, it means that the best specialists, physicians, and dentists in civilian practice in the country will be serving the Veterans Administration on a fee-for-service, part-time, or consultant basis

In terms of education, it means that doctors will be training for Specialty Board examinations in residencies established at Veterans Administration hospitals, while also giving care to veterans

In terms of the Congress, it means that our legislators will be satisfied that the funds they have appropriated for the care and treatment of eligible veterans are being wisely administered for benefit of veterans.

In terms of the general public, it means that those who have loved ones eligible for medical or hospital care or treatment will be getting that care or treatment

In terms of sick or disabled veterans, it means the ultimate in physical or mental rehabilitation that is possible in each individual case

You have heard the goals. Now let us see how far along the road toward these goals the Veterans Administration has come.

Although the broad, overall objective for the general medical, the general surgical, the tuberculosis, and the neuropsychiatric services is the same, the procedures for reaching that goal vary

with each service. However, the general pattern of procedure is sufficiently similar to permit the citing of one, in order to give you a glimpse of them all

Let us take a look, for instance, at the General Surgical Service. The goal is a surgical service that in every way meets the standard for general surgery that has been set by the American College of Surgeons

It is inconceivable that General Hawley could accomplish this alone. So, he has appointed a Board of Consultants, composed of a representative from each of the twelve surgical specialties, to assist him

They, in turn, have appointed a representative in each of the twelve surgical specialties to advise and work with the Branch Medical Directors in the Veterans Administration Branch Offices. These Branch Office Consultant groups are responsible for surveying and evaluating the surgical service in each Veterans Administration hospital in the Branch Office area, and making such changes, as may be required, to bring the surgical service in these hospitals up to the standard

It should be remembered that the problem is twofold, because certain Veterans Administration hospitals have, or will have, residency training programs, while others, too far removed from medical centers to make cooperation feasible, will have no residency program.

At the present time, all of the Branch Office Surgical Consultants have been appointed and are beginning to survey the hospitals within their areas. The hospitals with residency programs, either under way or in the formative stage, will be the last to be surveyed, as the responsibility for the standard of residency is now resting with the medical schools that are engaged in establishing teaching programs at our hospitals

It is self-evident, of course, that no hospital program can succeed without hospital beds

In December, 1941, the Veterans Administration was operating 92 hospitals in three main clinical types: 50 general medical and surgical, 30 neuropsychiatric, and 12 tuberculosis—a total of 72,000 beds. In addition, there were 12 Veterans Administration homes with approxi-

General Hawley, chief medical director of the Veterans Administration, and Dr. J. C. Harding, assistant medical director, regret that owing to circumstances beyond their control neither was able to be in New York to address the meeting in person.

* Delivered at the Banquet of the 140th Annual Meeting of the Medical Society of the State of New York May 1, 1946.

mately 19,000 beds for the use of ex-servicemen and -women, permanently disabled to a degree which prevented them from following any gainful occupation, yet, whose disabilities had reached a static condition not requiring actual hospital care

As the war progressed, rapid and heavy demands for more hospital beds had to be met. The Veterans Administration attempted to solve the immediate problem by installing, in existing hospitals, emergency or expansion beds, over and above normal standard capacity. By V-J Day, 11,000 expansion beds were added, increasing the capacity to 83,000 beds. Use of expansion beds will be discontinued when new units to existing hospitals or new hospitals with sufficient capacity to care for the patient-load, now provided for under the authorized emergency bed allocation, can be acquired.

Hospital expansion plans call for the construction of new hospitals and the transfer of others from the Army and Navy. Under the present building program, the Veterans Administration will add 74 permanent hospitals of all types, with a bed capacity of 52,110 beds. As of April 4, 1946, we had 101 hospitals with a total of 85,302 authorized beds.

In addition to the construction and acquisition of new Veterans Administration hospitals, contracts are being let for the use of beds in civilian hospitals and other Federal hospitals when these are in surplus, over and above the needs of the respective community or service, for it is not the purpose of the Veterans Administration to hamper civilian hospitalization. We hope soon to have 20,000 contractual civilian hospital beds, although, as of February 26, 1946, only approximately 9,000 such beds were under contract. The exact total of beds that ultimately will be available in civilian hospitals is not known. At the present time, hospital associations in Kansas, Michigan, Oregon, and North Carolina have signed contracts and 36 other States are negotiating, either directly or indirectly, for participation in this program.

The goal for our Outpatient Service does not differ in the standard of treatment from that of the hospitals. But the problem is complicated because of the tremendous number of physical or mental examinations, which must be given on an outpatient basis. Examinations are required to determine the need for medical treatment and care, for the adjudication of claims, to determine need for hospitalization, to provide records from which percentage of disability may be evaluated for compensation and pension purposes. It is estimated that during 1947, more than 2,000,000 veterans will require complete physical or mental examinations.

With a potential veteran population of more than fifteen million from World War II, it readily can be seen that there will never be enough doctors in the Veterans Administration to give the necessary examinations. Nor will there be enough Veterans Administration outpatient clinics. General Hawley has appealed to civilian doctors for help in solving this major problem.

General Hawley has received magnificent response to his appeal, and several State plans for outpatient examinations and treatment have been worked out.

The Kansas State Plan is a notable example of this cooperation, and will work in the following manner.

The Kansas State Medical Society has submitted a list of their qualified members, who desire to render service to the Veterans Administration, in accordance with a predetermined schedule of fees. From this list, those vouched for by the Society are appointed as Veterans Administration physicians on a fee basis and their work for the Veterans Administration will be supervised by the Society in the various zones throughout the State. Medical service will be given to the veteran by the nearest qualified physician, under authority granted by the Veterans Administration representative designated for that purpose, and fees for treatments will be paid by our agency to the physician who renders the service. For convenience in operating this plan, the designated Veterans Administration representative is located adjacent to the office of the Kansas State Medical Society in Topeka.

One of General Bradley's and General Hawley's first objectives has been attained—the passage of legislation to enable them to establish educational and professional attractions for the finest caliber of hospital personnel and to permit them to employ doctors, dentists, and nurses without reference to the rules and regulations of the United States Civil Service Commission.

Public Law No. 293, of the Seventy-Ninth Congress, created a Department of Medicine and Surgery in the Veterans Administration, effective January 3, 1946. Since then, educational programs in the form of residencies have been established for doctors, and standards, independent of the Civil Service Commission, have been set for personnel in what are called the Auxiliary Services, that is, dietetics, social service, etc.

Long-range estimates of personnel needs are, to mention a few, 7,000 full-time Veterans Administration physicians, 750 dentists, and 30,000 nurses. Although still a long way from meeting these goals, the Veterans Administration has added hundreds of full-time doctors to its staff.

VETERANS ADMINISTRATION BEFORE REORGANIZATION

With Control of 97 Hospitals and 53 Regional Offices
Centered in Washington

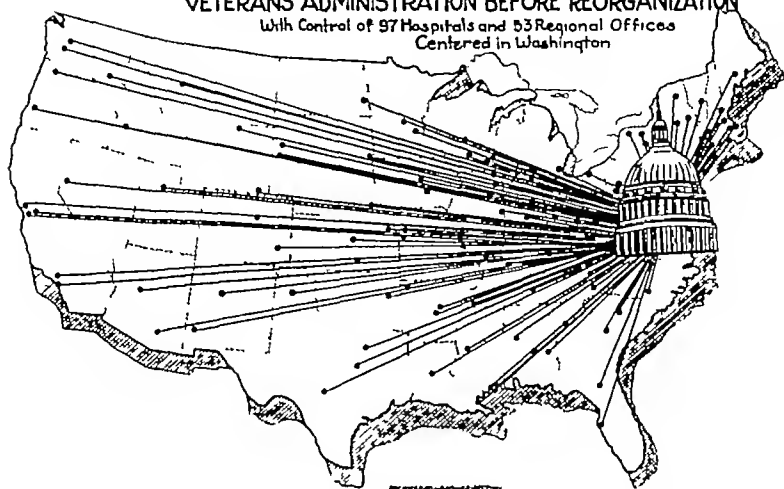


FIG 1

since the first of the year. A net gain of about 100 nurses a week is helping to alleviate, although not meeting, our need for nurses and the Dental Service reports more applications on hand than it will have positions to fill in the next eighteen months.

When General Hawley said, "Without the assistance of Class A medical schools, it would be impossible for the Veterans Administration to operate its present hospitals at a satisfactory standard," he had reference to the residency program in process of establishment at Veterans Administration hospitals that are located near medical schools or teaching centers, and the selection of physicians who are teachers in Class A medical schools or outstanding specialists to act as consultants on a part-time or fee basis.

The ultimate goal of these programs is 1,000 full time resident physicians and 500 part-time attending consultants.

On April 18, 1946, 63 out of the 77 Class A medical schools in the United States were co-operating in the residency program, 224 resident physicians were on full time duty in 12 Veterans Administration hospitals and 536 consultants and attending specialists were serving 17 Veterans Administration hospitals. For detailed information about the residency or consultant programs, doctors should consult the Dean of any Class A medical school.

One of the most interesting and important

phases of the General Hawley program is the medical rehabilitation of patients in Veterans Administration hospitals. The goal for this service is the ultimate physical and mental rehabilitation possible in each individual case. It is an interesting challenge because of the necessity of meeting the special problems involved in the rehabilitation of the tuberculous patient, the neuropsychiatric patient, the amputee or otherwise disabled, and the paraplegic, or spinal cord cases.

Because there had been no comparable program in the Veterans Administration, a completely new section or service had to be created. Today, we have come a long way down the road. The Medical Rehabilitation Service has been established. Field personnel is just beginning to be appointed, but the Medical Rehabilitation Service already has become an integral part of the medical program.

Of major importance to the whole program of the Veterans Administration is General Bradley's decentralization plan for streamlining the operations of all of the functions of the agency.

Where, previously, all activities were administered from Washington, under decentralization they will be administered on an area basis from 13 Branches of Central Office, with headquarters in each of what are, roughly the 13 Civil Service Districts throughout the country.

There has not been sufficient time, as yet, to

VETERANS ADMINISTRATION AFTER REORGANIZATION

With Control and Supervision in 13 Branch Offices to Break the Washington Bottleneck

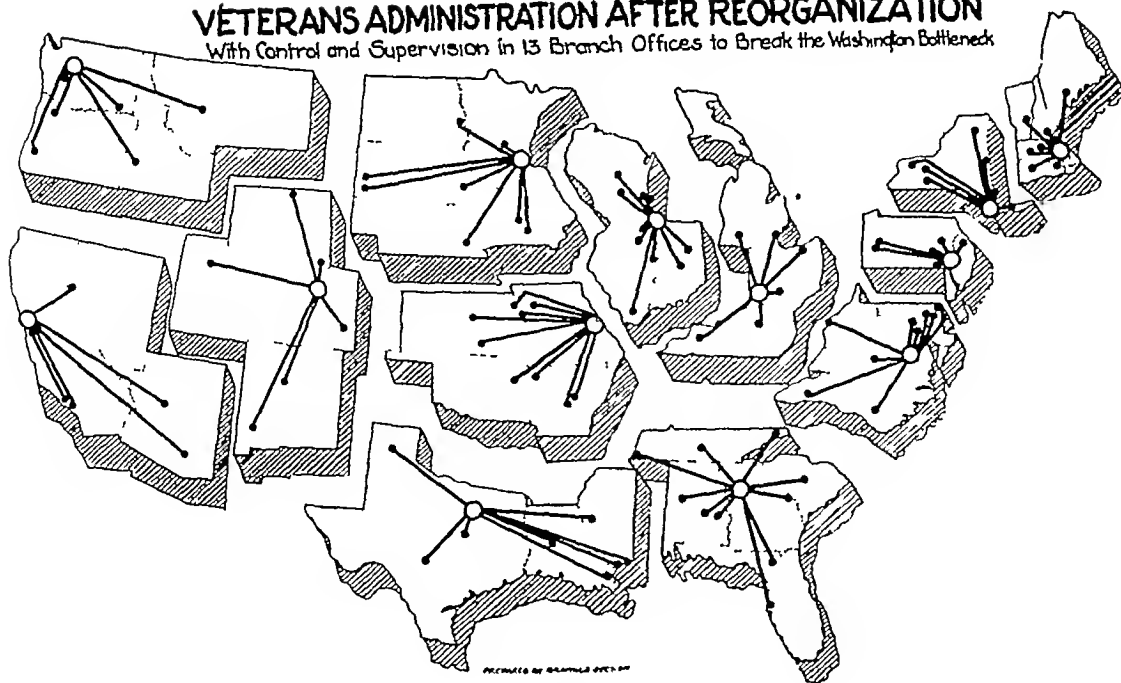


FIG 2

determine the effectiveness of decentralization, but the 13 Veterans Administration Branch Offices are open and began to function, officially, as of April 1, 1946

General Hawley is sincere in his praise of the American doctor, both individually and collectively. He has repeatedly said, "There is no substitute for a good doctor." And he means it.

In an address before the House of Delegates of the American Medical Association, General Hawley recognized and paid tribute to the medical teaching centers of this country. He recognized them as the source from which the American doctor has drawn, and is drawing, his medical knowledge and skill—knowledge and skill so gloriously reflected in the saving of a higher per-

centage of wounded during World War II than has ever been possible in the whole history of previous warfare.

Today, General Hawley is leaning heavily upon the qualified American doctor engaged in civilian practice. He needs his help in giving outpatient treatment. He is dependent upon him for assistance in Veterans Administration hospitals.

He needs the help of the organized State Medical Societies in encouraging communities where there are unused hospital beds to make these beds available to the Veterans Administration. In that, he needs your help in providing for veterans "A Medical Service Second to None."

OSLER SAID IT

The well-conducted medical society should represent a clearing-house, in which every physician of the district would receive his intellectual rating, and in which he could find out his professional assets and liabilities. We doctors do not "take stock" often enough, are very apt to carry on our shelves stale, out-of-date goods. The society helps to keep a man "up to the times," and enables him to

renew his mental shop with the latest wares. Rightly used, it may be a touchstone to which he can bring his experiences to the test and save him from falling into the rut of a few sequences. It keeps his mind open and receptive, and counteracts that tendency to premature senility which is apt to overtake a man who lives in a routine.—Sir William Osler

THE PHYSICIAN IN THE PATIENT-PHYSICIAN RELATIONSHIP*

ALPHONSE M. SCHWITALLA, S.J.

(Dean, St. Louis University School of Medicine, President, Catholic Hospital Association)

THE patient-physician relationship is fundamental in medical practice. This almost axiomatic truism would seem to be so palpably obvious as to make redundant, futile, and even platitudinous, any repetition of emphasis or re-statement. Yet, true as the statement seems, its translation from mere verbal formulation is a challenge to the sincerity, the competence, and the character of the physician. Today, it is true that even some physicians will pay lip service to the principle but will in their actual practice not only completely disregard the principle but will even deny its validity in medical practice.

Yet, it must be insisted that this principle is fundamental, fundamental in the ethical relationships between the patient and his doctor in so far as this principle establishes the reciprocal privileges and obligations of two individuals, fundamental in the professional relationships between the patient and his doctor in so far as this principle establishes the dependence of the patient with his biologic and psychologic needs, on the one hand, and the physician with his capacity and his willingness to meet those needs, on the other hand, fundamental in the profoundly human relationships between the patient and his doctor arising from the interplay of thoughts, emotions, and feelings emerging from sufferings and anxieties, on the one hand, and the readiness to apply remedial measures and physical, as well as psychologic sedation on the other hand. Medical practice obviously would not be medical practice if there were only patients without physicians or only physicians without patients, if there were only unmet needs or unapplied capacities, if there were only scientific truths instead of human needs to which these truths could be applied, or if there were only human needs without the competence to meet them. It is the patient and the physician who make the relationship possible and lay the foundation stone for the superstructure of the most intimate, the most searching, and the most extensive relationship between the practitioner of medicine and the beneficiary of that practice. It is the foundation of medical ethics, the basic reason for the maintenance of competence in the physician, the basic reason also for the demand of the art of medical practice that the physician must be a man of character and integrity beside being a man of knowledge.

The relationship is obviously a relationship between two human beings. Like all relationships, it is an explicit or implicit contract. The relationship is founded on a *quid pro quo* on either side. It involves a giving and a taking on both sides, it demands clearness of understanding, of obligations and responsibilities on both sides, as well as of benefits and privileges on both sides, it requires certain functions on both sides, certain mental and emotional attitudes. While, therefore, the contracting parties in the relationship are on a one-to-one basis, patient and physician being equally the contractors, nevertheless, with reference to ethical demands, the two cannot be equal for the patient is in need of something which the physician can help him to secure, not of something which the physician can give. The physician does not give the patient health. He aids the patient's organism in the readjustment which results in health, but that aid is something so much beyond anything for which the patient can render a commensurate *quid pro quo* that the patient is utterly incapable of remunerating the physician, even approximately adequately for the intangible but emphatically real benefits which the aid of the physician has effected within the patient's organism or his personality. In other words, the physician does not give health for a dollar, the patient does not pay a dollar for his health, but the physician assists the human organism of the patient through the procedures suggested by the physician's competence and his self-dedication to his vocation to a restoration of the equilibrium between the organism and the environment or to a restoration of that internal equilibrium between the diverse parts or functions of the organism. Both of these restorations we designate as restorations to health, for which aid the patient gives or may give a token payment to the physician, but he must give the physician his appreciation, gratitude, and acknowledgment of an obligation which are the physician's only real remunerations.

If this is a valid and an approximately correct analysis of the relation between patient and physician, we may well raise two fundamental questions. First, what does the patient-physician relationship demand of the physician, and second, what does the patient-physician relationship demand of the patient? The answer to both of these questions taken together, should throw the intense light of a complete revelation

* Delivered at the Banquet of the 140th Annual Meeting of the Medical Society of the State of New York, May 1 1946.

into the alleged or assumed vaguenesses and uncertainties in this patient-physician relationship. There will not be time, in the time at our disposal this evening, to attempt an answer to both of these questions. We shall, therefore, restrict our inquiry this evening to the discussion of the first of these questions and attempt such an answer as may be possible to the problem. What does the patient-physician relationship demand of the physician?

And first, let us raise a subquestion. What does the patient demand of the physician in this patient-physician relationship? If we have a clear understanding of this question, we may attempt an analysis of the further question of what society expects of the physician in the patient-physician relationship and finally, what the physician himself does or should or must demand of himself in this patient-physician relationship.

What does the patient demand of his physician in this patient-physician relationship? This question could be worded less abstractly in a vast variety of different ways depending largely on whom the patient is, whether he is an educated or a less well-educated individual, a wealthy man or a medically indigent individual, a discriminating man or a man who takes matters more or less for granted, a timid or bold, a fearful or trusting, a truth-loving or cynical man, in other words, a man who lives on the peaks or in the valleys of human emotions or, on the other hand, of a man who lives on the emotional flatlands and prairies of human experience. The question is asked, how does a person choose a doctor? And what is a good doctor? And why do I wish to choose my doctor? And why do I discriminate between my doctor and a consultant or a specialist? I am inclined to say that Dr Smith is my doctor, emphasizing the possessive pronoun but much less seldom do we hear the expression "Dr Jones is my laryngologist or my surgeon." We do say that "Dr Jones operated on me" or "I go to Dr Smith for my nose."

The question may again be worded in terms of popular discussions of the competence of physicians, the criteria and standards applied by the people as measures of professional efficiency. Or it may be reworded in terms of popular discussions of the physician's character as indicated by his approach to his patients or his discrimination between the different classes of his patients or his personal behavior toward his patients in his office or his examining room. The popular conversations about doctors are indicative of the demands which individuals or society make upon the physician.

It would seem that such thoughts as these might well have been suggested to those who would draft a national health bill since it is

through discussions of such questions as I am here raising that the feasibility or the impossibility would have been discovered of ever even approaching such concepts as the interchangeability of doctors as demanded by a panel system or the regulation of the numerical size of the physician's practice or the method of financial remuneration through a system of rules and regulations.

How do people judge a good doctor? It must be admitted that the question is extremely difficult to answer and still more difficult is it to answer the question how should people judge a good physician. Will I be misunderstood if I say, first of all, that there is little if any relationship between public action with reference to a doctor and the doctor's intrinsic worth? In other words, patients do not necessarily choose the objectively best doctor available to them anymore than people choose the objectively best banker or lawyer available to them. Reputation of physician, lawyer, or banker has much to do with his being chosen by many persons but that reputation may be established not on the basis of qualifications but on the basis of advertising, it may be established on the basis not of real professional competence but on the basis of popular appeal. Where crowds of patients flock, the crowds are apt to increase, where fees are large, they are apt to become still larger. Far be it from me to even imply that large fees are unworthy of the good doctor or that a large practice is indicative of relative inadequacy. The damnable thing about all this is that any criterion which is applied popularly in the judgment of the competence of a doctor may be indicative of sound worth just as it may be indicative of professional unworthiness. For the most part, however, this question, fortunately, need not be given a final answer because the true answer to the problem lies, it would seem, in quite a different direction.

Theoretically, and I would say even practically, there are no two doctors who are equally good for the same individual patient and to complete my thought, there are no two patients upon whom any one doctor is going to have precisely the same professional or personal effect. From a very reasonable point of view, we should have a teacher for each child and that fact is the real psychology as well as pedagogic educational reason why parents and, perhaps, particularly the mother should be the real teacher of the child. But when the child goes to school, we have a teacher teach a class of children because of the exigencies and limitations of society. We do not expect, however, that the teacher will have precisely the same effect upon each of her twenty-five or thirty children. We fondly hope

that the teacher will have at least a minimally beneficial effect upon that one of the children of her class upon whom she has the least effect. But with medical practice, there is no possibility of placing patients into classes. Each patient is a problem to himself not merely because disease entities manifest themselves in an almost infinite variety of variable presentations, but because the physician does not treat disease entities but treats rather an individual who has or thinks he has a disease, whatever the word disease might mean in this connection. That is the reason why there always must be a free choice of physicians by a patient and that is also the reason why there must always be a free choice of patients on the part of the physician.

My doctor is the doctor who is good for me. The fact that he is good for me with my special traits, my weaknesses, and strengths, does not mean at all that my doctor is good for you. How difficult it would be and practically impossible to bring this all home to the people at large, for the reply would be that the people are not familiar with a lot of doctors but, on the other hand, there still is in this analysis a depth of truth which one would hope might in the course of time through the processes of education be brought with greater emphasis to the attention of the lay mind.

Nevertheless, there still is an identifiable measure of truth in the expression "a good doctor." There is something corresponding to this phrase. It is the professional excellence of the doctor implying both competence and character, both scientific achievement and readiness to forget personal interests in his dedication to the interests of his patient. A good doctor is a doctor who lives up to the expectations of his profession even though he recognizes that standards set by an organization must necessarily be standards for the average and cannot be standards for the superior individual. He is a man who will value what his profession values as a general rule, a man who will not set his judgment against the judgment of his colleagues, a man who will be respectful to a colleague even though he must be critical of him. A good doctor will not spare himself, will not resent the requests of his patient or of the relative of the patient but will see in these requests the manifestations of deep human concern rather than of selfishness, and the indications of a profound anxiety arising from affection for the patient on the part of his dear ones rather than a morbid curiosity of a lay mind to understand a technical point.

How entirely different this thinking is from the thinking in the National Health Bill in which ostensibly the patient is given full freedom in the choice of his physician but must then choose

a physician who has qualified under the regulations and who has not as yet exceeded a quota of patient allotments for that particular area in which the patient is told that he may have any physician but then it is left to other authorities to determine when a patient should have a general practitioner or a consultant or a specialist, and when the patient is told that he has a freedom of choice of physician but then the pay for specialist or consultant or practitioner is regulated by rule, thus translating into an administrative problem the real needs and desires of the patient and subjecting these needs and desires to administrative and perhaps sometimes even coercive rule.

If the answer is made that it is only by such rules and regulations that we can have a national health program, let the subassumption be made as vigorous as possible: why must I have a national health program regulated by administrative enforcement if I must sacrifice some of my most profoundly valued and deeply rooted ethical ideals concerning the practice of medicine, and thereby sacrifice my independent responsibility for my health care and the health care of my dear ones?

And what does society expect of the physician in the patient-physician relationship? That society has a voice to which the medical profession must listen with reference to this matter no one will deny gainfully. On the other hand, the society's right to a voice in this matter must certainly be limited and must not come into conflict with the basic rights implied in the patient-physician individual relationship. What are society's rights and how do they modify the patient-physician relationship? This question raises the further one, upon what are the mutual rights of the patient-physician relationship founded? We have said that they are founded upon the contract but we have not defined the *quid pro quo* in the contract with sufficient definiteness to make such a definition the basis of further reasoning.

Now the *quid pro quo* is certainly not the stipend paid by the patient to the physician. This statement I regard as most essential in our thinking about this matter. It is for this reason that this code of medical ethics of the American Medical Association lay down as its first prescription that the service which the profession can render to humanity is the prime object of medicine while reward or financial gain is only a subordinate consideration. Needless to say, therefore, when the physician's desire for a reward comes into conflict with the good of the patient, it is always the latter that must take precedence. Proper ethics demands of the doctor that no consideration can ever be allowed

to come between himself and his patient if such a consideration is extrinsic to the welfare of the patient as the doctor seriously and sincerely in conscience understands the welfare of his patient. The first Code of Ethics of the American Medical Association, as far back as 1847, calls the doctor's attention to the necessity of having his mind and heart "imbued with the greatness of his mission, and the responsibility he habitually incurs in its discharge." But then, that first formulation of 1847 goes on to say "those obligations are the more deep and enduring, because there is no tribunal other than his conscience to adjudge penalties for carelessness or neglect."

Moreover, what really is the nature of the financial recompense which the patient gives to the physician and what is the nature of the financial gain. It is not and should not be a stipend in the sense that it is a payment of a stipulated sum fixed upon antecedent to the service to be rendered by the physician. I know that in certain quarters it is extremely unpopular to emphasize this point because, through a misconception of the fee schedule, the popular mind and in certain instances, even the professional man, has gained the impression that the fee schedule represents payments for certain services which imply medical responsibilities. No impression can be farther from the truth. In those medical societies that have best evaluated their own philosophy, the fee schedule is looked upon as a minimal demand of a physician for his services not as an obligatory fee, the understanding being that the physician in his relationship with the patient or with an agency which acts for the patient, will receive in recognition of his services at least the amount suggested in the fee schedule.

The reason for this interpretation lies in the nature of the payment to the physician. There is no common denominator between the services of the physician and the dollar. You cannot evaluate health nor life nor restoration to health, you cannot evaluate the intangibles associated with the health of a wife or child or of any of one's dependents. Therefore, it follows of necessity that any payment made to a physician for his services is in the nature of a token payment, no matter how large it is because even if it is a seemingly huge fee, the benefit of the personal self-sacrificing devotion to the physician bears no relationship whatsoever to even the largest financial fee. The payment to a physician, therefore, as a token payment, is a token of the patient's appreciation, gratitude, or the recognition of the physician's competence.

If this analysis again is correct, it would seem to follow that the more immediate are the rela-

tionships between the patient and the physician with reference to this payment, the more ethical are they. When, therefore, the benefits of the physician's services are received by the patient and the payment is made by some other agency extraneous to the two parties between whom the real contract exists, we are endangering the sanctity and the exclusiveness of the patient-physician relationship and we are exposing that relationship to the desecration of commercialism. We are degrading the services of the physician, the personal devotion of the doctor, his competence, the indescribable responsibility which he holds for life and limb, welfare and happiness of his patients, to purchasable commodities which surely, of their very nature, they are not and cannot be. We are thus materializing intangible goods, spiritual entities and we are bartering for coin the devotion and loyalty and confidential intimacy of the physician, together with the confidence and trust and the need for sympathy of the patient.

And this leads to the further consideration that an agency extrinsic to the patient-physician relationship cannot be a fit agent for a physician. It is for this reason that even the hospital, close as it is to the relationship, cannot adequately represent either the patient or the physician, least of all when the hospital, forgetful of its real nature as an aid to both the physician and the patient, presumes to become a corporate practitioner of medicine and recklessly enters into medical practice itself. I, frankly and straightforwardly, here wish to go on record, even though my interests are so wrapped up with the hospitals, as favoring the dissolution of any understandings or agreements or contracts between hospitals, on the one hand, and certain physician-specialists, on the other hand, which suggest commercialism rather than the ideals of which we are here speaking. And I deplore, with equal emphasis, the substitution of prepayment plans for hospital or medical care if in those prepayment plans there is bartered away the service of the radiologist or the laboratory pathologist or the anesthetist. Such paying agencies cannot escape criticism by saying that they are simply accepting the relationships that are presently existing between physicians and hospitals. The criticism should, however, fall not only upon the paying agency nor only upon the hospitals, but also upon those physicians who will lend themselves to these arrangements and who for the sake of avoiding inconveniences will simply follow the easier pathway.

There is, of course, much more to be said about all of this which cannot be touched upon briefly. In speaking of society's expectations of the physician in the patient-physician relationship, we

should have to touch upon the relations of the patient and physician to local, state, and federal governments, the obligations of the state in licensure, the protection of the people through not only licensure but through examination for competence, the possibility of licensure in the specialties and a vast number of subsidiary questions. The point I want to emphasize, however, even though I must omit these far-reaching discussions, is that complicated as all of this becomes in a complicated society, the obligations of the physician toward the patient are inevitably clear if we reduce them to the physician's basic responsibility in the patient-physician relationship.

And what does the physician expect of the physician in the patient-physician relationship, what does he expect of himself? If each physician had to answer this question, he would have to do so by writing his professional autobiography. Only in this way could the physician give us an adequate concept of his own ideals and ambitions, of his own expectations of himself, of his own demands upon his personal unselfishness, self-sacrifice, and capacity for whole-hearted dedication to his ideals. It is one thing to measure one's responsibilities in terms of legal obligations, another thing to measure in terms of moral obligations, quite another thing to measure them in terms of professional excellence and, finally, in terms of professional perfection. Some of us are content to walk haltingly and in stumbling fashion on the broad highroads of ethical practice, there are others who will find the harder way and who, in the desire to put first things first, will listen to counsels of perfection and to the self-imposed dictates of

one's own exacting conscience. Some of us will do the high and the right and the noble end the unselfish thing without ethics committees or without a publicly formulated code of ethics, some of us will not ask whether what we are doing is conformable to a code but whether it is conformable to ideals.

Of course, I am talking about professional competence and the progressive desire of the physician to penetrate more and more profoundly into the human being, not only through the avenues of knowledge but even more through the avenues of imaginative insight and emotional interpretation. But I am talking, also, for the development and maintenance of the physician's character in this deeply important area of human interest. No, I am not sympathetic with time studies except as broad guides. How long is the average time spent by a physician in meeting his patients in his office? How long does it take a physician on the average to see a patient in the hospital? What is the influence of a physician's patient density in the patient concentration in a hospital upon the time spent by the physician in seeing his patient? Is it worthwhile for a physician in urban or in rural practice to travel to see his patient, or must we develop other methods of effecting the contact between patient and physician?

Yes, these are important questions but even so much more important is what and who the physician is, his self-respect is important, the respect of his patients is important, the respect of society is important, but most important of all, is the fact that he carries a responsibility for which one day he will be held accountable before God.

PLANS ANNOUNCED FOR 1946 CLINICAL SURGEONS IN NEW YORK CONGRESS OF AMERICAN COLLEGES OF

The American College of Surgeons announces that arrangements have been completed for the holding of its Thirty-second Clinical Congress at the Waldorf Astoria, New York, September 9 to 13 inclusive. Plans include the usual extensive program of demonstrations, scientific sessions, panel discussions, symposia, forums, Hospital Standardization Conference, medical motion pictures, business meetings, and educational and technical exhibits, which will be held in the headquarters hotel, and operative and nonoperative clinics in the local hospitals.

This will be the first Clinical Congress since the meeting in Boston in 1941. Since that time 2,744 surgeons have been received into fellowship in absentia, and to them in particular the Convocation on

the opening night of the Congress will be a long anticipated event. Many of these new Fellows will have recently returned from service with the armed forces.

The formal initiation ceremonies, always impressive, will be exceptionally so this year because of the large number of new Fellows admitted during the past four years who are expected to be present.

Dr. Howard A. Patterson and Dr. Frank Glenn, of New York City, are chairman and secretary, respectively, of the Committee on Local Arrangements. Dr. Henry Cave of New York, a member of the Board of Regents of the College, is also active in directing the local plans for the meeting.

THE PROGRESS OF WOMEN IN MEDICINE*

ELISE S. L'ESPÉRANCE, M.D., New York City

WHEN I was asked to speak this evening for five minutes on "The Progress of Women in Medicine," it recalled to me an incident of my early college days when the professor of rhetoric said to me, "Young lady, your time is three minutes, your subject, The Immortality of the Soul." Just how can I crowd in so short a time all the vast opportunities that have been opened to medical women in the past generation?

I find that age has its compensations as it permits me to recall with great satisfaction the progress that women have made in this difficult profession during the past thirty years, and to view with pride this splendid gathering of medical men and women who are closely associated in a great profession, all looking forward equally toward the future of medicine, each willing to bear his or her part in maintaining and ever raising the standard of medical care today.

I must admit that this was not always the case. In the early days there were many limitations placed on our activities. Opportunities for medical educations were scarce. In fact, when I studied medicine there were only three standard medical colleges in the Eastern part of the United States that admitted women, they were Johns Hopkins, The Woman's Medical College of Pennsylvania, and The New York Infirmary for Women and Children. My selection was the Infirmary, which I have never regretted.

The chances for advancement after graduation in our chosen field were meager. We were a new element in a very old profession and there was a natural scepticism on the part of the medical men as to the seriousness of our intentions. This is well illustrated by an incident in my early career. In 1912, when I chose a future in pathology, one of the distinguished professors said to me that it takes twenty years to become a pathologist, and no woman would seriously consider one subject for that length of time. It may have been that remark which inspired me to remain in the field of pathology for over thirty years.

This doubtful attitude of the medical men was perfectly natural. Medicine is a serious profession and we have had to demonstrate our willingness to accept the challenge of this rigid competition. With the acceptance of this challenge, the doors of opportunity gradually began to open.

It is impossible in the short time allotted me to give you an accurate picture of the progress we have made during the past generation. It is sufficient to mention just a few important milestones.

First, medical education is coeducational in the colleges and universities in practically every large institution in the United States today, and I am proud to say that women students are maintaining a high scholastic record. Second, at present, there are very few hospitals that cannot proudly refer to their women interns and residents. Only recently, in a conversation with one of the members of the staff of a large metropolitan hospital, I mentioned the difficulty some of our women interns are having in securing residencies. He immediately replied "but we have two excellent women residents in our hospital." Third, within the past few years many women physicians have reached the high position of attendings on the staffs in some of our large hospitals and occasionally have attained the enviable status of director of a department.

These facts show the trend of the times to regard equally, without discrimination, all medical graduates.

One of the most significant achievements occurred during the past war when medical women were granted equal rank and opportunity with men in our armed services. This great advance was largely the result of the cooperation and enthusiastic support of our colleagues in the Medical Society of the State of New York who fought valiantly with us. This placed the State of New York as the first to sponsor such a step. It has also established for all time the position of women in medicine in the United States.

No great advancements are made except through a process of evolution attained through patience and perseverance. When we could demonstrate that medical women had those qualities, the acceptance of us on an equality by the medical profession was assured. Many distinguished medical women have laid the foundations for our progress in the past, the future rests with the young women of today.

The cordial feeling now existing between our two medical associations is a healthy stimulus to the success of each other. It is to this spirit of cooperation that we owe many of the successful campaigns against disease, many victories won, and many still greater to be achieved by this unity of effort.

* Delivered at the Banquet of the 140th Annual Meeting of the Medical Society of the State of New York, May 1, 1946.

PRESENTATION OF THE SOCIETY'S GOLD MEDAL TO THE OUTGOING PRESIDENT*

GEORGE W. KOSMAK, M.D., Chairman of the Board of Trustees

IT IS one of the pleasant and agreeable duties of the Chairman of the Board of Trustees of the State Society, on the occasion of its Annual Dinner, to present to the outgoing President a medal in recognition of his services to the organization during his term of office. This is a duty which I am very happy to fulfill.

Dr. Cunniffe has had a difficult path to follow since his elevation to the highest office in the gift of the Society, and he has pursued this task most efficiently and effectively. During this year, he has defended us against the imposition or attempted imposition of several measures that would have been detrimental to the progress of medicine. This has entailed great and

even unreasonable demands on his time and energy and strength. It required travel throughout the State under conditions not always too pleasant in order to bring before the doctors in various parts of the State his own views of the problems which beset the profession, coupled with exhortations which would make them realize of what an important organization they were members. Such personal contacts are of great value. In addition, he has presided over the meetings of the Council with patience and consideration. As I have said before, to properly fulfill this job is not as easy matter, and Dr. Cunniffe has acquitted himself well. We are pleased to extend to him this memento of his incumbency of the office and to wish him for the future continued health, happiness, and prosperity.

* Presented at the Banquet of the 140th Annual Meeting of the Medical Society of the State of New York May 1, 1946.

THE PATIENT DIAGNOSES THE DOCTOR

Thanks to persistent good health, I have always viewed the medical profession with calm detachment. But if I should become ill I would then be interested in your medical education, your experience and judgment, and above all, your ability to effect a quick cure—at, of course, a reasonable cost to me.

I should be alert for any neglect, delay, or supposed error on your part, since it might affect my welfare or my very existence and should expect you to give me your first and if possible, your undivided attention. As for your other patients, they and their comparatively trifling ailments would be a matter of the most profound indifference to me.

From the layman's point of view, it would seem that the smaller communities offer the doctor interested in general practice far greater opportunities for a varied and satisfying life. Small town practice places the maximum responsibility on the family doctor and gives him the maximum opportunity to know his patients and their real needs.

There is nothing in my past contacts with government bureaus which makes me enthusiastic about state medicine. I am the master who retains an expert, not a slave of a great impersonal machine.

I am much interested in prepaid insurance plans for medical, surgical, and hospital care.

The patient wants you to take him into your confidence. Barring the very sick, and the occasional unstable relative who cannot be depended upon you stand to gain by frankness. Take time to explain the patient's condition to him and to his family in simple English terms, and explain why the treatment is being ordered. This takes a few moments but it pays in every way. You are not dealing with children or imbeciles but many physicians habitually treat patients and their families as if they were.

Why do some men fossilize, others keep always in the foreground of professional progress? One man sees medicine as something static, in which all the great discoveries have been made, the other sees it as something dynamic—he eagerly awaits the proved advances. He is active in his county, state and national medical societies.

The general physician needs broader knowledge, embracing the whole field of medicine, so that he is prepared to take intelligent steps regardless of the emergency confronting him. He must have keen judgment, special ability in diagnosis, genuine interest in people, infinite patience and sympathy. In medicine the most scientific man is the one who applies the best techniques in the light of the patients' personal attributes.—J. R. Van Pelt, in *J. Missouri M.A.* Oct. 1945—*Clinical Medicine*, April, 1946.

Annual Meeting

Medical Society of the State of New York

ADDRESS OF THE PRESIDENT*

EDWARD R. CUNNIFFE, M D

I AM SPEAKING to you as the very retiring President of what may be considered the parent organization of the American Medical Association. You may recall that our state organization is forty years older than the national one and that leading members of this Society were predominantly active in the original effort to create a national organization, which now has become the largest and most important medical association in the world, far surpassing in size and extent of activities its original progenitor.

The principles of proper behavior in any walk in life, and particularly in the profession of medicine, are timeless and immutable. For forty years before the American Medical Association was formed, members of the New York State Society had adhered to certain concepts of ethics which ultimately became the "law of the land," so to speak, when formally phrased in Article 2, of the Constitution of the American Medical Association, which reads:

The objects of the Association are to promote the science and art of medicine and the betterment of public health.

And in the first section of Chapter One of its *Principles of Professional Ethics*, which reads:

A profession has for its prime object the service it can render to humanity, reward or financial gain should be a subordinate consideration. The practice of medicine is a profession. In choosing this profession, an individual assumes an obligation to conduct himself in accord with its ideals.

This language did not constitute an original promulgation at the time it was first uttered as a canon of ethics. It was merely the crystallization of the characteristics of behavior of the best medical men at all times and in all ages, embodied formally in the foregoing words.

I have presented these considerations for the purpose of making the point that it is nothing new in our tradition for emphasis to be placed on the maintenance of standards. Medicine would not have advanced through the centuries if this had not always been the motive activating the physician. For a comparatively brief period—almost a century and a half—the New York State Society has met annually for the purpose of increasing the quality of medical care, so we are indeed well fitted by a long tradition to

continue to safeguard the best interest of the public today, when pressures for social novelties have become very great.

It is interesting to compare our background and long experience in providing medical care with that of those who are so vocal in new plans to completely revolutionize the practice of medicine. It happens that the training for fitness in this pursuit resides exclusively in the medical profession and none of it inheres in the principal promoters of the schemes who can be, at best, only administrators or salesmen of the services we render. Nor are they bound by any rule of responsibility for the statements they make in espousing their cause. Ex-Mayor LaGuardia of New York City, appearing and testifying at the hearing on the Wagner-Murray-Dingell Bill in Washington, recently said that if the bill were passed, he would then stop his New York program for delivering medical care. It is extremely difficult for me to understand how he can stop anything that was never started, for this plan has never sold a policy or treated a patient. In addition, he claimed that a baby cost \$100 a pound in New York City. This, in spite of the fact that 13,459 babies were delivered in the municipal hospitals of our city during the year 1945.

That 1945 was a poor year for obstetrics in municipal hospitals can be realized, when a service delivering 200 babies per month in previous years delivered but 75 per month in 1945. I want to emphasize that for the 13,459 babies born in municipal hospitals, no doctor received any compensation, but in accordance with the time honored tradition of the medical profession, their services were freely given. This good proponent of the bill apparently did not realize that thousands of babies were delivered under the E M I C program, a program developed for the wives of men in the military forces. For these patients, the doctor's fee was \$50, except in cases where complications demanded a specialist, then the amount was \$75. The average baby weighs about six pounds. If Mr LaGuardia's charge were true, the expense would be \$600. When so many babies are delivered at such a small fee or for no fee at all, it is plain to be seen that there is something wrong with the good man's mathematics. Apparently the statement was made merely because it would attract attention by its sonorous phrasing, and advance

* Delivered at the 140th Annual Meeting of the Medical Society of the State of New York, May 1, 1946

the cause of socialized medicine, but not at all because there was any real basis to support it. Another example of this habit of overstating the truth is illustrated in the testimony of Mrs. Caroline Ware, president of the National Women's University Club, who claimed she represented 80,000 women and testified her society was in favor of the bill. Upon examination, she admitted that her society had not held a convention since before the war, and finally, she was forced to admit that she had canvassed but twenty women and the question asked was not about the bill but if they favored the extension of medical service. If they answered in the affirmative, they were supposed to favor a bill on which they had not offered an opinion. Yet she glibly reported her society in favor of it. The prize witness, however, was former Secretary Ickes who appeared in behalf of the bill and admitted that he had never read it but was in favor of it. When chided for this, he answered that most senators did not read bills before voting on them. I, myself, doubt very much whether Senators Wagner or Murray ever read the bill, and so far as Mr. Dingell is concerned, if he has read it, I am sure he does not understand it.

Mr. Altmeyer, of the Social Security Board, explained to the committee that the bill would provide medical care cheaper than the existing system because the government and the employer would help pay for it. It might be pointed out that the government gets its money from taxes only and it is a simple rule of economy that increased costs of production can only come with increased prices. Even Mr. Wallace rather belatedly admits that fact. While speaking of expense, it has been reported by some members of the Congress that for the administration of this plan it would be necessary to spend more than two billion dollars annually before a dollar goes to nurse or hospital or doctor. This expense would be for such items as directors, inspectors, paymasters, auditors, statisticians, stenographers, clerks, equipment, rent, and so forth. This figure is based on the supposition of having one inspector for every thousand patients, whereas in England experience shows there has to be one inspector for every hundred patients. Mr. Altmeyer, on questioning, was forced to admit that neither Messrs. Wagner, Murray, or Dingell wrote the bill but it was the brain child of Mr. Falk, who admits that he has spent ten years in preparing it. This is the fifth bill for socialized medicine that Mr. Falk has written and had presented to Congress by some of the New Deal representatives, the last bill being the second one he had introduced in 1945. The first four bills presented were admitted to be unsatisfactory, so, with all the government resources behind him

and an abundance of time, working for ten years, it is now shown that he has failed to succeed in this attempt. A few days after the current bill was presented, the *New York Times* published an editorial that was somewhat critical, whereupon Mr. Wagner wrote a letter to the paper stating that he knew it was not a perfect bill but hoped it would be better after the hearing.

The bill, as you know, was skillfully maneuvered away from the Appropriations Committee and into the Committee on Education and Labor, of which Mr. Murray is chairman. It would take a considerable length of time to hear all those who wanted to testify, so the chairman in his goodness and generosity decided that only those representing national organizations could appear before the committee, consequently, the New York State Medical Society, consisting of nearly 20,000 doctors who deliver medical care, is not permitted to appear but can send a statement to be placed on the record. On the other hand, the Physicians Forum, an organization which claims to have a membership about 700 and a Boston group, the remains of the old Committee of 400, were allowed to testify. These were the only physicians to testify for the bill and represent less than 2,000 members, while those doctors testifying against the bill represented 125,000. Practically all the testimony for the bill has been presented by government employees and women who represented very little. The committee, however, contains some very discerning members and it has been a daily occurrence to have the direct statements of the witnesses appearing in favor of the bill absolutely discredited upon cross-examination on their own statements.

Mr. Altmeyer, Mr. LaGuardia, and others proclaim that the doctors would make more money under this program than they receive in the present system. As a matter of fact, the definition of a profession, which is one of our principles of ethics, stresses the fact that money is not the prime object, but rather the services it can render to humanity is its goal. They say that more money will be received by the doctors and yet the program will cost the people less. It is hard to understand how pay to the physicians can be increased, plus the expense necessary to establish the enormous bureaucracy necessary to administer it and still have the cost to the people lower than at present. This will require some further explanation on the part of the proponents of the bill.

There is no substitute for experience. The experience of every country in the world that has tried compulsory health insurance has been unsatisfactory. Now they propose to give this inferior medical care to the American people, in the Wagner-Murray-Dingell Bill. It can be

likened to a hope and a wish for Utopia to arrive, coupled with an unlimited spending program to try to bring it about. It is the most unrealistic act ever proposed to the Congress, and assumes that government regulation in this country can be run more successfully than it has been in others where it has been tried. Today, the people of our country get medical care by going directly to their doctor. Under this bill a government clerk steps in between the doctor and his patient, with memoranda, schedules, rules, regulations, directives, thousands of them, changed from day to day, all instituted by the little bureaucratic gods that are appointed in droves of hundreds of thousands by the Social Security Administrator. Under this bill, the Social Security Administrator will have more power over the health of the people of the United States, vested in his own person, than could ever be assumed and exerted well by a single individual.

Let us look over the record of the countries which have accepted compulsory health insurance. Germany, which was the first country to be burdened with this program, was at one time the mecca of students from all over the globe, seeking postgraduate education. In seventy years the cost of their program multiplied one hundred times. Practically 50 per cent of all the money collected was used for overhead expenses to administer the program, the doctors receiving the benefit of practically one half. The total social taxes subtracted from the wages in Germany left the employees with little, barely enough for living expenses, and rendered it impossible for them to even leave the country and seek what offered them a more fertile field.

In England, in forty years, the cost has multiplied seventy times. A New York physician of my acquaintance who worked for a while with a London doctor reported that they had an office on one side of the house for panel patients and another on the opposite side for private patients. In a three-hour period this doctor would see 100 patients under the compulsory health insurance plan, ask them what their trouble was, give them a stock prescription, and let them depart. He never saw a single patient take off his shirt and receive an examination with a stethoscope. The secretary of the British Medical Association is responsible for the statement that no system of medical care will be successful if control of it is in the government. The failure of the system in England should be a lesson to us in this country. We see the people of England rapidly socializing everything, and preparing, perhaps, to go over in time completely to the Russian system. If that is the direction in which we are also drifting, a good way to begin is with medicine, taxing that and then moving along to the coal mines and the other industries, each new step calling for more taxes, so that the burden becomes

so great that nobody has any money left to buy anything and we all live on the largess of a beneficent and all-wise government which not only takes care of us from the cradle to the grave, but supplies us with living quarters, food to eat, clothes to wear, and rations everything out to those it likes and those it doesn't like, from shoe-strings to automobiles. I say, if that is what the American people want, the Wagner-Murray-Dingell Bill will take us a long way toward it and make each further step easier toward complete regimentation, domination, and dictatorship. This law will prepare us for such a situation by a series of headaches produced by our efforts to get a doctor when we are sick, from a government that has taken over the job of running and ruining the medical profession.

New Zealand's experience in so short a time as six years is another lesson to us, if we wish to be warned in time. According to the Minister of Health of that country, it has degenerated into a racket. He describes hospitals filled with patients with minor ailments. Doctors no longer seek improvement of their skills in postgraduate education, because they have no chance to put their abilities into practice, there is not sufficient time to spend with each patient, so extensive is the overuse of insurance facilities. Patients go to insurance doctors mainly for certificates enabling them to get paid for being sick, rather than to get over their sickness. People who are really seriously ill seldom think of using the compulsory insurance system. They go to a practitioner who does not take panel patients, and, therefore, has time to treat sick people. They would rather pay more to receive treatment from a physician who will have time to give a proper examination.

Austria and Italy have inferior medical service for their people. Dr. Dublin of the Metropolitan Life Insurance Company recently returned from a trip to Europe where he inspected the medical needs of France. He has reported that medical care delivered to the French people under compulsory insurance is very poor, and also reiterates that the medical care delivered to the people of the United States is the best in any country in the world. If such is the case, and he should be a good judge, it is hard to understand why the people of this country would listen to a proposal to establish a foreign system which has proved to be unsatisfactory.

I would like to speak on the other side of this question and tell of the great advantages that have been brought about by the medical care of the people of this country in the past seventy years under the leadership of the American Medical Association, but time will not permit. I can only say that the people of this country should consider long and carefully before they saddle such tremendous expense upon themselves and their children for inferior medical care.

Medical Society of the State of New York

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House of Delegates

Minutes of the Annual Meeting

April 29 to May 1, 1946

THE 140th Annual Meeting of the House of Delegates of the Medical Society of the State of New York was held at the Hotel Pennsylvania, New York, New York, on Monday, April 29, 1946, at 10 20 A.M. Dr Louis H. Bauer, *Speaker* Dr F Leslie Sullivan, *Vice-Speaker*, Dr Walter P Anderton, *Secretary*, Dr W Guernsey Frey, Jr, *Assistant Secretary*

SPEAKER BAUER The House will be in order Mr Secretary, are there any disputed delegations?

SECRETARY ANDERTON There are no disputed delegations, sir

SPEAKER BAUER I declare the 140th Session of the House of Delegates of the Medical Society of the State of New York open for the transaction of business.

Section 1

Report of Reference Committee on Credentials

SPEAKER BAUER The Chair recognizes the Chairman of the Credentials Committee, Dr McCarty

DR. CHARLES F MCCARTY, Kings At the last count there were eighty-four County Delegates, fifteen Officers, one District Delegate five Section Delegates and one Ex President registered.

SPEAKER BAUER Is there a quorum present?

SECRETARY ANDERTON There is a quorum present, sir

SPEAKER BAUER There being a quorum present, we will proceed with the order of business.

Section 2

Approval of the Minutes of the 1945 Session

SPEAKER BAUER The first order of business is the approval of the minutes of the 1945 Session

SECRETARY ANDERTON Mr Speaker, I move that the reading of the minutes be dispensed with, and that they be approved as published in the December 1 and December 15 1945, and the January 1 and January 15, 1946 issues of the NEW YORK STATE JOURNAL OF MEDICINE.

DR. EIRA A. WOLFF, Queens I second the motion.

There being no discussion, the motion was put to a vote and was unanimously carried.

Section 3

Reference Committees

SPEAKER BAUER Mr Secretary, will you read the appointments of the Reference Committees? Gentlemen, will you please pay close attention, because there are several changes from the printed list which appeared in the JOURNAL.

SECRETARY ANDERTON The Reference Committees for the 1946 House of Delegates are as follows

REFERENCE COMMITTEE ON CREDENTIALS:

Charles F. McCarty, *Chairman* Kings County
Goodwin A. Dwyer, *Queens County*
Felix Ottaviano, *Madison County*
Alexander N. Selman, *Rockland County*
E. Kenneth Horton, *Nassau County*

REFERENCE COMMITTEE ON REPORT OF PRESIDENT

Eira A. Wolff, *Chairman* Queens County
John A. Pritchard, *St Lawrence County*
Raymond F. Kircher, *Albany County*
Thurman B. Olvan, *Kings County*
Ralph Sheldon, *Wayne County*

REFERENCE COMMITTEE ON REPORTS OF SECRETARY CENSORS AND DISTRICT BRANCHES

Morris Mason, *Chairman* Warren County
Robert C. Simpson, *Montgomery County*
Frank Telford, *Richmond County*
Charles H. Loughran, *Kings County*
J. Lewis Amster, *Bronx County*

REFERENCE COMMITTEE ON REPORTS OF TREASURER, TRUSTEES AND FINANCE COMMITTEE

Fenwick Beekman, *Chairman* New York County
Morris Ant, *Kings County*
Benjamin Abramowitz, *Sullivan County*
Roger A. Hemphill, *Livingston County*
Bradford P. Golly, *Oneida County*

REFERENCE COMMITTEE ON REPORT OF PLANNING COMMITTEE FOR MEDICAL POLICIES

Albert F. R. Anderson, *Chairman* Kings County
W. Walter Street, *Onondaga County*
Edward C. Veprovsky, *Queens County*
Harry C. Quam, *Erie County*
John R. MacElroy, *Saratoga County*

REFERENCE COMMITTEE ON CONSTITUTION AND BYLAWS AMENDMENTS

Peter J. Di Natale, *Chairman* Genesee County
Clifford F. Lee, *Chemung County*
Joseph C. O'Connor, *Erie County*
Donald E. McKenna, *Kings County*
Francis G. Riley, *Queens County*

REFERENCE COMMITTEE ON REPORT OF COUNCIL—PART I:

Postgraduate Education (also Supplementary)
Joseph Tanoppy, *Chairman* Kings County
Vincent Juster, *Queens County*
Joseph H. Diamond, *Richmond County*
George C. Vogt, *Broome County*
Stockton Kimball (Section Delegate)

REFERENCE COMMITTEE ON REPORT OF COUNCIL—PART II:

Maternal and Child Welfare (also Supplementary)
Joseph A. Oels, *Chairman* Essex County
Alfred K. Bates, *Cayuga County*
Blahon C. Halleck, *Otsego County*
William J. Orr (Section Delegate)
Alfred M. Hellman, *New York County*

REFERENCE COMMITTEE ON REPORT OF COUNCIL—PART III:

School and Industrial Health
David W. Beard, *Chairman* Schoharie County
John C. Brady, *Erie County*
Irving S. Banda, *Kings County*
William J. Tracy, *Schenectady County*
Samuel M. Kaufman, *New York County*

REFERENCE COMMITTEE ON REPORT OF COUNCIL—PART IV:

Public Health Activities
Blood and Plasma Exchange Bank
Cancer (also Supplementary)
Hard of Hearing and the Deaf
4 H Clubs and Youth Health Activities
Frank La. Catutta, *Chairman* Bronx County
Jacob Warner, *Queens County*
Donald Malvern, *Dutchess County*
Arthur M. Johnson (Section Delegate)
Edgar O. Boggs, *Lewis County*

REFERENCE COMMITTEE ON REPORT OF COUNCIL—PART V

Rehabilitation
Rural Medical Service
Kenneth F. Bott, *Chairman*, Greene County
Charles S. Lakeman, Monroe County
Robert B. Archibald, Westchester County
Madge C. L. McGuinness, New York County
Theodore W. Neumann, Orange County

REFERENCE COMMITTEE ON REPORT OF COUNCIL—PART VI

Public Relations and Economics
Public Medical Care
Women Medical Students and Interns
Medical Service and Public Relations
Roy B. Henline, *Chairman*, New York County
John M. Galbraith, Nassau County
Lyman C. Lewis, Allegany County
Archibald K. Benedict, Chenango County
Elton R. Dickson, Broome County

REFERENCE COMMITTEE ON REPORT OF COUNCIL—PART VII

Medical Care Insurance
Special Committee on National Casualty and Indemnity Insurance
Herbert E. Wells, *Chairman*, Erie County
Benjamin M. Bernstein, Kings County
Joseph D. Hallinan, Queens County
Oswald J. McKendree, Oneida County
Clarence G. Bandler, New York County

REFERENCE COMMITTEE ON REPORT OF COUNCIL—PART VIII

Veterans' Affairs
Joseph P. Henry, *Chairman*, Monroe County
John P. O'Brien, Bronx County
Leo E. Gibson, Onondaga County
Edwin A. Griffin, Kings County
Reginald A. Higgons, Westchester County

REFERENCE COMMITTEE ON REPORT OF COUNCIL—PART IX

Legislation (also Supplementary)
Frederic W. Holcomb, *Chairman*, Ulster County
Thomas B. Wood, Kings County
Sylvester C. Clemons, Fulton County
Andrew A. Eggston, Westchester County
B. Wallace Hamilton, New York County

REFERENCE COMMITTEE ON REPORT OF COUNCIL—PART X

Workmen's Compensation
William B. Rawls, *Chairman*, New York County
Bernard S. Strait, Yates County
Stanley E. Alderson, Albany County
Renato J. Azzari, Bronx County
G. Kirby Collier, Monroe County

REFERENCE COMMITTEE ON REPORT OF COUNCIL—PART XI

Publications and Medical Publicity
George C. Adle, *Chairman*, Westchester County
Stephen H. Curtis, (District Delegate)
Louis A. Friedman, Bronx County
Scott Lord Smith, (District Delegate)
Charles C. Trembley, Franklin County

REFERENCE COMMITTEE ON REPORT OF COUNCIL—PART XII

Malpractice Defense and Insurance
Report of Legal Counsel
Eugene H. Coon, *Chairman*, Nassau County
Donald D. Prentice, Albany County
Joseph A. Landy, Bronx County
Gny S. Philbrick, Niagara County
John L. Sengstack, Suffolk County

REFERENCE COMMITTEE ON REPORT OF COUNCIL—PART XIII

Miscellaneous Matters
Convention
Medical Licensure
Nursing
Woman's Auxiliary
Office Administration and Policies
Joseph H. Cornell, *Chairman*, Schenectady County
Charles A. Prudhon, Jefferson County
Abraham Koplowitz, Kings County
Philip D. Allen, New York County
Richard P. Doody, Rensselaer County

REFERENCE COMMITTEE ON NEW BUSINESS A

Thomas M. D'Angelo, *Chairman*, Queens County
Leo F. Schuff, Clinton County
John J. Ganev, Kings County
Harold B. Davidson, New York County
James E. McAskill, (Section Delegate)

REFERENCE COMMITTEE ON NEW BUSINESS B

Leo F. Simpson, *Chairman*, Monroe County
Edgar Bieber, Chautauqua County
Arthur A. Fischl, Queens County
John Dugan, Orleans County
A. Wilbur Durfee, New York County

REFERENCE COMMITTEE ON NEW BUSINESS C

Frederick W. Williams, *Chairman*, Bronx County
Charles A. Anderson, Kings County
Denver M. Vickers, Washington County
John L. Edwards, Columbia County
Theodore J. Curphey, Nassau County

SPEAKER BAUER Thank you, Mr. Secretary (Announcements concerning time and place of meeting of various Reference Committees)

SECRETARY ANDERTON I move that the reports and supplementary reports of Officers, Council, Trustees, Legal Counsel, and District Branches, that have been published and distributed to the members of the House, be referred to the respective reference committees without reading.

DR. GEORGE W. KOSMAK I second the motion.
SPEAKER BAUER You have heard the motion. Most of the reports were sent to you in printed form prior to the meeting. There are several reports that have been distributed to you this morning. Is there any objection to their being referred without reading? If not, they will be so referred, but take notice of the following. All of the printed reports are referred to the respective Reference Committees with the exception of one portion of the Report on Malpractice Defense and Insurance pertaining to amendments of the Bylaws, which is referred to the Committee on Amendments to the Bylaws, otherwise, the report is referred to Reference Committee on Report of Council, Part XII. Also, the report on the Finance Committee is referred to the Reference Committee on the Reports of the Treasurer and Trustees. Otherwise, the supplementary reports are referred to the respective committees as noted in the titles.

Section 4 (See 57)

Supplementary Report of Secretary

To the House of Delegates—Gentlemen,

It gives your Secretary pleasure to draw your attention to a matter which has developed since presenting his Annual Report.

Owing to an increase in the incidence of diphtheria in several localities in this State, your Secretary attended, on April 17, 1946, with Mr. Dwight Anderson, Executive Secretary of the Medical Society of the State of New York, a meeting organized by Dr. Donald Armstrong, Vice-President of the Metropolitan Life Insurance Company, at his offices. Also present were other representatives of the Metropolitan Life Insurance Company, the New York State Health Department, and the State Charities Aid Association.

A program was discussed, aiming toward increasing the number being immunized against diphtheria and in increasing the immunity of those previously immunized against diphtheria in New York State.

Your Secretary petitions the House of Delegates to direct the Treasurer of the Medical Society of the State of New York to pay Dr. J. Stanley Kenney \$153.23 for his expenses incurred as delegate to the American Medical Association House of Delegates,

also \$77.27 for his expenses, while attending the House of Delegates meeting at Buffalo, New York, making a total of \$230.50. As Dr. Kenney's voucher was submitted more than ninety days after he had incurred these expenses the Council and the Board of Trustees have not the power to direct payment (Chapter X, Section 1, Bylaws of the Medical Society of the State of New York.)

Respectfully submitted,

W. P. ANDERSON, M.D., Secretary

April, 1946

Section 5 (See 48)

Supplementary Report of the Council—Part I Postgraduate Education

To the House of Delegates—Gentlemen,

As Chairman of the Council Committee on Public Health and Education, I herewith submit a supplementary report to include the activities of the Committee since March 13, 1946.

Postgraduate Education

In addition to the instruction mentioned in the report of the Council Committee on Public Health and Education submitted on March 5, 1946, instruction has been arranged for and given in the following county medical societies:

| County | Instruction | Number of Lectures |
|--------------|---------------------------------|--------------------|
| Broome | General medicine | 1 |
| Jefferson | General medicine | 2 |
| Oneida | General medicine | 1 |
| St. Lawrence | General medicine | 1 |
| Schoenectady | Chemotherapy and the antibiotic | 1 |
| Seneca | General medicine | 1 |
| Steuben | General medicine | 1 |
| Tompkins | General medicine | 1 |
| Ulster | Tropical diseases | 1 |
| Warren | Traumatic surgery | 1 |
| Wyoming | Cancer | 1 |

Since the meeting of the House of Delegates in Buffalo in October 1945, the Committee has arranged for postgraduate instruction to be presented in thirty-one counties with a total of ninety-eight lectures.

At the request of the Convention Committee, the Council Committee on Public Health and Education has arranged for a Teaching Day especially for the members of the Medical Society of the State of New York who served their country during World War II, to be held at the time of the Annual Meeting on Tuesday, April 30, 1946, Hotel Pennsylvania, New York City. This Teaching Day will consist of eight lectures—four lectures will be given in the morning and four lectures will be given in the afternoon. Subjects were selected which will not conflict with the Scientific Section and Session programs, to be held Wednesday, Thursday, and Friday.

Section 6 (See 47)

Supplementary Report of the Council—Part II

Maternal and Child Welfare

Child Welfare—A nation-wide child health survey is being conducted by the American Academy of Pediatrics, the Children's Bureau of the United States Department of Labor, and the United States Public Health Service. An outline of the plan was submitted to the Subcommittee on Child Welfare. It was decided to recommend to the Council approval of the plan and request the Medical Society of the State of New York to assist in the study. These suggestions were approved by the Council of the Medical Society of the State of New York at the meeting on March 14, 1946. Since that time,

several conferences have been held with representatives of the agencies conducting the survey and the Medical Society of the State of New York has already given considerable assistance.

A meeting of the Subcommittee on Child Welfare was held in New York City on Thursday, April 11, 1946 to consider a program for "Pediatric Institutes for General Practitioners." The Subcommittee approved the program as did the Council Committee on Public Health and Education. The necessary arrangements are now being made to hold these Institutes in various parts of the State under the joint auspices of the Medical Society of the State of New York and the New York State Department of Health.

Section 7 (See 53)

Supplementary Report of the Council—Part IV

Public Health Activities

Cancer—At the time of the meeting of the Subcommittee on Cancer and the Council Committee on Public Health and Education on March 13, 1946, a request was made to Dr. Louis C. Kross, Chairman of the Board of Directors of the New York State Unit of the American Cancer Society, to submit a plan of reorganization and operation to be developed in New York State. This has been received and will be considered at a meeting of the Subcommittee on Cancer and the Council Committee on Public Health and Education to be held in New York City on Sunday, April 28, 1946.

4-H Clubs and Youth Health Activities—Dr. J. G. Fred Hiss, Chairman, Subcommittee on 4-H Clubs and Youth Health Activities, reports his correspondence with Mr. B. R. Rickards, Director, Division of Public Health Education, New York State Department of Health and with Mr. Albert Hoefler, State 4-H Club Leader. Dr. Hiss has been active for several years to change the plan for judging the health of boys and girls in 4-H Clubs. The suggestions made by Dr. Hiss were accepted by the New York State group of 4-H Clubs and, recently at a meeting of the leaders at the National 4-H Club Congress, the following action was taken as reported by Mr. Hoefler:

"At that time I did raise the question and you and your colleagues will be interested to know that the Subcommittee has recommended discontinuance of the health screenings as have been conducted in the past and recommended the New York State plan. For 1946 we are recommending that the health screenings be made on the basis of improvement based on the Standard Report form and some additional information and that a blue award group be selected based on health improvement from the records submitted. Health records will be submitted at the same time and all other records are due and will be scored by the committee. States will be permitted to submit records of one boy and one girl."

Section 8 (See 78)

Supplementary Report of the Council—Part V Rehabilitation

A meeting of the Subcommittee on Rehabilitation and the Council Committee on Public Health and Education was held in New York City on April 9, 1946. Also present at this meeting were officers of the Medical Society of the State of New York, representatives of the New York State Departments of Education and Social Welfare and Dr. Victor H. Vogel, Chief Medical Officer for the Federal Office of Vocational Rehabilitation. Because of illness, the

New York State Department of Health was not represented

The usual discussions regarding the fee schedules took place. Comment was made by Dr. Vogel and others that there should be additional activities carried on under the Office of Vocational Rehabilitation of the New York State Education Department. Provision for physical examination of all applicants for rehabilitation is required. It was agreed that a fee for this examination would be submitted and that a physician devoting his time to internal medicine would be recommended to the Council for appointment to the Subcommittee on Rehabilitation.

It was also agreed that a fee schedule should be submitted for psychiatric patients who are now applying for care under the Rehabilitation program. This report was made to the Council at its meeting on April 11, 1946.

Dr. Albert F. R. Andresen, Brooklyn, was appointed a member of the Rehabilitation Subcommittee.

Provision for the psychiatric part of the program is being developed.

Section 9 (See 56)

Supplementary Report of the Council—Part IX.

To the House of Delegates—Gentlemen,

The Council Committee on Legislation respectfully submits a supplementary report.

The preliminary report was made on March 1. As the legislative session lasted through March 26, the total number of bills introduced in both houses and those in which we were interested could not be reported at that time, also, we could not give you the final action on many of the bills in which we were interested. There were 2,437 bills introduced in the Senate and 2,774 bills introduced in the Assembly, a total of 5,211 in both houses. Your Legislative Committee followed 136 bills in the Senate and 166 bills in the Assembly, or 302 bills in all. Of these bills, 122 were concurrent, leaving 280 separate bills.

At the time of the preliminary report, we could give you final action on very few of these bills. In that report we mentioned that the antivivisection bills had been defeated in the committee in the Senate, but remained in the Judiciary Committee in the Assembly. The final action was defeat in committee in the Assembly on both antivivisection bills. We also reported to you that a bill for the licensure of chiropractic had been introduced in the Assembly on February 27. No bill for the licensure of chiropractic was introduced in the Senate and this bill in the Assembly was defeated in committee.

In the earlier report we also called your attention to the very large number of compensation bills that had been introduced this year. At this time we can report to you that a very high percentage of these bills were either not reported out of committee or were defeated in committee. The fate of those that were passed by both houses has not been good in the hands of the Governor. In other words, there seems to have been a general attitude throughout the Legislature this year, not to make any marked changes in the Compensation Law this year. The Society was interested in sponsoring at least one-half dozen bills pertaining to workmen's compensation and these bills suffered the same fate as the great majority of the other workmen's compensation bills. Senate Int 612—Condon, which amended the Workmen's Compensation Law and, among other changes, struck out provision for committee of ex-

pert consultants, passed both houses but was vetoed by the Governor. We were on record as not being in favor of this bill and were pleased with the action of the Governor.

A bill was introduced on Thursday, March 14, Assembly Int 2739—Rules Committee, to authorize the State Tax Department to receive Federal moneys for construction of public and other non-profit hospitals, including health centers, postwar public works planning commission or other agency designated by Governor shall be sole agency for administration if Federal law requires that State agency be designated. This bill provides for the State to administer Federal funds under the Hill-Burton, or a similar bill, if such Federal legislation is passed. Your Legislative Committee went on record as being in favor of this bill, which was passed by both houses, signed by the Governor and becomes Chapter 666 of the Laws of 1946.

The Legislative Committee, on the advice received from the Advisory Committee on Ophthalmology, went on record as being opposed to the bill, Senate Int 1563—Wicks, which provided for the practice of ophthalmic dispensing. The opposition was based on the provision in this bill permitting the fitting of contact lens by optometrists. The disapproval of that provision in the bill was made known to the committees in the Legislature and on March 15 the bill was amended, removing that provision. Your Legislative Committee, after further consultation with the Advisory Committee on Ophthalmology, went on record with the committees of both houses that they were then in favor of the bill as amended on March 15. The amended bill passed both houses and was signed by the Governor and now is known as Chapter 697 of the Laws of 1946.

Your Legislative Committee went on record as being opposed to the bill, Senate Int 1695—Condon, which changed the definition of the practice of podiatry. It was thought that the new definition did not contain the limitations to the practice of podiatry that are now in the present definition and the removal of these limitations would be a danger to the public. Responses from many members of the State Society and members of the Legislative Committees of the County Societies in registering their opposition to this bill apparently were effective, as the bill which had passed both houses was vetoed by the Governor.

The bill, Senate Int 1319—Griffith, which amends the present law governing the selling and prescribing of barbiturates and other hypnotic and somnifacient drugs, was passed by both houses and signed by the Governor and becomes Chapter 597 of the Laws of 1946. The Society was on record as being in favor of this bill.

At the time of writing this report, there are still a few bills remaining in the hands of the Governor on which he has not acted. Among these bills is Assembly Int 802—Ryan, which amends the present Narcotic Law in regard to manufacture and sale of narcotic drugs, preparations, and defines exempt narcotic preparations. It is understood that this bill has an excellent chance of being signed by the Governor, but at the time of writing this report, this action has not been taken and we cannot give you the final action by the Governor or the chapter number. There is, also, the bill, Senate Int 1651—Griffith, which transfers from the Education Department to the Health Department jurisdiction of the care and treatment of physically handicapped children. Again, this bill has not been signed by the Governor at the present date and we cannot give you the final action.

The bill, Assembly Int 2274—Maffior which is known as the "tuberculosis bill," provides for care and treatment by state, county, or city, of persons suffering from tuberculosis without cost unless the person volunteers to pay, and which provides that localities may retain their institutions or transfer them to the State, and, also, that the State will pay about 60 per cent of expenses on patient-day basis, passed both houses and is in the hands of the Governor. To the present date the Governor has not signed this bill, but we understand that there is little likelihood of its being vetoed. We regret at this time that we cannot give you the final action or chapter number.

To sum up the report of the Council Committee on Legislation for this year it can be said that your Committee has been very busy following a large number of bills, has registered its recommendations on those bills with the committees in both houses and with the Governor. The results of this legislative session would appear to be highly satisfactory. It is regretted that some of the workmen's compensation bills in which we were interested were not acted on favorably but it is realized that their fate was no different than the great majority of the workmen's compensation bills that were introduced this year. The action taken by members of the Legislature in both houses and by the Governor has been to a very large extent along the lines which your Legislative Committee has desired.

Respectfully submitted,
HARRY ARANOW, M.D., Chairman,
Council Committee on Legislation

Section 10 (See 55)

Additional Annual Report—Report of the Finance Committee

To the House of Delegates—Gentlemen,

The House of Delegates at its last session adopted the following resolutions

Resolved, that the House of Delegates of the Medical Society of the State of New York requests the Board of Trustees to establish a fund for the advanced education of the children of our colleagues who have died in the service of our country, and be it further

Resolved, that said fund may be raised by a small increase in dues or annual levy over a period of years, for example, one dollar per year for ten years, in order that each member may have a part in the memorial."

The Council referred this to the Finance Committee for study

The Finance Committee found itself unable to make any concrete recommendations without knowing more about the scope of the problem

The Committee sent a questionnaire to each county society requesting information as to the number of doctors who had died in service and the names, ages and sex of any children. So far, replies have been received from 54 of the 61 county societies.

From the counties reported, there are a total of 54 children who would be effected by the resolution. Twenty nine are boys, and 25 are girls. Their age groups are as follows

| Age | Number | Boys | Girls |
|-----------|--------|------|-------|
| 0-5 years | 19 | 13 | 6 |
| 6-10 | 19 | 10 | 9 |
| 11-15 | 9 | 3 | 6 |
| 16-20 | 5 | 2 | 3 |
| Over 21 | 2 | 1 | 1 |
| Total | 54 | 29 | 25 |

Of the seven counties not reporting, only one will materially affect these figures. That county is New York, and it may be expected that as a rough estimate we may have 20 children and possibly more from that county to provide for. No definite estimate, of course, can be given until all counties have reported.

It will be seen from the above listings that there will be only a few children who are in the advanced education stage and, therefore the peak load will not come for several years.

Before the Committee can proceed any further even after all questionnaires have been returned, it will be necessary for the House to clarify the resolution.

First, what is meant by "advanced education"? Does it mean college, professional school, or both? The Finance Committee recommends that the plan be restricted to college education for all and, in addition, professional education only for those who wish to study medicine. The House should also place a limit on the number of years of education to be provided.

Second, should financial need be a determining factor? The Finance Committee recommends that this education be provided only for those who otherwise would not be able to obtain it.

Third, how extensive provision for financial help does the House wish to make? Should there be a straight scholarship of a fixed sum, or should the amount cover tuition and other obligatory fees, or should it cover the latter plus a fixed allowance for board and room?

Fourth, the final paragraph of the Resolution does not confer the authority on either the Council or Trustees to raise the annual dues as its content is too indefinite.

With reference to this the Finance Committee recommends that voluntary contributions be asked for, during the next five years. Each county society may be requested to add a plea on their annual bills for voluntary contributions to the War Memorial. It is believed that sufficient money can be raised this way without any increase in dues or compulsory assessment. If not, the balance should come from the general funds of the Society.

The Committee also recommends that the plan be limited to sons and daughters of deceased veterans and not to include grandchildren.

Finally, the Committee recommends that authority be conferred by the House on the Council to determine the method of administration of the Program and to make appropriate recommendations regarding the financial aspects to the Board of Trustees.

Respectfully submitted,
LOUIS H. BAUER, M.D., Chairman
J. STANLEY KENNEY, M.D.
F. LESLIE SULLIVAN, M.D.

Section 11 (See 71)

Additional Annual Report—Report of the Planning Committee for Medical Policies—1946

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To the House of Delegates—Gentlemen,

Organization—The Planning Committee for Medical Policies was continued by the House of Delegates at its Annual Meeting in 1945, and its organization was on the same basis as in the previous two years. Its personnel therefore was as follows:

J Stanley Kenney, M D, *Chairman*, New York
 Edward R. Cunniffe, M D, Bronx
 William Hale, M D, Utica
 W P Anderton, M D, New York
 A. A. Gartner, M D, Buffalo
 Louis H. Bauer, M D, Hempstead
 Peter J. Di Natale, M D, Batavia
 Norman S. Moore, M D, Ithaca
 Walter S. Mott, M D, White Plains
 O W H Mitchell, M D, Syracuse
 Leo F. Simpson, M D, Rochester

The period covered by this report is from October 8, 1945, to April 10, 1946. This represents a period of six months since the rendering of your Committee's last annual report, which was a very comprehensive survey and covered a wide range of topics. For this short year it seemed wise and consistent with the trends for your Committee to confine its studies to what it considered the more important problems requiring clarification. It elected, therefore, to concentrate its efforts on two major programs—Diagnostic Aids and Health Centers, and Group Medical Practices. In addition, it has studied the National Health Program and again reviewed the current Wagner-Murray-Dingell Bills, and has commented briefly on a few of the other subjects which were carefully considered in its 1945 report.

Interim Report—We are rendering this as an interim report. Both of the above-mentioned subjects represent continuing programs and our study of them, therefore, is necessarily incomplete. Because of the inherent complexity of these two problems we found ourselves confronted with obstacles which precluded any hasty or ill-considered recommendations, and much more time for their solution will be required.

Diagnostic Aids and Health Centers—The Council of the Medical Society of the State of New York on November 8, 1945, voted that the following recommendation be referred back to the Planning Committee with the request for more detailed information as soon as possible:

Centers for Diagnostic Aids

The Planning Committee recommends as an experiment that a Center for Diagnostic Aids to physicians practicing in the rural districts be set up in a selected location in either or both of the following designated areas:

- (1) The counties of Schuyler, Chenango, and Tioga
- (2) The north and northeastern part of Delaware County, the southwestern part of Otsego County, and the southeastern part of Schoharie County

This specific recommendation from the Council has formed the basis for this study.

For purposes of clarification it would seem advisable to restate what is meant by "centers for diagnostic aids." The Hill-Burton Bill defines a public health center as a "publicly owned facility for the provision of public health services and medical care, including related facilities such as laboratories, clinics, and administrative offices operated in connection with public health centers."

That portion of the Planning Committee report of 1945 which related to diagnostic centers reads as follows: "The term 'laboratory facilities' means in addition to routine chemical, bacteriologic, and serologic examinations and other pathologic work, the related clinical tests such as x-ray examinations, electrocardiograms, basal metabolism tests, and similar clinical procedures. Blood transfusions also should be made available, but this facility is being provided by a particular setup now developed as the result of legislative action at the 1945 annual session."

"The primary purpose of these centers is not to furnish a diagnosis, but rather to make available to the physician in attendance the results of all such tests, thereby enabling him to make his own diagnosis. No treatment is to be provided. No member of the staff of such a center is to be permitted to engage in the private practice of medicine."

A subcommittee of this Planning Committee, consisting of Dr. O W H Mitchell and your chairman, together with Dr. Leslie Sullivan and Dr. Robert Hannon, held a meeting in Albany which was attended by Dr. Godfrey, State Commissioner of Health, Dr. Rogers, Deputy Health Commissioner, Mr. Harry Page, representing Mr. Lonsdale, Commissioner of Public Welfare, Dr. Berkel of the Welfare Department, and Dr. Bourke representing Assemblyman Lee B. Mailer, Chairman of the Health Preparedness Commission, who was unable to attend himself, because of the necessity of being present at the legislative sessions. Dr. Bourke is the director of the study for the Joint Hospital Board of the New York State Postwar Public Works Planning Commission.

Dr. Bourke gave us a general survey of the planning the State is undertaking through this Joint Hospital Board and he furnished us with a copy of their preliminary report dated February 15, 1946, and known as "New York State Plan for Survey of Hospital Facilities and Program for Regional Hospital Planning for Postwar Hospital Construction" (See Appendix A).

These gentlemen evinced great interest in the survey made in 1945 by the subcommittee on Laboratory Services and Medical Care of which Dr. F. Leslie Sullivan was chairman. We reminded them that the State Society is deeply interested and concerned with methods to provide quality medical care in rural and outlying districts and in order to attract doctors to practice in these areas and to furnish them with the facilities to do so. The diagnostic aid center would be a means to this end. How to finance and administer such centers and insure efficient control of them by the doctors remains the crux of the problem.

They discussed in a general way the program of state aid for public health work, but believe that such plan or plans as may be evolved should be integrated with the program for regional hospital planning and postwar hospital construction which New York State contemplates. They anticipate having the local community, with state aid where necessary, maintain its own hospital facilities as far as possible, but again they retained the basic con-

ception of having these facilities tie up with the regional general hospital and medical center. They felt, therefore, that the diagnostic clinic or public health center—or whatever designation it ultimately will be given—should be an intrinsic part of the basic plan. Either such a center could be incorporated in an existing hospital or, where new ones are built, provision could be made for such centers in these hospitals. Dr. Bourke appeared sympathetic to the State Society's idea of a local experiment of setting up a diagnostic center in such a section as the Delaware-Scholastic area.

Much confusion still exists as to what a health center should be. The broader concept of it assumes such a facility to be prepared to house and furnish all technical services. This would include specialist and consultant services. Dr. Godfrey could not visualize these health centers without adequate provision for consultation service which would, of course, mean services of specialists. They stressed, also, the possible political and legal difficulties which would have to be overcome, and believed that great pains would have to be exercised to secure the full consent and cooperation of all local boards and local officials in the interested areas.

Your subcommittee brought out emphatically that whatever plans are being considered for any locality, we must know, first, what the professional groups think about it, second, what the local sentiment is toward such a "center", third, specific details of any facilities contemplated or needed, fourth, how to finance these schemes, fifth, that such centers at all times have competent professional guidance.

It was the consensus of everyone that more exploratory work would be necessary. Furthermore, it was not clear to these officials how the State could assist. The discussion also brought out the fact that there were many other difficulties to be met, especially in the municipalities which operate under their own laws.

The organization of district councils to work with local agencies to cope more promptly with important or urgent matters which might arise was suggested. Such councils, it was felt, might serve a purpose similar to that of the Coordinating Council of the Five County Medical Societies of Greater New York, and thus protect medicine's rights and interests. These councils would clear through some kind of central planning committee which, again, could be integrated into the general regional planning program.

Much, if not all, of the State planning appears to depend on the enactment into law by Congress of the Hill-Burton Bill S-191. At the time of the writing of this report (April, 1946) the status of this legislation is most dubious. While it has already passed the Senate, and though the House Committee has held hearings upon it, its passage by the House is by no means certain.

There was no provision in the bill which passed the Senate for financing the operation or maintenance of the hospital. Assuming that this bill fails of enactment, it would seem probable that the State planning would have to be revised, and necessarily would fall back on State aid programs adopted many years ago of appropriating monies for the development of hospitals and related facilities. Such appropriations would have to be granted by the State Legislature.

We expressed the hope that the Medical Society of the State of New York might be able to implement a diagnostic center as an experiment in one of the areas needing such diagnostic aid, with the State assisting, perhaps, in a financial way. It was sug-

gested that this might be done under the provisions of an old existing law.

The comprehensive report of the Committee on Rural Medical Service of the American Medical Association has been reprinted in full and appears in the minutes of the December 12, 1945, meeting of the Planning Committee. It is too long to incorporate in this report. It presents a detailed survey of the medical and health problems involved in the rural areas throughout the various states. It discusses problems which are comparable to those existing in many of our upstate rural communities and should be of considerable assistance in guiding our thinking and planning.

Regional conferences under the auspices of the Joint Hospital Board of the New York State Post-war Public Works Planning Commission have already started. The first one has been held recently in the Albany area and the second one for the New York area is scheduled at an early date. To these meetings have been invited representatives of the New York State Hospital Association and its local councils, trustees and superintendents of hospitals in the region, representatives of the medical and nursing professions, the deans of the medical schools and representatives of public health and social welfare, agriculture, labor, and industry. A 22-page inventory is being circulated among hospitals in the area which is to be filled out and returned as early as possible. After all these reports have been received, they will then start their planning. They ask particularly at this time that no region start either to expand its hospitals or build new hospitals or anything of that nature. While this organization and planning is contingent upon the passage of the Hill-Burton Bill, nevertheless, if it fails of enactment, it is probable that bills will be introduced into the next legislature to implement their program on State funds if Federal funds are not available.

The foregoing résumé will serve to inform you, at least superficially, of the difficulties encountered where State Society thinking and planning within the framework of our present medical practice clashes with the ideas and plans of health and related government authorities. Both seek the same objectives. How to achieve these objectives and correlate conflicting ideologies is a dilemma. The State Society desires competent professional guidance for such centers and control retained by the doctors. The administration and financing of these centers, based on this principle, with at least partial State aid and cooperation, poses our most vexing problem.

The State Society is anxious to assist in the working out of plans for the improved medical care contemplated for rural communities. The whole subject of centers for diagnostic aid will entail conferences with local professional and lay agencies in the communities concerned and further contacts with state officials and it may have to await the outcome of both the State's survey of hospital facilities and of the pending legislation. Your Committee proposes to hold such conferences, particularly with representatives from the areas recommended for experiment in the Sullivan Committee report. We cannot move in the development of any plan with preciseness or sureness until all these facts have been ascertained.

It was the sense of the Committee after considered deliberation to make no recommendations on this subject at this time, rather to bring before the House for their information these points brought out in our discussions, what the difficulties have been and why the directive to establish one or two experimental centers has not been put into effect.

Group Medical Practice—Your Planning Committee in its annual report in October, 1945, made general reference to the problem of group practice. Since that time, interest in this phase of medical practice continues to mount. This method of practice forms an integral part of at least one contemplated medical prepayment insurance plan in metropolitan New York. It intrigues other medical groups, including our large medical schools and teaching centers. Young physicians are now coming out of the military services in increasing numbers, and some are finding it difficult to enter private practice for the first time and others to renew their former practices. Many of these men are profoundly interested in group practice.

A special subcommittee of the Planning Committee under the chairmanship of Dr. Di Natale, has given considerable study to the over-all problem of group practice. There has been marked advance in the character of the practice of medicine in the past twenty-five years, and what originally started as a trend toward cooperative effort in rendering medical care has now become a major feature and probably will become increasingly so within the next few years. The impetus given public opinion along this line by developments coming out of the war effort has made it imperative for the medical profession to develop new methods of distributing medical care.

Experience in the past where group practice has succeeded has shown that in any group one member has been in absolute control and has demonstrated the ability to assemble a competent group around him which has submitted to his authority. Furthermore, such groups have maintained the highest standards of medical ethics. The principle must be definitely accepted, namely, that the ethics of a group must be the same as the ethics of an individual in the practice of medicine. That is one thing that must be insisted upon, because the relationship of a group to other practitioners is very important.

The advocates of group practice point out that it furnishes the answer to many of the personal problems of everyday working conditions, time for rest and relaxation, vacations, periods of study and investigation, and time for postgraduate work, social and financial safeguards, it prevents duplication of overhead and provides the public with more adequate medical care by having a doctor available at all times and having readily available consultation services.

It is true that a patient very frequently will get more laboratory procedures and more consultations than may be needed. Fifteen per cent would seem to be an ample estimate of those patients seen daily who require the broader and more specialized laboratory and diagnostic procedures. Medicine practiced in many groups is inferior to medicine practiced by many men outside of groups. Many groups have broken up because of the petty jealousies created where perhaps one man brought in more income than another member of the group. A physician must be built for group practice. There may be a tendency to exploit younger physicians and some feel that there is loss of individuality when one is part of a group.

Group practice must be a partnership in the sense that everyone who joins the effort must be willing to subordinate his own personal desires to the work of the group as a whole.

Group practice tends to make for impersonal medicine. This is the very thing that the American people have been sensitized against. We stress the doctor-patient relationship. Some one person in the group, usually the internist, must be designated to

be the one responsible for the assembling of all data and transmitting these findings to the patient. In other words, the patient must have his own doctor in the group.

There are many questions that involve the combination of independent group practice and group payment. Recognition within the group must be given to such matters as adequate income for each member and reasonable stable tenure as a member of the group. The method of compensation must be carefully worked out. These represent only a few of the administrative problems that must be met.

The Coordinating Council of the Five County Medical Societies of Greater New York recently has set up a set of principles for group practice. These principles are incorporated in this report as *Appendix B*. They constitute a reasonably sound framework which should guide the organization of any group. The Planning Committee approves these aforementioned principles. Organized medicine is frequently criticized as opposing group practice. We should like to correct that impression. Medicine does approve group practice, but insists it should be conducted on a highly ethical plane and should conform to such basic principles as those enumerated in *Appendix B*.

The Committee feels, also, that the formation of any group is entirely a local problem and should adapt itself to the situation in each community. We cannot recommend at this time any particular type of group practice.

Compulsory Sickness Insurance—On November 19, 1945, the country was aroused by the presentation to Congress by the President of the most comprehensive and revolutionary proposals for a national health program ever placed before this body. On April 2 last, Senator Taft, at the opening of the hearings on the current Wagner-Murray-Dingell Bill, S-1600, introduced on the same day as the President's program was announced, called this measure "the most socialistic legislation ever introduced to the Congress."

Collectivism raises its ugly head more ominously than ever. To our mind, trends toward national socialism appear to be more evident daily. Let us remind ourselves that this movement for the placement of American medicine under the control of the Federal government through a system of Federal compulsory sickness insurance is an entering wedge toward regimentation of banks, insurance companies, utilities, transportation, industry, and, perhaps, even labor itself.

Provisions 1, 2, 3, and 5 of the President's program, with certain constructive amendments, organized medicine will support. It is Section 4 on this program to be implemented by the current Wagner-Murray-Dingell Bill to which we are unalterably opposed. Title 2 of the National Health Act of 1945, carrying the caption "Prepaid Personal Health Service Benefits," is not materially dissimilar, except for provisions for financing the program, from the comparable sections contained in S-1050. The new bill imposes no taxes. The program it contemplates will be financed, at least as far as the present provisions of the bill are concerned, by appropriations from the general fund.

Nothing has occurred since the previous report of this committee to alter our stand on compulsory sickness insurance.

The President in his Health Message and the new Wagner-Murray-Dingell Bill have both called for compulsory sickness insurance, and both the President and authors of this bill insist that the program is not socialized medicine.

Careful examination of the proposal, however, indicates that it is just that. The program calls eventually for compulsory insurance to cover practically the whole population. It provides for lay administration of medicine, in that in the last analysis the Federal Security Administrator and the Social Security Board are the regulating agents. Once again, the Surgeon General of the United States Public Health Service is designated as the Administrator of the program, but he is subject to the above agencies. The so-called Advisory Board is appointed by him and it has no authority.

The free choice of physician provided in the program is no free choice at all. It offers free choice only if the physicians take part in the scheme. It is free choice if he takes part, only if his panel is not filled. If the majority of the physicians in an area elect to be paid on a capitation basis, it can be operated only by assigning people in a certain district to a certain physician. Here, again, there can be no free choice.

The statement that the physicians will decide how they will be paid is again an inaccurate statement. The majority of the physicians may decide. The minority, no matter how large that minority must abide by the will of the majority.

The patient has no voice whatever in the selection of a specialist. Whether or not he may have one is decided by a government agency.

Regulations governing patients, hospitals, and physicians are promulgated by the Administrator—again a case of rule by administrative law.

A tremendous bureaucracy will be set up with its consequent red tape and inefficiency. There is no premium on good medical care, only on quantity. Medical care will deteriorate. The Government collects money, pays it out, and prescribes the regulations under which physicians, patients, and hospitals operate. Whether it should be termed 'socialized medicine' or 'political medicine' is unimportant. It is regimentation.

The costs of the program are cleverly avoided in the latest version of the Wagner-Murray-Dingell Bill. The President suggested a four per cent payroll tax up to \$3,600. The previous Wagner-Murray-Dingell Bill called for an 8 per cent payroll tax, 4 per cent from the employer and 4 per cent from the employee and a 5 per cent tax from the self-employed up to \$3,600 income. Of this, 3 per cent of the 8 per cent was to be devoted to medical care. Under either suggestion it calls for expenditures of billions of dollars with no guarantee of efficient disbursement for good medical care.

The Committee disapproves any form of compulsory sickness insurance. The needs of the country can be met by an improvement in the economic status of certain groups, by extending public health and preventive medicine facilities, by increasing maternal and child health where needed, by increasing hospital and diagnostic facilities as needed, by the use of Federal funds to provide or extend these facilities where the state or local community cannot afford to provide them, the local communities to have supervision over the agencies created and finally by extending the prepayment of both hospital and medical care costs on a voluntary insurance basis.

The American Medical Association in 1945 adopted a 14-point program for improving the medical care situation in the United States. In 1946 it extended and clarified that program by the adoption of a ten point Health Program. (See Appendix C)

Your Planning Committee again reaffirms the Society's previous stand against compulsory sickness

insurance in general, and disapproval of the current Wagner-Murray-Dingell Bill, S-1600. We recommend the endorsement of this ten point program of the American Medical Association by the House of Delegates.

Public Relations and Medical Publicity—Apropos of the above statement on the Wagner-Murray-Dingell Bill, it seems most timely to the Committee that the distribution of a brochure or some other type of leaflet for public consumption, presenting clearly our points of view and the stand of the Medical Society of the State of New York, should be accomplished as promptly as possible. We continually tell the doctors all this but the public has had only one side of this most controversial subject. We should like, for the information of the Reference Committee and the House, briefly to summarize some of the discussion that the Committee has held regarding suitable publicity for these important matters.

Mr Dwight Anderson, our Public Relations Officer, attended the last meeting of the Planning Committee and he was in thorough accord with the idea and spoke frankly and tersely in favor of it. To quote him "I thought this statement on the Wagner-Murray-Dingell Bill was a perfect brief indictment of this measure which could be understood by anybody." He then expanded his ideas in some detail and suggested methods for implementing this project.

The Committee was privileged to have present at its April meeting Dr Joseph Lawrence, our former Executive Officer and now in charge of the Washington office of the Council on Medical Service and Public Relations of the American Medical Association. He contributed a number of practical suggestions which tended to clarify our thinking, and gave us the benefit of some of his experiences at the national level.

He expressed the opinion that "the sentiment is pretty general over the United States that people do not want things thrust upon them and especially not when they are thrust on them because it is said they could not themselves provide them. They would much rather try to provide for themselves. We particularly hear that is so through the Farm Bureau groups and other groups of that kind from the grass roots. They would rather have what they can provide for themselves than to take these grand conditions or things that are going to be thrust upon them." This was also the principle that actuated the Kelllogg Foundation in their collaboration in the rural hospital programs so successfully accomplished in Michigan and to which we referred at some length in the 1945 report. Their experience taught them that local professional and lay people concerned with social conditions had definite ideas as to what their problems were and what they wanted to do about them. They were more or less alive to their responsibilities and were equally cognizant of their deficiencies in training to meet their community obligations. They began, therefore, with the problems which the people recognized, rather than with those that someone else thought they ought to see. This meant education, and there was elaborated a definite method by which these people could study their problems, exchange experience, talk with others who had solved similar problems successfully and find their own answers through cooperative community action. Local opposition to arbitrary placement of hospitals or other facilities which run counter to their own ideas and plans will be stubborn.

The striking success of the State Society's anti-division campaign proved beyond question the

effectiveness of a well-organized and well-conceived public relations job. Your Planning Committee has in mind some sort of similar program on matters of general health, the practice of medicine, and more particularly at this time, on the Wagner-Murray-Dingell Bill. More and more questions are being brought to Congressmen and state legislators by their constituents, many of them of varied scope, and while often they represent generalizations they are based on specific instances in their own communities.

Medical publicity is an essential part of public relations. We need at the present time some way of conveying our programs to the people who would be friendly to us. These things must be done in a popular way, that is, written up in a popular form so that the people are ready to read them. It may seem to some of you that this is not dignified nor seemly, but we have now reached the point where we have to rely on public support. Government bureaus are sending out pamphlets all the time, stressing their own points of view, never ours. For example, note the booklets from the Department of Agriculture, from the Children's Bureau, from the Public Health Service, etc., which may be had just by writing in for them. We ought to have some ourselves to counteract the pernicious propaganda they are spreading. We should make more use of our statistics, interpreting them in our language.

We are in favor of an adult education program for all of the people in the community who have anything to do with health, education, recreation, or welfare.

We are aware that to make available to the laity material in a form which they will understand will, of course, create additional expense for the Public Relations Bureau. The bureau cannot do these things without additional funds, yet it is highly important that something of this sort be done. Such education of the public as will bring to them the truth about many of these matters and will clearly show what we are trying to do in the public interest should be heartily endorsed and encouraged.

We recommend to the House of Delegates that they make available for distribution to the laity educational or other suitable material on pertinent medical problems, and, specifically, the Society's position on the Wagner-Murray-Dingell Bills, and that the House instruct the Public Relations Bureau to prepare such material for the education of the public and we further recommend that the House invite the attention of the Council and the Board of Trustees to this proposal, reminding them that the Public Relations Bureau cannot do this without the appropriation of additional funds, to the end that this program can be implemented with the least possible delay.

Industrial Medicine—Your Planning Committee is cognizant of the increasing importance of Industrial Medicine and its relation to the practice of medicine. We feel that organized medicine should be very active in this field. The individual medical practitioner should be reminded that he is potentially an industrial physician, that he should evince more interest in the study of the whole health problem concerning the different diseases peculiar to industry.

We should restate here the tremendous amount of work and planning that the American Medical Association has done on this subject through its Council on Industrial Health. We would reiterate the following from last year's report.

1 Your Planning Committee again invites

attention to the Industrial Medicine program of the American Medical Association for state and county societies.

2 We would recommend to the Postwar Planning Committees of the state and county societies that they bring to the attention of physicians returning from the military services the facilities offered in the field of industrial medicine.

3 We would respectfully suggest to those responsible for undergraduate medical education that those diseases and afflictions peculiar to industry be given adequate recognition in their teaching program.

4 We recommend that the Council give this program its serious attention and urge upon the various county societies their cooperation in carrying out this program.

Miscellaneous Topics—As a result of studies and recommendations of the Planning Committee during the past two years, the State Society has set up its Bureau of Medical Care Insurance, with Mr. George P. Farrell as its director. It also was instrumental in causing to be established the Special Committee on the Relationship of the Hospitals to the Practice of Medicine, of which Dr. Carlton Wertz is chairman. We have directed the policy of the Society to a large degree in its pronouncements against the compulsory sickness insurance program. Your Committee has also devoted considerable time and study to such subjects as the nursing problem, medical education and licensure, physical medicine, and the problem of the care of the chronically ill.

Nothing has occurred since the last annual report of this Committee to add substantially to our knowledge of these topics. We would refer those interested to the last two annual reports of the Committee.

As many of the studies now on the agenda of your Planning Committee are continuing programs, we respectfully petition the House that the life of this Committee be extended and that the House authorize the reappointment of this Committee on the same basis as previously provided, and that in addition the Committee be authorized to invite members of Government or other agencies concerned with health problems to sit with the Committee from time to time whenever problems pertaining to their departments arise.

Appendix A

New York State Plan for Survey of Hospital Facilities and Program for Regional Hospital Planning for Postwar Hospital Construction and

New York State Postwar Public Works Planning Commission Joint Hospital Board

ROBERT T. LANDSDALE, *Chairman*
(State Office Building, Albany, New York)

February 15, 1946

Plan for Survey of Hospital Facilities and Regional Planning for Postwar Hospital Construction

In order to meet the requirements of the proposed Hill-Burton Bill, S-191, and to more efficiently plan for postwar hospital construction, the Postwar Public Works Planning Commission, through its Joint Hospital Board, is inaugurating an intensive survey of existing facilities and an appraisal of needed hospital construction.

To secure the assistance and advice available through individuals and groups responsible for the construction, operation, and use of hospitals, the work is to be approached on a regional basis.

For the purpose of facilitating the completion of the survey and for postwar hospital construction planning, the State will be provisionally divided into hospital regions and primary and secondary service districts within each region.

Representatives from each of the primary and secondary hospital service districts will be chosen at regional meetings to which will be invited all hospital administrators and others with interest and responsibility for hospital care. With the hospital service district representatives as a nucleus of the membership, Regional Hospital Planning Councils will be established in each of the regions.

This joint local and state action should result in an orderly and intelligent solution to the problem of meeting the needs for additional hospital and related facilities for the care of the sick.

The following is a résumé of the plan adopted by the Joint Hospital Board.

1 Purpose of the Joint Hospital Board of the New York State Postwar Public Works Planning Commission

1. To inventory the existing hospitals of every character.

2. To survey the need for the construction of hospitals.

3. To develop programs for the construction of such public and nonprofit hospitals as will afford in conjunction with existing facilities, the necessary physical facilities for furnishing adequate hospital clinic and similar service to all of the people.

II State Organization

1. The Governor has designated the New York State Postwar Public Works Planning Commission to act as the sole state agency. The Joint Hospital Board, consisting of the Commissioners of Health, Mental Hygiene and Social Welfare, is to assist and cooperate.

2. A State Advisory Council to the Postwar Public Works Planning Commission is being appointed and will be under the chairmanship of Assemblyman Lee B. Mailler, who has been designated by the Governor as Advisor to the Joint Hospital Board.

III Regional Hospital Plan for the State

(A) Purpose

1. To provide a decentralized method of completing the survey of hospitals.

2. To make available the results of the Survey to the local individuals and groups with responsibilities for hospital care.

3. To provide, through Regional Hospital Planning Councils, appraisals of existing facilities for hospital care.

4. To secure regional recommendations regarding the need for additional facilities.

5. To assist hospitals in their plans for expansion by coordinated regional hospital planning and to enhance working relationships between individual hospitals and services.

6. To take advantage of the position of the four upstate medical teaching institutions for improving facilities for undergraduate and postgraduate medical public health, and nursing education and for the provision of an adequate distribution of medical services requiring specialty training.

7. Through the work of the regional Hospital Planning Councils to assist the Joint Hospital

Board and the New York State Postwar Public Works Planning Commission in meeting its responsibilities.

(B) Organization

1. The provisional division of the state (exclusive of New York City) into four major hospital regions and two smaller regions for the extra metropolitan area.

2. The provisional division of each region into primary and secondary hospital service districts.

3. The Hospital Council of Greater New York, with its Postwar Hospital Planning Committee, and with the cooperation of the Greater New York Hospital Association, will act as the clearing house for New York City.

4. Establishment of Regional Hospital Planning Councils in each of the upstate regions. Regional Hospital Planning Councils should be composed of the hospital administrators, acting as representatives of the primary and secondary hospital districts, representatives of the New York State Hospital Association and its local hospital councils, boards of trustees of hospitals, representatives of the medical and nursing professions, the medical school and representatives of public health, public welfare, agriculture, labor and industry.

5. The appointment of a competent hospital administrator on a full or part-time basis, for a temporary period, for each of the Regional Planning Councils to act as secretary to Regional Planning Councils and to assist in completing the hospital inventory schedules. State funds will be available to cover this service and travel expenses.

6. One local hospital administrator from each of the hospital districts will be asked to volunteer as the representative of his hospital service district and to assist the local hospitals in completing the inventory schedules. This will mean that no one volunteer would be responsible for more than 10 or 12 institutions. These district representatives will receive instruction concerning the interpretation of the inventory schedules from the secretaries of the Regional Hospital Planning Councils and the Joint Hospital Board.

(C) Operation of the Plan

1. The 22-page inventory schedule will be sent directly to each of the hospitals of more than 25-bed capacity.

Hospitals of less than 25 beds will receive a short 9-page inventory schedule in duplicate.

Two copies of the schedule are to be completed, the hospital will retain one for its own use, the second copy will be turned over to the representative of the hospital service district, who will review it with the hospital superintendent, if necessary.

The secretaries to the Regional Planning Councils will meet with the hospital service district representative, check the schedules for the several hospitals within the district, and forward them to the Joint Hospital Board at Albany.

The Hospital Council of Greater New York will distribute the inventory schedules and complete the contacts with hospitals in New York City. Inventory schedules for maternity homes, nursing homes, and related institutions will be completed with the assistance of the several state departments concerned.

2. The completed inventory schedules will be forwarded to Chicago where the Commission on Hospital Care has volunteered to perform the coding, preparation of punch cards, and preliminary tabulations.

The statistical tabulations and completed inventory schedules and punch cards will then be returned for appraisal and planning uses in New York State

3 Shortly after the inventory schedules have been mailed to the hospitals, organizational meetings will be held in each of the regions. To these meetings will be invited representatives of the New York State Hospital Association and its local Councils, trustees, and superintendents of hospitals in the regions, representatives of the medical and nursing professions, the Deans of the Medical Schools and representatives of public Health and social welfare, agriculture, labor, and industry

At the regional organization meetings, the Regional Hospital Planning Councils are to be established, a secretary appointed, and the survey inaugurated. Each Regional Hospital Planning Council should be composed of the hospital service district representatives and representatives of the groups enumerated above

4 Subsequent meetings of the Regional Planning Councils are to be arranged through its chairman, as necessary and by request of the Joint Hospital Board

The Joint Hospital Board will make available to each of the Regional Hospital Planning Councils information secured through the survey and data pertaining to the social and economic factors in hospital planning

Appendix B

Principles for Group Practice Approved by the Coordinating Council of the Five-County Medical Societies, November 1, 1945

1 A medical group shall be defined as a number of licensed physicians engaged in the practice of medicine in a common organization, qualified to provide complete medical care as required, whether this care be in the patient's home, physician's office, or in the hospital

2 All features of medical service in any method of medical practice shall be under the control of the medical profession

3 Physicians may work whole or part-time for an approved group. Where there is only a small demand for a specialist's services, he may serve two or more approved groups

4 Patients may obtain the services of approved groups according to one of two methods

- (a) Through an insurance plan approved by the county medical society in which the group operates
- (b) By payment of fees for services. In the latter case, such fees shall not be lower than the established Workmen's Compensation Schedule fees

5 No third party may be permitted to come between the patient and his physician in any medical relation. All responsibility for the character of medical service must be borne by the medical profession.

6 A patient shall be free to choose any group or individual practitioner of medicine

7 Any method of rendering medical service must retain a permanent, confidential relationship between the patient and a family physician, either as an individual practitioner of medicine or a member of a group

8 Medical care shall be under medical control. Hospital services shall be controlled separately

9 The chief executive officer in charge of ad-

ministration of the medical policy of an approved group shall be a physician

10 The organization and operation of all approved medical groups shall emphasize preventive medicine.

11 Physicians serving in approved groups are to be allowed to assume only responsibilities in the care of patients for which they are qualified according to standards established by the county medical societies

12 Staff conferences of approved groups shall be held at regular intervals

13 No approved group shall provide for payment of commissions or fees to any one for referring patients to the group

14 Chapter II, Section 4, of the Principles of Medical Ethics of the American Medical Association, states "Solicitation of patients by physicians as individuals, or collectively in groups by whatsoever name these be called, or by institutions or organizations, whether by circulars or advertisements, or by personal communications, is unprofessional"

It is equally unprofessional to procure patients by indirection through solicitors or agents of any kind or by indirect advertisement, or by furnishing or inspiring newspaper or magazine comments concerning cases in which the physician (or group) has been or is concerned. This principle shall apply to any approved group

15 Income which accrues from the group practice of medicine shall, after necessary expenses are paid, be paid to physicians working in the group and not to any other organization or individual

The following has been suggested as an addition by the Queens County Medical Society: Groups having members who are not members of county medical societies may secure the approval of the county society upon their application for such approval.

Appendix C

National Health Program of the American Medical Association

(Promulgated February 23, 1946, by the Board of Trustees of the American Medical Association)

The following is the restatement of the 14-point program of the American Medical Association adopted by the Board of Trustees on February 23, 1946, which clarifies still further the position of the American Medical Association on some of these points, and brings into the program more definitely maternal and child welfare, medical research, medical care of the veteran, and the part to be played by the voluntary health agencies

1 The American Medical Association urges a minimum standard of nutrition, housing, clothing, and recreation as fundamental to good health and as an objective to be achieved in any suitable health program. The responsibility for attainment of this standard should be placed as far as possible on the individual but the application of community effort, compatible with the maintenance of free enterprise, should be encouraged with governmental aid where needed

2 The provision of preventive medical service through professionally competent health departments with sufficient staff and equipment to meet community needs is recognized as essential in a health program. The principle of Federal aid through provision of funds or personnel is recognized with the understanding that local areas shall control their own agencies as has been established in the field of education. Health departments should not assume the care of the sick as a function, since ad-

ministration of medical care under such auspices tends to a deterioration in the quality of the service rendered. Medical care to those unable to provide for themselves is best administered by local and private agencies with the aid of public funds when needed. This program for national health should include the administration of medical care, including hospitalization to all those needing it but unable to pay, such medical care to be provided preferably by a physician of the patient's choice with funds provided by local agencies with the assistance of Federal funds when necessary.

3 The procedures established by modern medicine for advice to the prospective mother and for adequate care in childbirth should be made available to all at a price that they can afford to pay. When local funds are lacking for the care of those unable to pay, Federal aid should be supplied with the funds administered through local or state agencies.

4 The child should have throughout infancy proper attention, including scientific nutrition, immunization against preventable disease, and other services included in infant welfare. Such services are best supplied by personal contact between the mother and the individual physician, but may be provided through child care and infant welfare stations administered under local auspices with support by tax funds whenever the need can be shown.

5 The provision of health and diagnostic centers and hospitals necessary to community needs is an essential of good medical care. Such facilities are preferably supplied by local agencies, including the community, church, and trade agencies which have been responsible for the fine development of facilities for medical care in most American communities up to this time. Where such facilities are unavailable and cannot be supplied through local or state agencies, the Federal government may aid, preferably under a plan which requires that the need be shown and that the community prove its ability to maintain such institutions once they are established (Hill-Burton Bill).

6 A program for medical care within the American system of individual initiative and freedom of enterprise includes the establishment of voluntary nonprofit prepayment plans for the costs of hospitalization (such as the Blue Cross plans) and voluntary nonprofit prepayment plans for medical care (such as those developed by many state and county medical societies). The principles of such insurance contracts should be acceptable to the Council on Medical Service of the American Medical Association and to the authoritative bodies of state medical associations. The evolution of voluntary prepayment insurance against the costs of sickness admits also the utilization of private sickness insurance plans which comply with state regulatory statutes and meet the standards of the Council on Medical Service of the American Medical Association.

7 A program for national health should include the administration of medical care, including hospitalization, to all veterans, such medical care to be provided preferably by a physician of the veteran's choice, with payment by the Veterans Administration through a plan mutually agreed on between the medical association and the Veterans Administration.

8 Research for the advancement of medical science is fundamental in any national health program. The inclusion of medical research in a National Science Foundation such as proposed in pending Federal legislation, is endorsed.

9 The services rendered by volunteer philanthropic health agencies, such as the American Cancer Society, the National Tuberculosis Association, the National Foundation for Infantile Paralysis, Inc., and by philanthropic agencies, such as the Commonwealth Fund and the Rockefeller Foundation and similar bodies, have been of vast benefit to the American people and are a natural outgrowth of the system of free enterprise and democracy that prevail in the United States. Their participation in a national health program should be encouraged, and the growth of such agencies when properly administered should be commended.

10 Fundamental to the promotion of the public health and elevation of illness are widespread education in the field of health and the widest possible dissemination of information regarding the prevention of disease and its treatment by authoritative agencies. Health education should be considered a necessary function of all departments of public health, medical associations, and school authorities.

Section 12 (See 55)

Supplementary Report of the President

SPEAKER BAUER Dr Landy and Dr Azzari, will you form a committee of two to escort the President of the Medical Society of the State of New York to the platform?

(The delegates arose and applauded as Drs. Joseph A. Landy and Renato J. Azzari, of Bronx County escorted Dr. Edward R. Cuniffle to the platform.)

SPEAKER BAUER. Gentlemen, of the last meeting of the House of Delegates, I remarked that so far as I knew this was the first instance in which a President of the Medical Society has been president during two sessions of the House of Delegates. That was due to the fact that our session of 1945 was postponed from its usual time. Therefore, Dr. Cuniffle, to show you how much we think of you and regret your departing we are tolerating you twice. Gentlemen, the President of the Society, Dr. Cuniffle (Applause).

PRESIDENT CUNIFFLE That is a very nice introduction. Thank you very much, Mr. Speaker!

Members of the House of Delegates, sometimes it is hard to start something over again, as you know I asked how to begin a speech one time on the Wagner-Murray-Dingell Bill. It had been talked and mulled over so much, that I was at a loss how to start. The suggestion was, "Well you might tell them a story."

In those days of atomic bombs and various instruments of warfare that have been devised and developed and will destroy practically everything if used there was a bomb dropped over every city, county, state, and hamlet of the world. The powers got double-crossing each other, and they finally got touch buttons to set off these bombs, and everything was destroyed. The earth was nothing but a bare globe. There was not a house or building in it. There was not a tree, there was not a bird. Man was destroyed. Finally out in the Pacific on an island which was devastated, from a cave came a little monkey. He looked around, and could not see a tree or another animal. As he was thinking about it and studying the situation, a female monkey walked out, and he turned around and looked at her and said, "Do we have to start this damned thing all over again?" (Laughter). That is probably the way this shapes up in Speaker Bauer's mind. I have to start this damned thing all over again.

I am very fortunate to be allowed to speak again to this body. This privilege is really a very great honor, for not often does one have the opportunity to address the 140th Annual Meeting of a medical society. It is well to remember that this Society was organized to increase the scientific knowledge of its members, to devise ways and means of achieving better protection of the health of the people of our State and improvement in the quality and delivery of medical care to its citizens. These ideals have been eagerly followed as exemplified by the actions of every meeting of this House, and I am perfectly sure that the present meeting will be no exception.

In my report of the activities of the State Society, I discussed the very vigorous campaign which was waged against the proposed so-called antivivisection bill, calling attention to the good work done by our Committee on Publicity, a work which cannot be praised too highly. This campaign led to the promotion of a national society, called the Friends of Medical Research, with a branch in New York State, under the aegis of the Medical Society of the State of New York and the New York Academy of Medicine. I am not at all sure that this is the best way in which to meet the threat that will again be presented at the next meeting of the Legislature. The national organization is very valuable in the protection that it may give to some of the weak states that are unable to properly protect themselves and, also, in providing scientific men to aid in the educational part of the work. However, I am quite certain that it would be unable to protect our State against the danger of having such a bill being enacted into law. Nor do I believe that an organization in New York City can afford us sufficient protection. It would seem to me that a committee in New York City with only one member from outside the City, no matter how valuable he may be, would present a very weak front for such an important defense. I think it is readily admitted that this is a matter for the entire State. Legislative bills are presented to a legislature composed of representatives elected from every portion of the State. It will be necessary to have men in every county who will discuss this matter and convince the legislators that such an act would weaken and destroy the progress of medicine in our State. It seems to me the part of wisdom for our Society to keep the committees already appointed in several counties and to organize them in counties which have none at present. This framework of committees under the direction of the Council Committee should lead the campaign against such legislation and, of course, accept and encourage the help of any other organization interested.

At the last meeting of the House of Delegates in October, a plea for a universal insurance contract for the State, including surgical, obstetric, and medical care for in-hospital patients was presented to this body. The policy was to be accepted by the different insurance groups of our State. There seems to have been some misunderstanding in what was intended by this policy. It was certainly not intended to interfere in any way with the local policies made to suit the conditions of that locality. The intention was for the medical plans to retain their individual policies but to have one contract that was universal and would be accepted throughout the state. I still believe that this is not only possible, but that it is absolutely necessary if we are to accomplish what we are trying to do with voluntary medical insurance. I trust that this

matter will not be discarded but that the committee having this work in hand will be continued until further study finally decides the question.

The activities toward providing the means of administering the program of the Veterans Administration in regard to the treatment by private physicians of veterans suffering from service-connected disabilities has progressed very favorably. The committee has had several meetings under the chairmanship of Dr. Hale. A fee schedule has been prepared and is ready for presentation to Colonel Harding. Funds have been appropriated by the Board of Trustees and a certificate of incorporation and bylaws of a membership corporation to be formed by the Medical Society of the State of New York for the purpose of dealing with the Veterans Administration has been prepared. The objects and purposes, for which this corporation is formed, are to be promoted, transacted, and earned on without pecuniary profit. The territory in which its operations are principally to be conducted is the State of New York and its principal office is to be located in the Borough of Manhattan, City of New York, State of New York. The directors have been appointed and the certificate will be completed during the next few days. It is well for me to advise the House that it is a vast undertaking that will be very difficult to carry on successfully but that must be done, not alone to show our patriotic feeling of loyalty and gratitude to the veterans, but, also, to prove that our Society can direct and furnish medical care throughout the entire State under this program.

During the past session of our legislature, a large amount of money was appropriated and an extensive program outlined for the construction of county health units throughout the State, to be supervised by fulltime men, and a vigorous attempt was made to completely banish tuberculous disease. I am sure the Society approves very much this plan of improving medical conditions in our State and will earnestly support it.

I would be remiss at this time if I did not call your attention to that part of the report which contains the discussion of the Governor's Commission for the Study of Medical Care. It is well to note the men who signed the majority report, which is a practical endorsement not alone of our criticism of compulsory health insurance but is, also, an approval of the many changes we have been advocating for the past several years. It is well to bear in mind the fact that many matters approved by our Society as being worthwhile are not always adopted and, consequently, are not enacted into law. I must also say a word of praise for the two men of our Society, Dr. Harold Brown, of Buffalo and Dr. Andrew E. Eggston, of Westchester County, who were appointed to the Commission after it was in existence one year, for the very able way in which they represented our Society and the amount of work they were compelled to do on account of their late appointment. I cannot emphasize that too strongly because I know that they completely dominated the Committee with the facts they presented after their appointment, and they deserve a great deal of credit.

After a number of years a society having a great many committees seems to get into trouble with the misunderstanding consequent upon an overlapping of these committees with reduplication of work. Several complaints have been brought to me of this condition in this Society at the present time, and I would like to petition the House of Delegates to

request the Council to appoint a committee to study the system of committees and if it is found necessary, to publish any proposed amendments to the Bylaws in time so they may be acted upon next year.

I want to extend greetings to the incoming President with my very best wishes and forecast for him a very successful administration. I would like to call attention to the very earnest and extremely valuable work of the past-presidents who are among the most active of our members, some of them past-presidents for many years. Such an example would urge us to do likewise and continue to work actively in the affairs of the Society. I pledge my assistance I can give to the incoming president and hope that I can be as valuable to him as the immediate Past-President Dr. Bruckus has been to me.

I have enjoyed very much my year as your President. In spite of the fact that hotel accommodations were not always available and traveling conditions presented some difficulties. However I have been amply repaid for any inconvenience by the pleasure of meeting so many members of our Society. I have a very high opinion—much greater than ever before—of the New York State doctor of medicine. I am thinking not only of his scientific ability but, also, of his sterling character. I have received the most sincere cooperation and assistance from the members of all the committees and of course, have been guided, advised and ruled by the Council whose loyalty and helpfulness I appreciate more than I can say. I am sure that no organization exists with higher ideals and ethics, which means honesty and uprightness in dealing with all.

Thank you very much! (Applause)

SPEAKER BAUER Thank you, Dr. Cunniff! I hope you are going to remain on the platform throughout the session.

The remarks of the President are referred to the Reference Committee on the Report of the President.

Section 13 (See 55)

Report of the President-Elect

SPEAKER BAUER Dr. McKendree and Dr. Golly, will you form a committee of two to escort the President-Elect of the Medical Society of the State of New York to the platform?

(The delegates arose and applauded as Drs. Oswald J. McKendree and Bradford F. Golly of Oneida County, escorted Dr. William Hale to the platform.)

SPEAKER BAUER Members of the House, I feel that Dr. Hale is really entitled to two introductions. I say that for this reason. It has always been customary after a man has been elected President-Elect to escort him to the platform and present him to the House. Last year you will recall that our closing session was pretty hectic. In fact, it was so hectic that we did not even have time for one report which had to be read by title only. Therefore, there was no opportunity to present him at that time. I regret that so I am going to introduce him twice now, once for last October and again now, gentlemen, the President-Elect, Dr. William Hale. (Applause)

PRESIDENT-ELECT HALE Mr. Speaker thanks for both introductions.

One cannot be in this House very long without appreciating that there is a tremendous amount of business being transacted. I am reminded of a story that was told by one of the visitors at the House of Delegates meeting of the American Medical Association. He was referring to some of the boys overseas in uniform who when they had

an opportunity, visited the neighboring towns to see what was going on. In one of these towns a lad looked up at a fine brick building turned to a man in the street and said, "Hey, Bo, what is this building?"

"Oh, that's our crematorium."

"Gee whiz, is that where they make cheese?"

"Oh, no, no go inside and have a look."

So the lad went inside, and after about two minutes he landed out on the sidewalk on all fours. The man picked him up and said, "What happened to you?"

"I don't know but I went inside, and I saw this grand big building, and over in one corner there were a bunch of sourpusses so I went over and slapped a couple of them on the back and said, 'Hey Bos what's cooking?' (Laughter)

There's no question but that there's a lot cooking here, and from some of the committee meetings that I happened in on yesterday, I think we are going to require three days for this session.

I should express my gratitude to this House for the confidence they have placed in me by electing me to this office. I certainly do appreciate it. I want to assure you that I think this Society is run by every member of this House of Delegates. Your officers are constantly looking for advice from the entire membership. During the months when you are not assembled, it is your representatives in the form of the Council that carry the advice to your presiding officer. That advice has been excellent in the past, and I know I am going to need that same type of advice in the next few months. I anticipate your support in every way, and I assure you I will do my utmost to carry out the wishes of this House and of your Council.

We meet today in an atmosphere of hope and challenge. At no other time in medical history have there been so many problems demanding action by the medical profession and inviting the interest of individual practitioners as we have at this time. During the war, our greatest interest was with the recruitment of necessary personnel in order to have the best that medical science could give to the men and women upon whom we depended to win one of the bitterest wars the world has ever seen. Now we must turn our attention to the needs of a peacetime society.

At no other time has the profession needed so urgently to stand firm and united. The threat of government-controlled health insurance is still making itself felt in no uncertain way. Hearings have been held during the past month on the third Wagner-Murray-Dingell Bill in a period of three years. As physicians who are vitally involved in medical care we know the danger to which both our patients and ourselves will be exposed should this mammoth bureaucratic plan be foisted upon our country. Not one of us can be unconcerned, for it would touch on the lives of every person from coast to coast. The doctor certainly would be effected by the inevitable red tape, with the issuance of orders from lay administrators, the changing of responsibility from the patient to the government bureau. Medical care would no longer be in the hands of the medical profession.

The patient would by the same token suffer from the mediocrity which is the very core of compulsory health insurance. He would be required to pay large sums into the health insurance treasury but he would have very little to show for it. The quality or quantity of medical care would be determined by the amount of money he could pay.

patient and physician would be gone. Scorned as this patient-physician relationship has been by the proponents of socialized medicine, we know that in the majority of cases it is the very cornerstone of success in dealing with the sick person.

The cost of a compulsory health insurance program we can guess. Not only would there be a payroll tax, but there would also be a drain on the general treasury, the sum of which cannot possibly be estimated. Perhaps such a blank check would not be too high a price for the American people to pay for a sure return, but to sign such a blank check for a kind of medical care which, in short order, would be ridden with politics, is tragedy indeed.

The Medical Society of the State of New York has not been content merely to warn the people against political medicine. My predecessors have given leadership to the movement within our State to establish adequate facilities for prepaid medical care insurance. Today, we have six plans in operation throughout the State of New York under Medical Society sponsorship. This development has come within the comparatively short period of six years. We intend to continue to strengthen these plans and to extend them so that every person in New York State will know that this coverage is available. Employers will know more and more that they can offer medical care protection to their employees just as they now can offer hospital care protection.

While we continue to promote the various plans in our own state, we have the additional responsibility, this year, of coordinating them with the over-all national plan which the American Medical Association launched several months ago. Perhaps, in this way, we can help to put across the ideal of non-profit medical care insurance to the entire nation. We owe every cooperation to this purpose and we will give it.

In connection with voluntary medical care insurance, we think inevitably of the veteran of this war who has been promised medical care by the Veterans Administration. The Veterans Administration has shown great interest in a plan by which veterans may be able to secure needed medical care from their own home town physicians and in their own hospitals. Already arrangements have been made with several state medical societies and negotiations are in process with others. Your President has referred to the work that has already been done under his administration, and I trust that work will continue during the next year. The Medical Society of the State of New York has already held conferences with officials of the Veterans Administration several months ago, and studied this question in great detail. We have been truly concerned that the veteran should receive his due without his becoming a political football to be kicked around. He should receive the medical care to which he is entitled, in a way which will completely assure him his dignity as an individual. We hope to work out these negotiations with the Veterans Administration so that every doctor in the State may provide medical care for veterans who are his patients. You will hear much more about this in the coming months.

I would like to mention here the work of Major General Hawley in providing first-class medical care for veterans. From the time of his appointment he was determined to keep veterans' medical care out of politics. In the past, veterans' hospitals have been located too often according to the needs of political patronage. General Hawley, however, is determined that they shall be located in areas which offer the best medical facilities and the best

medical personnel. You may well imagine that this has not been easy for him. Politics intrude even on so sacred a matter as the medical care of men who sacrificed much for their country and to whom we acknowledge a great debt of gratitude. I am sure that every one of us as individuals, and the Society as a professional organization, assures General Hawley of every support we can give him in his program.

We cannot talk about veterans of this war without remembering members of our own profession who have been in the armed service. The medical profession looks with pride upon the accomplishments of these men. Many are still serving the peacetime needs of the Army and Navy.

Many physicians found a great opportunity for service during the war. Every new advance known to medical science, all the skill developed over years of practice, went with them when they became physician-soldiers. All the advantages resulting from our high educational standards in medicine were put at the command of the armed services.

It is true that many physicians did not find military service rewarding. They had the same amount of skill, the same devotion, and the same energy as the others, but in the allotment of tasks in a period of great pressures and preparation for great emergencies they were often in positions where they had little or no opportunity to give what they had to offer. For many this was a bitter disappointment.

Doctors in service have been returning in the past six months, slowly to be sure, but returning. In many cases they can slip back into practice with a minimum of effort. In far more cases they come home to find their practice practically gone, no office space to be had, almost no equipment obtainable. In many instances, they can find neither office space nor living space for their families. Both individually and as a Society, we have a deep obligation to these men who are finding it difficult to become re-established.

The Medical Society of the State of New York has rendered considerable service by giving returning physicians information as to refresher courses, residencies, and partnerships available. It has also been able to give information about practices which might be taken over. It has kept in touch with co-operative agencies which could direct physicians to parts of the State and, sometimes, to locations outside the State which needed physicians.

I believe every county society should re-examine its program to assist returning doctors who are striving to assume their rightful places in their profession, and to change or augment that program in the light of their experiences during the past six months or so. I also urge every physician who has cared for patients whose doctors have been to war to return those patients to the physician who is now trying to find his way back again.

There is one subject which will draw much discussion from this House, namely the American Cancer Society, which is in the process of a campaign for a large sum of money. We have a committee of this Medical Society, and we should have a committee in each component county society, to partake of this great problem. It is proposed to spend 60 per cent of the money raised in the state where it was subscribed, and it is to be spent directly for service to the cancer patient. This may go far in keeping the control of the cancer problem from the hands of the uninformed.

As President of the Medical Society of the State of

New York, I do not plan to carry the torch for any particular interest of my own. Rather, it is my purpose to try to reflect the interests of every physician in our State and to represent those interests well. In this, I hope for the cooperation of every individual physician and of every constituent medical society. Only thus can I serve well as President of your State Society. (Applause)

SPEAKER BAUER The remarks of the President-Elect are referred to the Reference Committee on the Report of the President.

Dr Hale, in the five years you were Vice-Speaker, I am sure you took root up here and would not feel at home anywhere else, so I hope you will remain here during the session.

PRESIDENT ELECT HALE Thank you, sir

Section 14 (See 67)

Introduction of Representatives from Other State Societies

SPEAKER BAUER Are there any delegates here from the States of Connecticut, New Jersey, or Vermont?

(There was no response)

SPEAKER BAUER If any delegate discovers there are such present at any time during the session, the Chair would appreciate it if you would call his attention to them.

Section 15

Introduction of New Members of House of Delegates

SPEAKER BAUER Are there any new members present who have never sat in this House before? (Approximately 18 delegates arose.)

SPEAKER BAUER We are very glad to have you here. I am sure you will find that you are most cordially welcomed by the older delegates. We hope that you will feel free to take part in our discussions at any time if you have anything to say. Seniority in the House is not necessary to get the attention of the chair.

Section 16

Presentation of Dr Joseph S Lawrence to the House

SPEAKER BAUER We have this morning a very distinguished gentleman present, whom I am sure the House wants to welcome. It seems funny to think of him as a guest when for twenty-one years he was Executive Officer of the Medical Society of the State of New York. He left us to enter a larger field as Director of the Washington Office of the Council on Medical Service and Public Relations of the American Medical Association. He was very successful here when he served us, and he is becoming equally successful in Washington as all of us who knew him were sure he would. If I should say I was going to introduce Joe, some people might not know whom I meant, but if I said Joe Lawrence, I think there is no one in the room who would not know him, so Joe, come up here and greet a lot of old friends. (Applause)

Dr. JOSEPH LAWRENCE Mr Speaker and Friends of the Medical Society of the State of New York, you cannot imagine how happy I am and how honored I am in being asked to come before you. Just to look you in the face again is a pleasure. As your Speaker said, for twenty-one years I never missed a meeting of this House, but I sat in the back row somewhere listening to what you were saying and going along with you.

I know that you are going to be a busy body today

You have a lot of work in front of you. I could probably entertain you for half an hour, but I am not going to do it. From here, however, I should like to say that while I am here, if any of the Reference Committees wants to talk with me about things that are happening in Washington—and there are plenty—I will be at their service, and delighted to tell them what I know about the subject under inquiry. However, I cannot before sitting down refrain from that old habit of mine, which my wife says was born in me as a schoolteacher, and that is I must tell people what to do. There is just one thing I would like to mention to you and that is, in your deliberations this week, be realistic. You know what that means being realistic. I think we have reached the point where we have got to be realistic. Let us pick up two or three things that need doing, but be realistic in our approach.

I thank you again for your attention and for the pleasure of being here. (Applause)

SPEAKER BAUER Thank you very much!

(Further Announcements regarding times of meeting of various Reference Committees, as well as places of meeting)

Section 17

Appointment of Committee on Scientific Awards

SPEAKER BAUER The President announces the Committee on Scientific Awards to consist of Dr George C. Adie, Dr Abraham H Aaron, and Dr Alfred M. Hellman.

The floor is now open for the introduction of resolutions.

Section 18 (See 60)

Study of Advisability for the Establishment of Minimum Medical-Surgical Fee Schedule

Dr. JOHN C. BRADY, Erie This is introduced on behalf of the Erie County Medical Society.

"WHEREAS, in many quarters of New York State there is a swelling demand from medical organizations and practitioners for the establishment of a schedule of minimum charges and fees for diagnostic, medical, and surgical services, and
"WHEREAS, it is the considered judgment of these professional elements that such a minimum schedule would

(1) Serve to set an absolute minimum charge for each type of care or service thereby curbing or minimizing unfair and unwholesome competitive practices which are especially prevalent in populous communities,

(2) Tend to prevent or reduce criticism of the medical profession for making charges deemed out of proportion to the degree of professional responsibility assumed, the time expended and the financial ability of the patient to pay, and

(3) Eliminate to a substantial degree, the extreme variations in charges for the same type of services among physicians of equal professional competence, and

"WHEREAS, it is recognized that minimum fee schedules for Workmen's Compensation practice and care of persons under voluntary prepayment insurance and Veterans Administration plans are based, to a greater or less degree, upon charges that prevail in the zone or locality for similar treatment of patients of like standards of living, that is, the charges made in private practice, and

"WHEREAS, the adoption of a minimum fee schedule for private practice undoubtedly would further and facilitate the establishment of really

fair and reasonable as well as satisfactory minimum fee schedules for services in the Workmen's Compensation and the other enumerated fields, now, therefore, be it

"Resolved, that the Medical Society of the State of New York, represented in this duly convened session of its House of Delegates, hereby goes on record as favoring and requesting that its Council explore and study fully the necessity and advisability for the establishment

(1) Of a minimum medical-surgical fee schedule for the entire State of New York, or

(2) A series of minimum medical-surgical fee schedules designed for and limited to defined areas of the State, or

(3) A minimum fee schedule for each County of the State "

SPEAKER BAUER That resolution is referred to the Reference Committee on New Business A, of which Dr D'Angelo is Chairman

Section 19

Creation of Membership Classification for Physicians Employed by Veterans Administration or Serving in the Regular Army or Navy Medical Corps

DR SAMUEL B BURK, *New York* The subject of this resolution is the Creation of Membership Classification for Physicians Employed by Veterans Administration or Serving in the Regular Army or Navy Medical Corps

"WHEREAS, a considerable number of American physicians are now being employed by the Veterans Administration on fulltime service or have decided to accept permanent appointments with the medical corps of the regular Army or Navy, and

"WHEREAS, many of these physicians desire to establish and maintain a membership affiliation with organized medicine, and

"WHEREAS, the Constitution and Bylaws of the Medical Society of the State of New York at present makes no provision for a membership classification for these physicians, therefore be it

"Resolved, that Article II of the Constitution of the Medical Society of the State of New York be amended by the addition of the following '(D) Associate', and be it further

"Resolved, that a new section to be designated as Section 8 shall be added to Chapter I of the Bylaws of the Medical Society of the State of New York to read as follows

"Section 8 The Associate Members of this Society shall be graduate physicians who are affiliated fulltime with the Veterans Administration or are serving on permanent appointments in the regular Army or Navy Medical Corps, who are stationed temporarily or indefinitely within the State of New York and who shall have been admitted to a corresponding form of Associate Membership, without vote, in a component county medical society Associate Members of the Medical Society of the State of New York shall pay the regular assessments of the State Society in the same manner as active members The specific requirements for admission as an Associate Member shall be established by each of the component medical societies "

SPEAKER BAUER That resolution, involving an amendment to the Constitution and Bylaws, cannot be referred to a Reference Committee but will re-

main in the hands of the Secretary when, after being duly published, it will come up for consideration next year

Section 20 (See 63)

Group Plan of Malpractice and Defense Insurance—Yearly Audit

DR THOMAS F MCCARTHY, *Bronx* I have three short resolutions to introduce

"WHEREAS, the Bronx County Medical Society sponsors the Group Plan of Malpractice and Defense Insurance of the Medical Society of the State of New York, and

"WHEREAS, as such sponsor, the Bronx County Medical Society is vitally interested in the financial status of the Group Plan, therefore be it

"Resolved, that the House of Delegates of the Medical Society of the State of New York direct that a yearly audit including an inspection of vouchers of the Group Plan be made by a certified public accountant and submitted to the Comitia Minora of each County Medical Society, thirty days previous to the Annual Meeting of the State Medical Society "

SPEAKER BAUER This resolution will be referred to the Reference Committee on Report of Council, Part XII, which deals with Malpractice Defense and Insurance in part, of which Dr Eugene R. Coon is Chairman

Section 21 (See 62)

Group Plan of Malpractice and Defense Insurance—Report from Counsel Re Final Disposition of Malpractice Suits

DR THOMAS F MCCARTHY, *Bronx* The second resolution reads

"WHEREAS, the Bronx County Medical Society is concerned with the final disposition of suits brought against its members for malpractice, therefore be it

"Resolved, that the House of Delegates direct that the Medical Society of the State of New York through its Counsel submit a report to the Comitia Minora of each County Medical Society on the number of members insured in the group plan in said county, number of suits in said county (against insured, against noninsured), number of suits dropped, number of suits settled and amounts, and the number of judgments and amounts "

SPEAKER BAUER This resolution will likewise be referred to the Reference Committee on Report of Council, Part XII, of which Dr Eugene R. Coon is Chairman

Section 22 (See 61)

Group Plan of Malpractice and Defense Insurance—Establishment of Fund for Sole Purpose of Meeting Counsel Fees in Defense of Malpractice Suits

DR THOMAS F MCCARTHY, *Bronx* The third resolution reads

"WHEREAS, the Bronx County Medical Society considers inequitable the present arrangement for the payment for Malpractice Defense of members of the Medical Society of the State of New York therefore be it

"Resolved, that the House of Delegates of the Medical Society of the State of New York direct that a separate and distinct fund be established for the sole purpose of meeting counsel fees in the defense of all malpractice suits against members of the Medical Society of the State of New York."

SPEAKER BAUER This resolution will also be referred to the Reference Committee on Report of Council, Part XII dealing in part with Malpractice Defense and Insurance, of which Dr Eugene R. Coon is Chairman

Section 23 (See 80)

Change in Federal Compensation Act

DR. BENJAMIN M. BERNSTEIN, Kings This resolution concerns itself with a change in the Federal Compensation Act

"WHEREAS, the Federal Compensation Act does not provide for free choice of physician, thereby violating one of the most important tenets in the relationship between doctor and patient, and

"WHEREAS, the New York State Compensation Law has always recognized the necessity for such a regulation and embodies such permission in its provisions, and

"WHEREAS, numerous complaints have been received from our membership because of the difficulties in treating patients injured in Federal service and covered only by the Federal Compensation Act, therefore, be it

"Resolved, that the House of Delegates of the Medical Society of the State of New York memorialize the House of Delegates of the American Medical Association urging that this body advise the proper Federal authorities concerning this provision and urge that a change in the Federal Compensation Act be made to permit all injured persons to go for treatment to a doctor of his or her own choice."

SPEAKER BAUER That resolution is referred to the Reference Committee on New Business of which Dr Frederick W Williams is Chairman, Reference Committee C

Section 24 (See 83)

Establishment of Speakers' Bureaus

DR. BENJAMIN M. BERNSTEIN, Kings The second resolution concerns itself with the establishment of Speakers' Bureaus

"WHEREAS, no organized body can carry forth its message of service to a community without adequate dissemination of knowledge concerning its activities and functions, and

"WHEREAS the trend of the times requires an ever-broadening relationship between the medical profession and the public so that the physician's point of view shall be placed before the public in proper perspective at all times, therefore be it

"Resolved, that a Speakers' Bureau be set up as part of the Council or Committee on Medical Service and Public Relations in county, state, and national societies to act as spokesmen for these bodies, and be it further

"Resolved, that these speakers' bureaus be adequately informed of all phases of medical practice so that a unanimity of opinion might be voiced, and be it further

"Resolved, that all interested lay county state and national associations be apprized of the existence of such a speakers' bureau for use at their meetings, conventions and conferences, on health matters as they effect both the physician and the public."

SPEAKER BAUER Referred to the Reference Committee on New Business A of which Dr Thomas M. D Angelo is Chairman.

Section 25 (See 74)

Establishment of County Health Departments

DR. OLIVER W H MITCHELL Mr Speaker and Members of the House, this is a resolution urging the establishment of County Health Departments

"WHEREAS, the Medical Society of the State of New York is cognizant of the limitations of public health service under part-time health organizations such as now exist in most townships, villages, and small cities of the State, and

"WHEREAS, the State of New York after January 1, 1947, through increased State financial assistance to counties will make it increasingly advantageous for counties to establish and maintain modern health services by organizing a county health department staffed by full-time professionally trained medical and auxiliary personnel on a merit system basis and at the same time permit the retention of local part-time health officers able to demonstrate their value as a part of a county wide organization, and

"WHEREAS, this Society approved on May 9, 1927, the county health department form of organization and subsequently reaffirmed said approval, and

"WHEREAS, the House of Delegates of the American Medical Association on June 10, 1942, passed a resolution urging the establishment of fulltime modern health services to provide complete coverage of the nation's area and population, be it

"Resolved that the House of Delegates of the Medical Society of the State of New York urge the voluntary establishment and maintenance of county health departments throughout the State at the earliest possible date in order that the existing deficiency in public health administration be corrected, and be it further

"Resolved, that a copy of this resolution be sent to the Honorable Thomas E. Dewey Governor of the State of New York, and to the Honorable Edward S. Godfrey, Jr., M.D., Commissioner of Health of the State of New York "

SPEAKER BAUER Referred to the Reference Committee on New Business B of which Dr Leo F Simpson is Chairman

Section 26 (See 83)

Amendment to Principles of Professional Conduct

DR. HAROLD B. DAVIDSON, New York This is the proposal of an amendment to the Principles of Professional Conduct of the Medical Society of the State of New York providing that splitting or refunding of fees in connection with medical care shall constitute unethical conduct

"WHEREAS, it is desirable that the Principles of Professional Conduct of the Medical Society of the State of New York shall be in harmony with the Workmen's Compensation Law and the Education Law with respect to the prescribing of rebates, splitting or refunding of fees, therefore be it

"Resolved, that the Principles of Professional Conduct of the Medical Society of the State of New York shall be amended as follows

"Strike out the second paragraph of Section 32 reading as follows

"Physicians shall not directly or by any subterfuge participate in or be a party to the act of the division, transference assignments, subordination, rebating, splitting, or refunding

'of any fee for medical, surgical, or other treatment'

"Enact and substitute in place of the above deleted paragraph the following

"It shall constitute unethical conduct for a physician directly or indirectly to request, receive, or participate in the division, transference, assignment, rebating, splitting, or refunding of a fee for, or to directly or indirectly request, receive, or profit by means of a credit or other valuable consideration as a commission, discount, or gratuity in connection with the furnishing of medical or surgical care, diagnosis, or treatment or service including x-ray examination and treatment, or fee in connection with the sale, rental, supplying or furnishing of clinical laboratory service or supplies, x-ray, laboratory services or supplies, inhalation therapy service or equipment, ambulance service, hospital or medical supplies, physiotherapy or other therapeutic service or equipment, artificial limbs, teeth or eyes, orthopedic or surgical appliances or supplies, optical appliances, supplies or equipment, devices for aid of hearing, drugs, medication or medical supplies or any other goods, services, or supplies prescribed for medical diagnosis, care or treatment. This shall not preclude a physician making a reasonable payment to a hospital or other medical institution for the use of its facilities in his professional work, nor shall it preclude the organization of physicians in partnerships or groups, provided such organizations are within the laws of the State of New York and are organized and operated in harmony with the Principles of Professional Conduct of the Medical Society of the State of New York."

SPEAKER BAUER That resolution is referred to the Reference Committee on New Business C, of which Dr Frederick W Williams is the Chairman

Section 27 (See 86)

Car Priorities for Veterans (and Other Physicians)

DR. J A LANDY, *Bronx* This resolution is in reference to car priorities for veterans and other physicians as well

"WHEREAS, physician veterans are finding it impossible to obtain automobiles for professional use except under black market conditions, and

"WHEREAS, priorities for physicians have been discontinued, and

"WHEREAS, some automobile manufacturers (Ford) and some district distributors have established a policy of supplying essential users with automobiles, based on the former priority standards, therefore be it

"Resolved, that the House of Delegates of the Medical Society of the State of New York petition the Council to contact the duly constituted governmental bureaus and agencies, acquainting them with the critical situation and urging an official return to priorities for the distribution of automobiles, and be it further

"Resolved, that the House of Delegates of the Medical Society of the State of New York petition the Council to contact automobile manufacturers and district distributors, explaining the urgency of the situation and requesting priority for physician veterans as well as other physicians requiring automobiles for the practice of their profession, and be it further

"Resolved, that the delegates of the Medical Society of the State of New York to the House of Delegates of the American Medical Association be instructed to press for similar measures at the next Annual Session"

SPEAKER BAUER That resolution is referred to the Reference Committee on New Business A, of which Dr Thomas M D'Angelo is Chairman.

Section 28 (See 78)

Remission of Dues for Medical Veterans

DR. EDWIN L HARMON, *Westchester*: This resolution concerns itself with the clarification of the remission of dues' provision for medical veterans

"WHEREAS, there is still confusion in the book-keeping departments of certain county medical societies concerning the remission of dues for veterans, and

"WHEREAS, the present ruling states that

"the existing procedure be revised and liberalized to provide remission by the State Society of its portion of dues for a full twelve-month period plus any additional months necessary to coincide with the fiscal year of the Society", and

"WHEREAS, this ruling allows great inequality in the periods of remission of dues following return to civil practice providing as much as two years for those 'relieved of active duty' in January, 1946, and only one year for those 'relieved of active duty' in December, 1945, now, therefore, be it

"Resolved, that dues for civil practice should be remitted only for the balance of any fiscal year in which less than six months were spent in active military service but where six or more months were spent in active military service, during the year of discharge, remission of dues should extend over the balance of that year plus one additional twelve-month period"

SPEAKER BAUER Referred to the Reference Committee on New Business B, of which Dr Leo F Simpson is Chairman

Are there any further resolutions?

(There was no response)

SPEAKER BAUER In my six years as Speaker, I have never seen so few introduced at the first session. I am very anxious to have as many resolutions as possible introduced this morning because the reference committees have all afternoon and evening to do their work, and if they are not introduced this morning they can only be introduced tomorrow, which means that the reference committees are going to work during the sessions of the House, which I am trying to avoid

CHORUS We are trying to have them typed. We will have some shortly

SPEAKER BAUER I will declare a recess for about five minutes to enable that to be done. Please don't go very far because I want to get all the resolutions introduced this morning that it is possible to do, so that the Committees on New Business will be able to consider them this afternoon and this evening and be ready with their report on them for tomorrow's session

(A short recess was had at this point)

SPEAKER BAUER The House will be in order

Section 29 (See 89)

Publicity for Veterans

DR. FREDERICK W WILLIAMS, *Bronx* I would

like to introduce this resolution on behalf of the Bronx County Medical Society

"WHEREAS, several hundred members of the Medical Society of the State of New York have returned from active military service, and

"WHEREAS, several hundred more are expected to return from military service within the next six months, and

"WHEREAS, these veteran physicians, because of the housing shortage, are being compelled to re-establish practice in neighborhoods where they are unknown, and

"WHEREAS, 50 per cent of their former patients have moved during the past five years leaving no forwarding address, and

"WHEREAS, there is no effective way of reaching this 50 per cent except through public notice that these physicians have resumed private practice, therefore be it

"Resolved, that the House of Delegates of the Medical Society of the State of New York approve newspaper publicity for veteran members by the local medical societies, and be it further

"Resolved, that this publicity be limited to the publication of the names, addresses, and telephone numbers in a local paper for three insertions"

SPEAKER BAUER Referred to the Reference Committee on New Business A, of which Dr Thomas M D Angelo is Chairman.

Section 50 (See 79)

Invitation to American Medical Association for 1949

DR. ROY B HENLINE, *New York* This resolution is from the County Society of New York regarding an invitation to the American Medical Association for 1949

"Resolved, by the Medical Society of the State of New York that a formal invitation be extended to the Board of Trustees and House of Delegates of the American Medical Association to hold the Annual Meeting of the American Medical Association in New York City in 1949"

SPEAKER BAUER Referred to the Reference Committee on New Business C, of which Dr Frederick W Williams is Chairman.

Section 31 (See 82)

Amendment to Principles of Professional Conduct

DR. ALFRED HELLMAN, *New York* This concerns a possible amendment to the Principles of Professional Conduct concerning criticism of one physician by another

"WHEREAS, gratuitous or adverse criticism by a physician of the character of another physician or the quality of professional services rendered by him to a former patient serves no constructive purpose and frequently gives rise to legal action of the nuisance variety against the doctor whose work has been criticized, therefore be it

"Resolved, that a new paragraph shall be added to Section 35 of the Principles of Professional Conduct of the Medical Society of the State of New York reading as follows

"Every physician should refrain from useless and adverse criticism or derogation of the character or quality of the medical services rendered by another physician in the course of his contacts or communications with former patients of another physician."

SPEAKER BAUER There being another resolution

on the subject of the Principles of Professional Conduct, which has already been referred to the Reference Committee on New Business C, of which Dr Frederick W Williams is Chairman, this likewise will be referred to that same Reference Committee

Section 52 (See 43-44)

Upward Revision of Workmen's Compensation Fee Schedule

DR. STANLEY E. ALDERSON, *Albany* This is a resolution from the Medical Society of the County of Albany regarding Workmen's Compensation Fee Schedule

"WHEREAS, the present compensation fee schedule was established in 1938 and has not been increased, and

"WHEREAS, the general costs of living, etc., have increased more than 35 per cent in the same period, and

"WHEREAS, our Compensation Committee has repeatedly called this to the attention of the State Society Compensation Committee, therefore be it

"Resolved that the House of Delegates of the Medical Society of the State of New York hereby requests, through the proper channels, that the entire Workmen's Compensation fee schedule be increased 25 per cent.

SPEAKER BAUER Referred to the Reference Committee on Report of the Council, Part A, having to do with Workmen's Compensation, of which Dr William B Rawls is Chairman.

Section 53 (See 75-103 for Reference Committee Report)

Promotion of National Health—Introduced by Dr A. Wilbur Duryee, *New York*

Section 54. (See 87)

Hospital Training for Professional Graduates

DR. ROGER A. HEMPHILL, *Livingston* This resolution concerns hospital training for professional graduates

"WHEREAS, hospital experience is universally recognized as a basic part of professional training, and

"WHEREAS, such training is not at present required by our Medical Practice Act, be it

"Resolved, that the House of Delegates actively promote legislation requiring the Medical Practice Board to grant a license only to those who have spent a year after graduation in a hospital approved by the Board of Regents"

Notice that the wording does not limit this specifically to the medical man, but refers to the Medical Practice Act. We feel in our County that hospital experience is something everybody licensed under the Medical Practice Act ought to have after he has completed his professional education. It is not, at present, required of physicians or anyone else. Since other than physicians can now practice medicine, possibly it might be advisable to make it mandatory for all to take that, whether physicians or not.

SPEAKER BAUER That resolution is referred to the Reference Committee on New Business A, of which Dr Thomas M D Angelo is Chairman.

Section 55 (See 75)

Session on Chest Diseases

DR. HERBERT E. WELLS, *Erie* This is a resolution asking for a Session on Chest Diseases

THE GRADUATE SCHOOL IN MATHEMATICAL PHYSICS AT BIRMINGHAM

IN 1956, a Graduate School in Mathematical Physics, leading to a diploma, was instituted in the Department of Mathematical Physics of the University of Birmingham. It had been noticed that students who graduated in the honours school of mathematical physics in the Department seemed well equipped, and considerably in demand, for work involving the applications of mathematics to physical problems in industry, government laboratories, etc., because of the training they received in the principles of physics, and particularly in the techniques of translating physical problems into mathematical terms, and of interpreting the solutions from a physical point of view.

Entry to the honours course at Birmingham is restricted to students of high ability, who must have the appropriate background in their school training, since the three-year course makes fairly heavy demands on the students. It seemed likely therefore that a one-year postgraduate course would be of advantage to students who had taken a degree in mathematics, because they could not—or did not choose to—enter the mathematical physics course, or who graduated from universities at which such a course was not available.

The three years of operation of the Graduate School have provided sufficient experience to judge that it can serve the purpose for which it was intended, and that it imparts to the students knowledge and experience which serves them well in their later work. The course extends over one academic year (October to July) and is normally intended for honours graduates in mathematics with subsidiary physics. In some cases it proved possible to fit in students with somewhat different qualifications. Lecture courses attended by the students include a course in methods of mathematical physics (given so far by Dr J. G. Valatin, who is in general charge of the Graduate School), which forms the central theme of

their introduction to the outlook of a mathematical physicist. In addition, students normally take selected parts of the lecture courses for honours physicists, and those parts of the final-year course for mathematical physicists (electromagnetic theory, hydrodynamics, quantum mechanics) which they have not previously covered, and which suit their particular needs. Other options include mathematical statistics, numerical methods, elasticity theory, statistical mechanics, and usually at least one course in one of the applied science departments. All students attend a weekly seminar arranged specially for the Graduate School in which they contribute themselves, and otherwise hear talks by members of the research group in mathematical physics and others. It has proved possible to arrange for each individual student a combination of courses which suits his particular interests and knowledge.

Although many of these courses are given for other purposes, students find it easy to synthesize their work and to build them into a common foundation of understanding.

The number of students in the course has remained small in the first three years, and is likely to continue small until the existence and purpose of the course become more widely known. It is therefore premature to give any statistics of the subsequent occupations of students who have obtained the diploma. These included work in industry and government laboratories as well as academic research. (One student took up postgraduate work in the Mathematical Physics Department at Birmingham, and two joined an applied science department in the University.)

The development of the Graduate School was greatly aided by the award of advanced course studentships of the Department of Scientific and Industrial Research, and in some cases by grants from the University of Birmingham.

R. E. PETERLS

WATER-RESOURCES AND WATER-USE SURVEY

THE study of the use and conservation of water resources is a relatively new geophysical science and one that impinges closely on other sciences such as meteorology and climatology, geology and geomorphology, agriculture, economic geography, demography, etc. The importance in the modern world of economic and land-use planning, particularly with reference to so precious a raw material as water, involves the collection of a vast and varied amount of data and information relevant to the assessment of water resources, on not only a national but also an international basis. Two papers*,

* World Meteorological Organization. Technical Note No. 25. Design of Hydrological Networks. Prepared by Max A. Kohler. Technical Note No. 26. Techniques for Surveying Surface-Water Resources. Prepared by Prof. Ray K. Linsley. Pp. v+16+vi+41. (WMO-No. 82 TP 32.) (Geneva: Secretariat of the World Health Organization, 1958.) 4 Swiss francs.

published by the World Meteorological Organization, are useful statements in this important field, particularly in view of the varying scientific standards of recording and observation that are available and possible in different world regions.

M. A. Kohler summarizes briefly the types of hydrological data, the network density of observations required, and network planning, and the techniques for estimating hydrological data that can be used. Attention is directed to the impracticability of devising a universally standardized procedure and a scheme is put forward for the creation of a minimum cover of permanent full, partial, and temporary observational stations.

The second, longer, technical paper is more closely concerned with techniques for the surveying of surface

water resources in a region, and providing estimates of usable water supply. Attention is given to methods which are adapted for use in the absence of adequate hydrological data and to simple techniques of observing hydrological phenomena which may provide useful data with least cost in time and money. Despite the importance of ground water circulation in all regions—and especially in arid regions—the survey is limited to the discussion of techniques with regard to surface resources. These are a guide to the estimation of requisite rates of replenishment of ground water that are necessary for the effective use of the latter over a period of time. The main topics discussed are the hydrological balance, precipitation, evapo-transpiration and its measurement, stream flow, sediment transport and water supply, and a summary direction for procedure in the matter of water resource surveys.

The special problems and peculiar needs of a densely populated and highly industrialized country such as Great Britain are summarized in an interesting discussion on a water use survey opened by Prof. W. G. V. Balchin (under the chairmanship of Prof. Dudley

Stamp), with contributions from experts representing a very wide range of technical interests in this important field (*Geog. J.*, 124, 476, 1958). Prof. Balchin directs attention to the dramatic increases in water consumption in Britain during the past century, culminating in an increase of 50 per cent in England and Wales and 41 per cent in Scotland during the short period 1938–50. The water storage capacity in the same time has increased by only 46 per cent and 31 per cent, respectively. The area where the consumption is greatest is the area where population is densest and the rainfall least, and where the local resources are already fully employed—that is, in lowland Britain and particularly in the great urban and industrial complexes.

These papers are a salutary reminder, through the many facets to the problem of water conservation that they reveal, of our ultimate dependence on water resources and our need to avoid over-exploitation of a raw material that in Great Britain at least, people assume all too readily is in abundant supply, and for which in many others the supply is already precarious.

ALICE GARNETT

CARNEGIE TRUST FOR THE UNIVERSITIES OF SCOTLAND

THE fifty-seventh annual report of the Executive Committee of the Carnegie Trust for the Universities of Scotland covers the year 1957–58 (pp. iv + 74, Edinburgh: Carnegie Trust for the Universities of Scotland, 1959) and includes the financial accounts for the year ended September 30, 1958. A major preoccupation of the Executive Committee during the year was the formulation of a policy to implement its new powers of investment. During the year there were on the books five senior research scholars, thirty-six research scholars in their second or third year, and twenty-five in their first year. For 1958–59 the value of the senior scholarship has been increased to £500 (with an additional £100 for expenses), while scholars at Oxford, Cambridge and London will receive £450, scholars living away from home, attending a Scottish or an English provincial university, £400, and scholars living at home and attending a Scottish university, £350. A grant of £4,000 a year for five years from the end of 1958 was made to the Scottish Dictionaries Joint Council subject to some conditions with regard to progress. Ten of the research grants awarded during the year were for expenses involved in illustrating the published results of research and five grants were made to authors as a subvention towards the cost of publishing their books.

Four grants are particularly mentioned. The Trust has provided a special heavy-duty vehicle and a 'Folboat' with outboard motor and a grant for running expenses to assist Prof. J. H. Burnett and Dr. D. H. N. Spence, of the University of St. Andrews, in preparing a comprehensive account of the aquatic vegetation of Scotland, a research which involves crossing many moorland roads to examine distant mountain lochs. A grant of £2,500 was made to Prof. R. H. Matthew, of the University of Edinburgh, for a study by a research team correlating the problems of the design of basic dwelling units, lay-out, siting and services

with social requirements, with specific reference to contrasting types of social grouping and including a cost study. Another grant was to the University of Glasgow North Rona Expedition, which spent about a month on North Rona and Sula Sgeir, paying particular attention to marine biology. Some very rare species of algae were found and a special census was made of Leach's petrel. A second successful expedition, assisted by a grant from the Trust, was one from the University of Aberdeen, led by Prof. A. C. O'Dell, to St. Ninian's Isle, Shetland, in June–July, 1958, in which a most important collection of silver ornaments was uncovered.

Of the ten grants for travel and maintenance made to members of university staffs engaged in research, three were to members of a faculty of medicine, four in science and three in arts. Among these may be mentioned those to Dr. W. I. Card to enable him to visit centres in the United States and Canada, where work of interest and importance in gastroenterology is proceeding, to Mr. Alastair Fraser to work in Copenhagen in the laboratories of Prof. M. Thomsen and Dr. F. Thomsen, leading authorities on insect endocrinology, and later in Liège, Brussels and Paris, to Dr. C. H. Gunningham to enable him to follow up in Scandinavia his investigations in Scottish heaths aimed at gaining a comprehensive picture of the ecology of heather, including its reactions to grazing and burning and influences of soil climate and at utilizing this information in an investigation of the ways in which heath lands have originated and are maintained, to Dr. Elizabeth D. Fraser, to enable her to test in America some of her hypotheses regarding perceptual constancy as a function of personality and learning and the effect of metabolic disturbance, and to Dr. P. H. Tait to discuss his experimental techniques in embryology in the United States.

THE SCHOOL HEALTH SERVICE IN BRITAIN

THE School Health Service is fifty years old. In the half-century of its existence there have been remarkable changes in the health of school children, and in the pattern of illnesses affecting them. Both boys and girls to-day are taller and heavier, better clad, better shod and cleaner. They reach physical maturity earlier and may expect to live twenty years longer. In sharp contrast to the conditions of malnutrition found only too commonly 50 years ago, medical attention is now being drawn towards an increasing number of school children who are too fat.

The annual report* of the Chief Medical Officer presents these facts and discloses among other vital statistics that the killing and crippling diseases prevalent at the turn of the century—tuberculosis, rickets and rheumatism—have been practically eliminated. The remaining causes of crippling and other forms of handicap are now mainly congenital or hereditary in origin. Accidents still kill twice as many children as die from disease, and road accidents are responsible for half the deaths recorded. Boys are more liable to death on the road than girls, leaving school in the afternoon is one of the most risky periods of the day.

Nearly 250,000 children were found to have verminous heads in 1957. This is about 4 per cent of the total school population. "This condition is preventable and there is seldom any excuse for it", says the report. "It is essentially a family problem, children being infested and re-infested by adults". The current question of smoking and its relation to lung cancer provides "a striking example of the need

* *The Health of the School Child. Fifty Years of the School Health Service* (Report of the Chief Medical Officer of the Ministry of Education for the years 1956 and 1957). Pp. 1+220+12 plates (London: H.M. Stationery Office, 1958) 10s. 6d. net.

for boys and girls, while still at school, to be taught something about healthy living—by example, perhaps, more than by precept. In spite of all that has been said and written about the close connexion between the two, many children still smoke cigarettes". A recent inquiry carried out at a mixed secondary modern school in the Isle of Wight disclosed that about a third of the boys and 15 per cent of the girls were regular smokers.

The incidence of dental decay has increased in the past few years among school children, and is due "probably to the greater amount of sweets and confectionery eaten since the end of sweet rationing". Fluoridation of water supplies probably offers the best hope of reducing this incidence, "but large scale benefits from this measure can hardly be expected for several years".

One consequence of the changing pattern of ill-health in childhood is that school health service staffs now devote more attention to children who are emotionally disturbed, or who suffer from some handicap which threatens to have a retarding effect on school progress from a psychological cause.

There is also the challenge of the delinquent school child which cannot be ignored by the school health service. The number of children charged before the juvenile courts has risen from 13,000 in 1913 to 38,000 in 1956. It is right, says the report, that the school health service should concern itself with the problem and co-operate with the other agencies involved. In 1957 more than six and a half million children attending about 30,000 maintained and assisted schools were covered by the service. More than two million have a periodical inspection during the year.

INCENTIVES IN THE BUILDING INDUSTRY

A RECENT Building Research Station report* on incentives in the building industry shows that bonus schemes have an important contribution to make to building efficiency. The maximum benefit can only be derived, however, if they are integrated into a rational pattern of management. The report enumerates principles on which an incentive scheme should be based as well as the method of operation if it is to be successful.

Operation targets, coupled with a recording system giving operation costs, should be used whenever possible. The operations should be the visual stages of work, of about one week's duration, and continuous jobs with no hold-ups for other trades.

The scheme should be designed to suit individual needs and local conditions. This calls for flexibility in targets to suit the local productivity of labour and

the distribution of bonus payments. The operatives on each site should decide the method of sharing within the bonus group or gang. It is necessary to safeguard the quality of work by making site staff independent of production bonus and improving site supervision of quality.

A number of conclusions were reached about the methods of operation of an incentive scheme. Accurate and well-balanced targets should be maintained by the systematic use of cost information from all the firm's sites and by close consultation with its site staff. The incentive effect of a scheme is greatest when it is given a central position in the organization of the firm, especially if administered by the contract management side. There should be close liaison between estimating and the fixing of target bonus-rates. The principles of the scheme should be kept simple and explained to the operatives so that they can calculate their own bonuses. The bonus units are small gangs.

* *Department of Scientific and Industrial Research. Building Research Station. National Building Studies Special Report No. 28. Incentives in the Building Industry*. By Allison Entwistle and W. J. Reiners. Pp. iv+43 (London: H.M. Stationery Office, 1958) 3s. net.

The bonus paid should be the actual amount of bonus earned, there should be no limit to the amount of bonus that can be earned, the bonus should be paid weekly and as soon as possible after the completion of the operation. The scheme should cover, so far as possible all the work on the site. Good labour relations on the site are an aid to productivity

and should be encouraged by presenting the targets to the operatives for agreement before work starts and a recognized channel for complaint should be established. Provision should be made to allow targets to be modified on a particular site if adequate reason is established. Disputes or complaints should be dealt with speedily and in consultation with the site staff

SURFACE OF THE OCEAN AS A SOURCE OF AIR-BORNE NITROGENOUS MATERIAL AND OTHER PLANT NUTRIENTS

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IN an earlier communication¹ the occurrence of organic nitrogen in New Zealand snows was reported, and it was suggested that this might represent a contribution to the nitrogen economy of New Zealand soils. This article presents further results on the subject and points to the most probable origin of this air-borne nitrogenous material.

Samples of snow have been collected from above the vegetation line to avoid possibility of contamination by plant or animal debris. This was done in preference to the more conventional rain water sampling which is open to large contamination errors. The analyses of these samples are shown in Table 1.

Since the samples described here were freshly collected snow from regions where no plants or animals exist, contamination from these sources should be negligible. No insoluble inorganic material was visible in the samples, so that cyclic terrestrial dust could not contribute appreciably to the nitrogen found in the samples. This is to some extent further supported by the lack of nitrate in the samples. The samples were collected in early and mid winter when the pollen contribution would be negligible. It seems that precipitation, at least in New Zealand, does in fact contain appreciable quantities of bound nitrogen which does not arise from contamination

and, if heavier, sinks to form sediments, and if lighter, rises to form this layer, which therefore contains micro-organisms and other plant-life in a state of partial decomposition and would be expected to be rich in organic matter. It would also be expected to have an increased potassium/sodium ratio, since many marine organisms concentrate potassium. It is known² that when a bubble of gas passes through a liquid gas interface the act of the bubble bursting throws up a small droplet from the surface of the liquid into the gas phase. This must occur in the phenomenon known as 'white caps' (that is, when a wave breaks). The haze produced by these particles is quite noticeable on a fine day when a heavy surf is running. Thus the composition of these droplets reflects that of the surface layer and not that of the bulk ocean.

It is reasonable to assume from the foam produced in rough ocean that some surface active material is present on the surface of the ocean. During strong onshore winds large quantities of foam accumulate on the shores of New Zealand which provides an opportunity to sample directly the surface layer of the ocean. A sample of ocean foam was collected on the west coast just north of Wellington. The foam was broken with a silicone anti-foaming agent and allowed to stand. It proved to be 25 per cent solid matter. On microscopic examination this material was found to be particularly rich in bacteria and also had large quantities of diatoms and fragments of phyto and zoo plankton. The chemical analysis of this material is shown in Table 1. It is interesting to note the high nitrogen content and that the potassium/sodium ratio is higher than that in sea water.

The relationship between the surface layer of the ocean and snow water is most clearly seen when one plots the excess potassium concentration against the 'albuminoid nitrogen concentration'. This is done in Fig. 1. The excess potassium concentration is obtained by subtracting from the potassium concentration 1/27 of the sodium concentration, that is, that amount of potassium which would be associated with the sodium in sea water. We see that the results from the ocean foam and the snow water samples lie on a straight line which can be extrapolated back to give the albuminoid nitrogen concentration in sea water. This is strong evidence in favour of a common origin and supports the

Origin of Organic Nitrogen in Snow

The problem immediately arises as to the origin of this material. When one considers the geographical position of New Zealand, situated as it is in a westerly air stream and surrounded by thousands of miles of ocean it is difficult to avoid the conclusion that the source is the ocean itself. The ocean however contains only about 0.003 ppm of albuminoid nitrogen. Further, if the snow is analysed in more detail, one sees that it is not merely diluted sea water but that its potassium/sodium ratio is an order of magnitude greater than that of sea water.

In order to explain these facts, it is necessary to postulate that the upper very thin layer of the ocean has a different composition from that of the rest of the ocean. In particular that it is enriched in potassium ammonium organic material and organic nitrogen and probably various other materials. It is suggested that most (for example, from plankton) is other than sea water

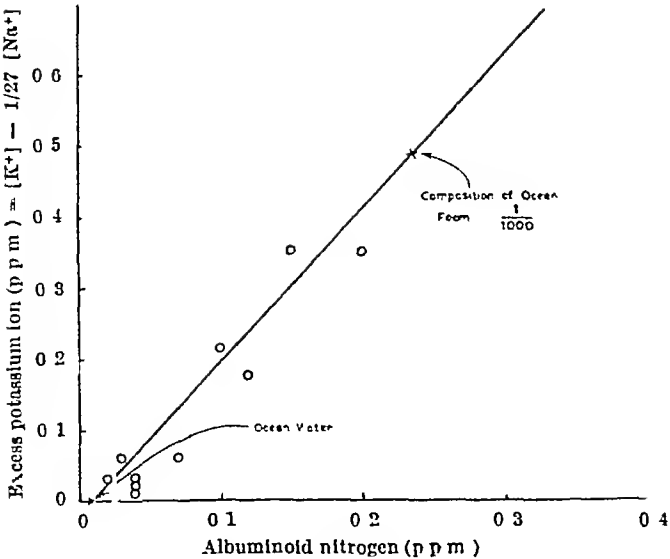


Fig 1

nitrogen in snow originates in the surface layer of the ocean

The above evidence suggests a new path in the nitrogen cycle, at least for New Zealand, and probably for other areas with rough oceans to their windward. Elementary nitrogen dissolves in the sea and is fixed by marine micro organisms. These eventually rise to the surface and are caught in the surface layer, where some are partly decomposed by other micro organisms into ammonia and other products. The micro-organisms and their decomposition products are carried into the air by a bursting air bubble in a 'white cap'. In the air the droplet would lose its moisture and a part of its ammonia, and as a small and light particle be carried far inland to settle out or to serve the very useful function of seeding rain clouds. On reaching the ground this material would contribute to the soil, nitrogen and potassium and possibly other materials necessary for plant growth. From the lack of NO_2 and NO_3 in the samples, this path in the nitrogen cycle might be considered more important than the conventional fixation of atmosphere nitrogen by atmospheric electrical discharges, at least for the areas covered by the sampling. This then might represent a net transfer of bound nitrogen from the ocean to the land.

Table 1

| Description of sample | Nitrogen content of snow samples (ref 3) | | | | | Na^+ (p p m) | K^+ (p p m) | Corrected $\text{K}^+ = \text{K}^+ - \frac{1}{27} \text{Na}^+$ (p p m) | K^+/Na^+ |
|---|--|----------------------------|----------------------------|--|----------------|--------------------------|-------------------------|--|--------------------------|
| | NO_3 (p p m) | NO_3^- (p p m) | NH_4^+ (p p m) | Organic (albuminoid) nitrogen (p p m) | Sum (p p m) | | | | |
| (1) Snow collected April 26, 1958, 6,000 ft (tree line 4,000 ft) during snowstorm on Mt Ruapehu (100 miles from sea) Wind W S W | 0 | trace < 0.002 | 0.03 | 0.15 | 0.23 | 1.36 | 0.4 | 0.35 | 0.29 |
| (2) Freshly fallen snow collected April 26, 1958, at 5,300 ft on Mt Ruapehu | 0 | trace < 0.002 | 0.03 | 0.2 | 0.23 | 1.35 | 0.4 | 0.35 | 0.296 |
| (3) Snow collected May 3, 1958, at 6,000 ft (tree line 4,000 ft) on Mt Egmont (20 miles from sea) | 0 | 0 | 0.03 | 0.1 | 0.13 | 0.68 | 0.24 | 0.215 | 0.354 |
| (3a) Snow taken under (3)—previous snowfall? | 0 | trace < 0.002 | 0.05 | 0.03 | 0.08 | 1.02 | 0.1 | 0.06 | 0.098 |
| (4) Snow collected April 27, 1958, at 7,000 ft (tree line 3,000 ft) on Tasman Glacier (25 miles from sea) | | | 0.1 | 0.12 | 0.22 | 0.20 | 0.18 | 0.175 | 0.90 |
| (5) Rain collected in Wellington in southerly storm on April 26, 1958. Distance up wind to open sea 10 miles, altitude 10 ft | 0 | 0.002 | 0.27 | 0.2 | 0.47 | | | | |
| (6) Snow collected July 20, 1958, at 5,750 ft (tree line 4,000 ft) during a snowfall on Mt Ruapehu (100 miles from sea) | 0 | 0 | 0.2 | 0.04 | 0.24 | 0.16 | 0.01 | 0.01 | 0.067 |
| (7) Snow collected July 21, 1958, at 6,575 ft. Same fall as in (6) | 0 | 0 | 0.33 | 0.07 | 0.40 | 0.16 | 0.06 | 0.06 | 0.375 |
| (8) Snow collected July 21, 1958, at 8,070 ft. Same fall as in (6) | 0 | 0 | 0.2 | 0.02 | 0.22 | 0.11 | 0.03 | 0.03 | 0.273 |
| (9) Snow collected August 2, 1958, at 6,000 ft during snowstorm on Mt Ruapehu | 0 | 0.001 | 0.02 | 0.09 | 0.11 | | | | |
| (10) Fresh snow collected August 22, 1958, at 5,000 ft at Temple Basin, Arthur's Pass (tree line 3,000 ft, 30 miles from sea) | 0 | 0.002 | 0.01 | 0.04 | 0.05 | 0.04 | 0.02 | 0.02 | 0.50 |
| (11) Fresh snow collected September 10, 1958, at 5,700 ft on Mt Ruapehu | 0 | 0 | 0.01 | 0.04 | 0.05 | 0.05 | 0.05 | 0.03 | 0.077 |
| (12) Ocean foam collected on rocky coast north of Wellington during strong on shore westerly wind | | | | | 235 | 12,000 | 930 | 485 | 0.078 |
| (13) Typical ocean water | | 0 | 0.004 | 0.008 | | 11,000 | 410 | 0 | 0.037 |

Application of Hypothesis to Other Problems

Origin of Ammonia in Air and Rain The presence of ammonia in air and rain has been known for many years. Its origin, however, has been in doubt.¹ The ocean seemed to be the most likely source except that calculations based on the equilibrium constant between air and water, together with the concentration of ammonia in the sea, rule out this possibility, even though in New Zealand's case there seems to be no other. The hypothesis presented in this article would imply that the ammonia is coming, not from the bulk ocean, but from the surface layer and from the evaporation of the small droplets which are thrown up into the air by the bursting bubbles. Variable quantities of ammonia will be lost by these droplets to the air, depending on their pH and composition. Indeed, the results in Table 1 seem to show that the higher the albuminoid fraction the lower the ammonia retained in the droplet and vice versa. This might be due to the buffering effect of the basic nitrogenous material.

Potassium/sodium ratio in rain water It is a well known fact that the potassium/sodium ratio in rain water is often larger by a factor of 10 than that in the sea—the obvious source. This can be readily explained in terms of the above hypothesis, since the rain would derive its salts from the surface layer of the ocean, which in turn is rich in marine organisms many of which are known to have much higher potassium/sodium ratios than the 1/27 of sea water.

Charge discrepancy in rain water The total sums of all the charges carried by the anions and cations in rain water sometimes do not balance. This can be explained by the presence of organic compounds balancing the excess charge.

Ocean foam The origin of the foaming agent in the sea is not certain, but it is possible that it is produced

by the bacteria themselves and serves to trap their food and also to aid in their aeration.

Many of the sheep stations on the New Zealand coasts and islands carry more sheep than might from other considerations be expected, and without aerial top dressing.² This effect decreases with distance from the sea, and applies only to areas lying within 10 miles of the coast. Could this be the result of wind blown foam carrying plant nutrients to these coastal areas?

Bacterial action of the sea There is a discrepancy between the supposed bacterial action in the sea and the very few bacteria found therein.³ Is it possible that a large fraction of these biological processes takes place on the surface layer of the ocean, and that these are not effectively sampled by the normal methods which sample the bulk ocean rather than the surface?

Life in the inter tidal zone The occurrence of large quantities of organic matter and nutrients in the surface layer of the sea might provide the food supply for the large amount of life that exists in and near the inter tidal zone.

I wish to thank Mr H. J. Wood of the Dominion Laboratory, Wellington, for the nitrogen analyses, and Mr A. J. Heyne and Mr G. Pallo Department of Scientific and Industrial Research, for collecting samples.

¹ Wilson A. T. *Nature* 163 318 (1950)

² "Standard Methods for the Examination of Water and Sewage" (American Public Health Association 1700 Broadway New York)

³ Woodcock, A. L., Kientzler, C. F., Arous, A. B. and Blanchard D. C. *Nature* 178 1144 (1953)

⁴ Edlison E. *Tellus* 3 215 (1955)

⁵ Aitken R. (private communication Otago College Station Waimu Otago New Zealand)

⁶ Harvey H. W. "The Chemistry and Fertility of Sea Water" (Cambridge University Press 1955)

COMBINED EFFECTS OF CORTISONE AND INSULIN ON DEVELOPING CHICKEN EMBRYOS

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THE injection of insulin into the yolk sac of chicken eggs after an incubation period of 4-8 days is responsible for the occurrence of a shortening of the long bones of the legs (micromelia) and of abnormalities of the beak, the mean body weight of such embryos is somewhat reduced. The severity of these symptoms varies with the amount of injected insulin.¹ The principal effect of cortisone, injected during the same developmental stages is a marked dwarfing of the embryos, but without the production of skeletal malformations.² When both insulin and a potent adrenal cortex extract (but of unknown cortisone concentration) were injected after 5 days of incubation it was found that the incidence of insulin specific skeletal abnormalities was significantly greater than after the injection of insulin alone.³ In similar experiments but done after 8 days of incubation and using cortisone in combination with insulin, Lunardo and de Bastiani did not find a potentiation of the insulin effect.⁴ It seemed of interest therefore, to determine if differences of developmental stages

are responsible for dissimilarities in the effects produced by simultaneous treatment with cortisone and insulin or if the discrepancies between our earlier observations and those of Lunardo and de Bastiani have other causes.

For our present tests we used eggs of White Leghorn fowls. Sterile solutions of cortisone (cortisone acetate, Merck) and of insulin (Lilly) were injected into the yolk sac after 4 or 8 days incubation. The details of our experiments are presented in Tables 1 and 2. In recording skeletal abnormalities all degrees of shortening of the legs were pooled similarly, all types of beak defects were grouped together. The incidence of other skeletal abnormalities was very small and was not separately recorded, these defects occurred with about equal frequency in all groups and, since there was no reason for believing that they owed their origin to our experimental procedures, they were added to the 'normal' groups.

Untreated eggs served as controls of the various experimental groups. For the test reported in Table 1 we had 37 fertile and untreated eggs; 33 of these

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Council.

Table 1 EXPERIMENTS IN WHICH CORTISONE, INSULIN, OR BOTH CORTISONE AND INSULIN WERE INJECTED INTO THE YOLK SAC OF WHITE LEGHORN EGGS AFTER 96 HR OF INCUBATION AND AT THE DOSAGES GIVEN BELOW

| | Cortisone | | | Insulin | | | Insulin and cortisone | | |
|--------------------------------------|-----------|--------|--------|---------|--------|--------|-----------------------|--------|--------|
| Experiment | 1 | 2 | 3 | 1 | 2 | 3 | 1 | 2 | 3 |
| Insulin units/egg | — | — | — | 3.2 | 3.2 | 4 | 3.2 | 3.2 | 4 |
| Cortisone, mgm/egg | 1.25 | 1.25 | 1 | — | — | — | 1.25 | 1.25 | 1 |
| Number treated | 20 | 27 | 30 | 26 | 27 | 30 | 54 | 48 | 90 |
| Survival to eighteenth day, per cent | 57.7 | 81.5 | 70.0 | 84.6 | 63.0 | 73.0 | 37.1 | 47.8 | 35.5 |
| Number survivors | 16 | 22 | 23 | 22 | 17 | 22 | 20 | 23 | 32 |
| Body-weight, gm | 14.20 | 13.73 | 13.00 | 19.59 | 15.15 | 13.37 | 12.70 | 8.71 | 10.14 |
| | ± 0.93 | ± 0.86 | ± 0.83 | ± 0.81 | ± 0.79 | ± 0.73 | ± 0.87 | ± 0.50 | ± 0.67 |
| Normal, per cent | 100 | 100 | 100 | 87.0 | 64.7 | 36.4 | 75.0 | 65.2 | 18.8 |
| Short legs, per cent | 0 | 0 | 0 | 13.0 | 35.3 | 51.5 | 25.0 | 34.8 | 59.4 |
| Abnormal beak, per cent | 0 | 0 | 0 | 13.0 | 11.8 | 27.3 | 5.0 | 4.4 | 25.0 |

In those groups in which both hormones were injected the ratio of cortisone to insulin amounted to 0.39 in experiments 1 and 2 and to 0.25 in experiment 3. All living embryos were weighed and examined after 18 days of incubation. Incidence of 'normal' embryos and of abnormalities of the legs or beak in percentage of survivors to eighteenth day. Standard errors of body weight.

Table 2 EXPERIMENTS IN WHICH CORTISONE, INSULIN, OR BOTH CORTISONE AND INSULIN WERE INJECTED INTO THE YOLK SAC OF WHITE LEGHORN EGGS AFTER EIGHT DAYS OF INCUBATION AND AT THE DOSAGES GIVEN BELOW

| | Cortisone | | | Insulin | | | Insulin and cortisone | | |
|--------------------------------------|-----------|--------|--------|---------|--------|--------|-----------------------|--------|--------|
| Experiment | 1 | 2 | 3 | 1 | 2 | 3 | 1 | 2 | 3 |
| Insulin units/egg | — | — | — | 3.2 | 3.2 | 4 | 3.2 | 3.2 | 4 |
| Cortisone, mgm/egg | 1.5 | 1.5 | 1 | — | — | — | 1.5 | 1.5 | 1 |
| Number treated | 40 | 10 | 55 | 40 | 20 | 55 | 70 | 40 | 80 |
| Survival to eighteenth day, per cent | 67.5 | 90.0 | 89.1 | 80.0 | 90.0 | 80.0 | 63.5 | 87.5 | 73.7 |
| Number survivors | 27 | 9 | 49 | 32 | 18 | 44 | 48 | 35 | 59 |
| Body-weight, gm | 11.87 | 13.02 | 16.56 | 18.20 | 16.95 | 17.75 | 13.53 | 13.24 | 14.85 |
| | ± 0.52 | ± 0.65 | ± 0.45 | ± 0.47 | ± 0.50 | ± 0.40 | ± 0.42 | ± 0.42 | ± 0.50 |
| Normal, per cent | 100 | 100 | 100 | 50.0 | 27.8 | 34.1 | 61.3 | 71.4 | 49.2 |
| Short legs, per cent | 0 | 0 | 0 | 50.0 | 72.2 | 65.9 | 17.9 | 23.6 | 50.8 |
| Abnormal beak, per cent | 0 | 0 | 0 | 0 | 5.0 | 0 | 5.1 | 0 | 18.6 |

In those groups in which both hormones were injected the ratio of cortisone to insulin amounted to 0.47 in experiments 1 and 2, and to 0.25 in experiment 3. All living embryos were weighed and examined after 18 days of incubation. Incidence of 'normal' embryos and of abnormalities of the legs or beak in percentage of survivors to eighteenth day. Standard errors of body weight.

(89.2 per cent) survived to 18 days and the embryos at that age had a mean body-weight of 20.95 ± 0.53 gm. As controls for the experiments of Table 2 we had 26 fertile and untreated eggs, 22 of the embryos (84.6 per cent) lived at 18 days and had a mean weight of 19.37 ± 0.56 gm. None of these 55 embryos showed skeletal malformations of the kind with which the present discussion is concerned.

Effects on survival. Among embryos treated at 4 days with both insulin and cortisone the mortality was consistently higher than it was in the groups treated with either hormone alone. In fact, the toxicities of insulin and cortisone were nearly additive, and most of the group differences in mortality (or survival) are highly significant. At 8 days, on the other hand, survival after the combined treatment did not differ significantly from that occurring after injection of either insulin or cortisone. Comparing the experiments at 4 and 8 days, and taking into account such dissimilarities of dosage as existed, no consistent or significant changes appear to have occurred in the toxicity of either cortisone or insulin. Highly significant differences are found, however, between the combined treatments at the two developmental stages. In experiments 1 and 2, in which the ratio of cortisone to insulin was higher at 8 days than at 4 days (0.47 vs 0.39), the differences amounted to 31.4 ± 8.65 and 39.7 ± 8.90 per cent respectively, in the two third groups, with identical ratios (0.25), the difference in survival was 38.2 ± 7.04 per cent.

Effects on body-weight. Following treatment after 4 days of incubation, the injection of both hormones led in all three groups to a greater retardation of growth than that produced by either insulin or cortisone. In groups 2 and 3, the mean body-weights, after combined treatment, fell significantly below those of the groups treated with either cortisone or insulin alone. At 8 days the combined treatment

led to a significantly lower body-weight in comparison with the insulin-treated embryos, but the differences between the groups that had been injected with both hormones and those that had received only injections of cortisone were neither consistent nor statistically significant. A comparison of the treatments at the two developmental stages reveals some interesting differences. Against the lowest amount of cortisone which we used (1 mgm/egg) the 8-day embryos had become significantly more resistant than those treated at 4 days, their mean body-weight being 2.66 ± 0.94 gm higher, the results of experiments 1 and 2 are not directly comparable because of dosage differences. The injection of 3.2 units of insulin at 4 and 8 days did not produce significant dissimilarities in body-weight, but after 4 units the 8-day embryos were less retarded (difference 4.38 ± 0.88 gm). The results for combined injection of insulin and cortisone in experiments 1 and 2, because of dosage differences, do not allow a comparison between 4 and 8 days, but the results of tests with 1 mgm cortisone and 4 units insulin (experiments 3) demonstrate that growth of the embryos treated at 8 days was much less retarded than it was following injection at 4 days (difference 4.71 ± 0.27 gm).

Teratogenic effects. As one would expect, the incidence of malformations increased with dosage in the groups treated with insulin alone and in those treated with insulin and cortisone. This was true at both developmental stages. A comparison of the effects of insulin treatment with the results of the combined injection of insulin and cortisone shows no significant differences in the incidence of skeletal defects at the 4-day stage, except for a slight but consistent trend of the abnormalities to be more extreme in the groups treated with both hormones, in the groups tested at 8 days, on the other hand, the combined treatment was less teratogenic than injection of insulin alone. For the pooled data of experiments 1 and 2 (with identical ratios of cortisone

to insulin) these differences were highly significant ($\chi^2 = 16.82$, $P < 0.001$), and the same is true for the combination of probabilities for experiments 1, 2 and 3 ($\chi^2 = 30.31$, $df = 6$, $P < 0.001$).

Our results demonstrate clearly that between 4 and 8 days of incubation a change occurs in the reactions of the developing chicken embryo to combined treatment with insulin and cortisone. The older embryos survive better, show less retardation of growth and a lower incidence of skeletal malformations. These differences in response presumably are a reflexion of the homeostatic forces which the incipient functioning of the endocrine systems brings into play. Our observations, secondly, confirm the

report by Lunardo and de Bastiani that cortisone does not potentiate the teratogenic action of insulin. Since our earlier experiments with an extract of adrenal cortex produced very striking potentiation, it must be concluded that this was due not to 17-hydroxy 11-dehydrocorticosterone (cortisone) but to one or more of the other corticosteroids contained in the extract. This we hope to verify in future experiments.

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⁴ Zwilling E. (unpublished observations)
⁵ Lunardo C. and de Bastiani G. *La Clin. Ortoped.* 8: 120 (1950)

MATERNAL CONTROL OF OVARIOLE NUMBER IN THE PROGENY OF THE MIGRATORY LOCUST

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AN integral part of the phase theory of locust transformations is the cumulative transmission of phase characters from one generation to another, so that fully *gregaria* or *solutaria* types can be obtained only when crowding or isolation of the locusts is maintained for several generations. The transmission of phase status to the progeny is held to occur through the accumulation of extra-chromosomal materials in the egg.¹ Early criticisms, understandably in view of the specific status given to the phases previously, held that they were genetically distinct but formed hybrids.

The weight of field and laboratory evidence has now accumulated to the point where the essentially non-genetic nature of this inheritance is taken for granted, although the capacity of expressing it depends patently on the genotype concerned. This striking illustration of what Thoday² has called phenotypic flexibility has received scant notice save for some remarks of Kennedy.^{3,4}

Hunter-Jones⁵ has shown that crowded female desert locusts reproducing parthenogenetically, produce offspring which in colour and weight are typically *gregaria* whereas the same stock of females when isolated, give *solutaria* type larvae. Our experiments show that talotikus parthenogenesis also occurs with the migratory locust, *Locusta migratoria migratoria* R. and F.⁶ Moreover, the number of ovariols in female offspring of isolated unfertilized females ranges from 95 to 105, whereas hatchlings from crowded mothers carry only 75-85 ovariols. We may look to the female reproductive system for some of the clues to this problem.

There seem, in fact to be two physiological processes at work, one of these operates through the vitellus of the egg, the reduction of which by ligaturing after blastokinesis produces larvae which have the *solutaria* coloration (pale green) from crowded stocks of the migratory locust, the normal larvae of which

would be black and heavy.⁶ Generally, weight and colour are closely associated,⁷ both with one another and with the subsequent rate of development and number of moults of some species of locust.⁸ The number of ovariols borne by these ligatured larvae is, on the contrary, typical of *gregaria* populations. Thus the inheritance of this important phase character⁹ seems to be independent of the amount of vitellus remaining in the egg. This distinction, however, may prove to be one of the timing of the processes of ovari formation and larval coloration; in *Melanoplus* and *Drosophila* at least, ovariole number seems to be determined prior to or during blastokinesis.^{10,11}

Table 1. MEAN REGRESSIONS OF OVARIOLE NUMBER ON HATCHLING WEIGHT OF THE MIGRATORY LOCUST REPRESENTING THE INCREASE OF POTENTIAL REPRODUCTIVE CAPACITY FOR A SACRIFICE OF 1 MM WEIGHT AT BIRTH.

| Generation | Regression and subsequent rearing density |
|------------|---|
| I | Crowded (Stock from Musée d'Histoire Naturelle Paris) |
| II | Crowded |
| III | Crowded |
| IV | Crowded |
| V | Crowded 1.27 Isolated 2.85 |
| VI | Crowded 1.90 Isolated 1.75 |
| VII | Crowded 1.27 Isolated 0.93 |

There is in general an inverse relation between weight at hatching and the number of ovariols in locust larvae.¹² The interlocking of these two characters depends on the consistency with which the earlier generations have been kept crowded or isolated. To the extent that we may think of this relationship as a measure of the interchangeability

of reproductive potential (number of ovarioles) and larval mobility (weight of occluded food reserves) the changes of its magnitude are of interest whatever the mechanism of inheritance. Table 1 shows the mean regressions of ovariole number on hatching weight for comparisons made among larvae issuing from one and the same egg-pod. Each pod contains up to 100 eggs derived from a single ovarian cycle in the female. Comparisons across egg-pods or across the progeny from different females are swamped by extraneous sources of variation which themselves depend on the consistency of ancestral density. Generation VI (crowded grand-parents, isolated parents) were 67 times as variable as generation VII, for which isolation was the parental and grandparental regime. Yet even generation VII was 9 times as variable, as a whole, than were contrasts made within egg-pods as are those in Table 1. These varied in precision scarcely at all throughout the experiment.

Crowding leads to a cumulative gain in weight at hatching for a given sacrifice of reproductive potential, and since this sacrifice has evidently not entirely been made good even three generations after crowding was ended we have the longest reach, of any yet recorded, of a density-dependent effect being transmitted to the descendants of the crowded generation. Similar inheritance has, however, been demonstrated in the shorter run with other characters^{6,7}. In a general and less-precise way this inverse relation may be extended to fully *solitaria* and *gregaria* females, the progeny of the *gregaria* are fower and heavier, and have fewer ovarioles compared with the progeny of *solitaria*, nevertheless, both phases produce about 1 gm of living material in each egg-pod.

Setting Limits to Selective Action during the Egg Stage

Our series of 6,000 preparations of the dissected ovaries of several generations of the migratory locust affords an opportunity to set limits to the action of any selective forces operating during the development of the eggs, for the number of ovarioles in the laying female is the upper limit to the number of her progeny from which the issue of any one egg-pod can have been selected, always excluding the possibility of pre-ovogenetic selection. In particular, the sequence of egg-pods laid by isolated females was studied either when the female was left with the male after copulation for the rest of her life, when the number of ovarioles in her progeny steadily diminished, or when the male was removed after 24 hr in the cage, to allow copulation to occur, when no such diminution was observed. The influence of the male, once fertilization has been accomplished, is mildly to disturb the female and to induce a modest amount of those inhibitory effects normally associated with crowding. The mean ovariole number of offspring from a female left with one male drops by one ovariole for each of the 15 or so reproductive cycles that the female undergoes. More drastic crowding augments this progressive loss but also shortens the sequence of reproductive cycles so that the net effect is not greatly different.

'Crowding' the females with a single male produces offspring of which the mean number of ovarioles eventually lies outside the range of the phenotypes initially produced by the same mating pair. At most, less than half this cumulative shift can be attributed to selection, and in fact there is no evidence that any of it is so induced. The absence of such a

shift, in females from whom the male is removed within a few hours of copulation, excludes any influence of age alone on the mother.

Regulation of Fertility and Fecundity in the Migratory Locust

Implicit in the phase theory of locust outbreaks is some autoregulation of fertility or fecundity according to the population density. Our results provide some idea of the nature of such regulation in the migratory locust, other species seem to differ in important respects, and caution is needed in extending these findings to them.

The influence of crowding operates both within and between generations. The distinction between larval and adult crowding is vital for these comparisons, since changes of density rather than the level of the density seem to elicit the regulatory processes. Crowding during the larval instars almost doubles the number of egg-pods laid by the ensuing adult females, whereas adult crowding inhibits the laying female either from fulfilling her potential delivery of egg-pods or from endowing her female offspring with their appropriate complement of ovarioles. In this way larval and adult crowding act in opposite directions, and may substantially nullify one another during consistent crowding. Yet when the larvae are crowded and the adults isolated, as occurs with stragglers from gregarious groups, as many as 1,500 eggs may be laid by each female, when the reverse regime is imposed, only about a tenth of this number is to be expected.

However clearly one may recognize that these ideas relate only to a few aspects of a much wider problem, the control of fecundity in the migratory locust may be regarded as a homeostatic mechanism tending to stabilize population density. In every generation we have found a significant negative regression of ovariole number on hatching weight, which we interpret as a latent ability to exchange larval food reserves for reproductive capacity. When grouped locusts are dispersed, this adjustment is called into play and only fades away when several generations of isolation have failed to restore the population density through an increase in fecundity of the offspring. The last word in these matters often lies with the climate, which can override the locusts' best endeavours at regulation¹³.

Generally, it appears that the ability to produce offspring, the average fecundity of which is well outside the phenotypic range of the parents, lies at the heart of the capacity of migratory locusts to cope with rapidly changing environments. An analysis of growth and of moulting polymorphism in the red and desert locusts led us to conclusions in the same vein⁸. A full account of the experiments on which the present conclusions are based is being published⁹.

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LETTERS TO THE EDITORS

PHYSIOLOGY

An Exteroceptive Block to Pregnancy in the Mouse

EXPERIMENTS on the effect of certain oral progestogens during early pregnancy, in continuation of previous observations¹ on non pregnant animals involved placing a recently mated female receiving oral progestogen with a strange male. In a number of the mice the procedure resulted in failure of pregnancy from the first mating and a new mating within 3-6 days. Control experiments showed that the same effect was produced by dosage with inert material or even without any treatment other than the introduction of a strange male at 24 hr after mating. 20 out of 40 females behaved in this way a far greater proportion than could be attributed to the expected incidence of anovular cycles. Only about 8 per cent of young females, as used, return to oestrus within 4-5 days if removed from the male after their first mating, or copulate again at this time if they are left with the male. Moreover, among the suspect females there was a failure of the pseudo-pregnancy which might have been due to poor stud males. Experiments were therefore undertaken to explore this effect.

Two test situations were devised. Situation A was as already mentioned that is, the recently mated female was paired with a strange partner 24 hr after copulation with the stud male. Situation B was one of proximity without contact, the female being housed in a small cage inside a stock box containing other mice which could climb about the cage but not enter it.

The stud males and all the females were albinos. The test males were either albino or wild type. Young virgin females were mated in pairs with a stud male, the females were removed from the male when the vaginal plug was found and housed together overnight. 24 hr later they were presented with the test situation. The females were generally left in the test situation for 7-10 days, and they were then removed to normal mouse boxes. The pregnant females were isolated before parturition, and females which became pseudopregnant or in which the pregnancy had been blocked received a fertility test with a stud male. The few females which proved to be infertile were excluded. Daily vaginal smears were examined.

The results of these investigations are briefly summarized in Table I.

Pregnancy was blocked and implantation inhibited in nearly 30 per cent of females by the introduction of a strange male within 24 hr of coitus. It was so blocked even by the presence of a castrated male. Pregnancy was not affected by the return of the female to her original stud male or by the presence of a strange female, whether parous or ovariectomized. Contact between the sexes was not necessary for this effect. Pregnancy was also blocked when the female was caged inside the male stock box. Among parous females, pregnancy was less readily blocked than among non parous by contact with a strange male

Table 1. PREGNANCY BLOCK IN THE MOUSE. The females were separated from stud males on finding vaginal plug and housed together until presented with the test situation 24 hr later.

| Test situation | Females having blocked pregnancies | |
|---|---|----------|
| | Proportion | Per cent |
| A Housed with | | |
| | Strange normal male (albino) | 10/69 28 |
| | Strange wild type male | 26/35 71 |
| | Castrated male (albino) | 13/50 26 |
| | Another female (parous or ovariectomized) | 0/48 — |
| B Proximity without contact that is in cage inside stock box containing | Original stud male | 0/32 — |
| | Albino males | 8/32 25 |
| | Wild type males | 52/68 76 |
| | Females | 0/49 — |

but apparently broke down as easily when the female was housed inside the male stock box. This suggests that the latter situation supplies a stronger stimulus.

In both test situations the superiority of the wild type males over the albinos as pregnancy blocking agents was highly significant. The reason for this difference is not understood and as yet male mice of other strains have not been tried. Two different strains of females, one albino and the other pink-eyed champagne, were tested in small numbers in situation B. Both exhibited pregnancy block in similar proportions to those found for the original mice.

The use of the genetically marked wild type test males showed that superfecundation did not occur. Of 35 females 15 mated with the test male. All 15 gave birth to black-eyed young only (123 young). This includes one female in which coitus with the test male took place within a few hours of introduction her litter of 8 black-eyed young being born 10 days later, 20 days after finding the vaginal plug from the stud albino male.

No mutual reaction between females as regards pregnancy block was indicated either when the test situation involved other females or when the mated females were themselves placed singly in pairs or in threes in the test situation. It is well established, however, that females exert a powerful effect upon one another in terms of the oestrous cycle² and the incidence of mammary cancer³ and that the presence of a male tends to synchronize the cycle of non-pregnant females⁴.

Further experiments designed to throw light on the mechanism involved in this pregnancy block of exteroceptive origin are in progress. The pituitary and the hypothalamus are probably both implicated.

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Retinal Responses of Pink Salmon associated with its Downstream Migration

THE seaward migration of juvenile Pacific salmon is usually nocturnal and confined to a relatively brief portion of the night¹. It has been suggested that "as the light intensity falls rheotactic responses, which are to a large degree dependent on vision, fail, and these fish pass down stream in shoals. The fact that such mass movements occur during a rather precise period of the night is probably due to the dark adaptation of the eye and a period of night blindness"². In support of this view, a recent histophysiological examination of the retinae from several species of *Oncorhynchus* has shown an incompletely dark-adapted condition of the retinae at the time of most active downstream migration^{3,4}. As a further test of this hypothesis, the retinae from fish killed at different light intensities during the evening and early morning have been compared with the retinae from fish which were completely adapted to the same light intensities in the laboratory. The pink salmon fry (*Oncorhynchus gorbuscha*), probably the most specialized of the downstream migrant salmon¹, was selected for the study.

Migrant pink salmon were collected from a trap in Jones Creek, British Columbia, and brought into a dark room of the laboratory. Groups of five fish were exposed for 90 min to each of seven light intensities, ranging evenly from 10^2 to 10^{-4} ft-candle. The period of exposure was sufficient to bring about a complete adaptation^{3,4}. Fish captured in the same place and in like manner were placed in glass aquaria which were located in an exposed position in the river where the fish had been migrating. The bottoms of the aquaria were covered with sand and gravel. From these aquaria, fish were sampled at seven times when the incident light intensity reached the same values used in the laboratory. This was done both at twilight and at dawn. Light intensities of 10^{-1} ft-candle and greater were measured with 'Photovolt' model 200 photometer and light intensities below this value with 'Photovolt' model 520-M electronic photometer.

The eyes of teleost fish adapt themselves to altered light conditions by pronounced changes in the distribution of the retinal epithelial pigment and the position of the rods and cones. When the light intensity falls below threshold values, the retinal pigment concentrates and the rods and cones migrate due to the contraction and expansion, respectively, of their myoids. These movements are in direct proportion to the logarithm of the light intensity. Thus in bright light, the rods are shielded by the pigment and the cones placed directly in the path of light, whereas in low light intensities and darkness, the rods are brought directly in the path of light and the cones migrate closer to the concentrated pigment. These processes can be followed by measuring the thickness of the pigment and cone layers. The cones are more obviously delimited for this purpose than the rods. The histological techniques and methods of measuring retinal changes have been described^{3,4}. The values presented here are means for 50 measurements made from 10 eyes in each case.

Fig. 1 shows that both pigment and cone layers of pink salmon retina are in a semi-adapted state when the light intensity is rapidly changing in the morning. The

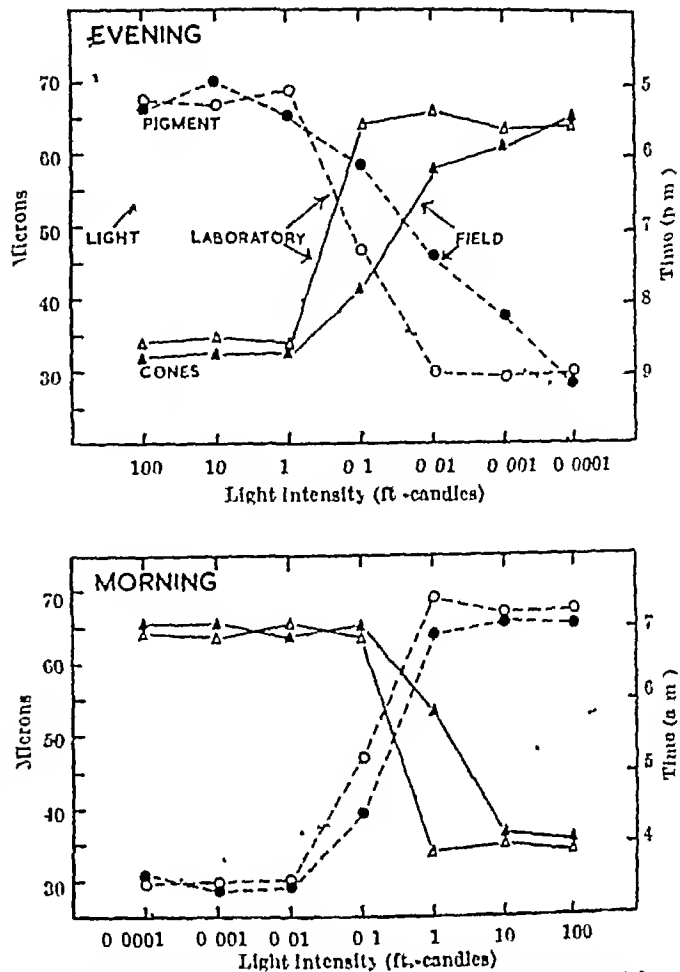


Fig. 1 Thicknesses of the pigment and cone layers of pink salmon retina when fully adapted to a series of light intensities in the laboratory and at the same intensities under conditions of rapidly changing morning and evening light in the field.

picture and the semi-adapted state in Nature is less at dawn than in the evening. This is in accord with an earlier demonstration that light adaptation is more rapid than dark adaptation in this species⁴. Under natural conditions, in the evening, both pigment and cones are in a fully adapted state at intensities above 1 ft-candle. However, between this level (the cone threshold) and 10^{-3} ft-candle the retinae of animals fixed in the field are not as completely adapted as those in the laboratory. At 10^{-4} ft-candle adaptation is the same in both groups. It requires about 45 min (Fig. 1) for the light intensity to fall from 1 to 10^{-4} ft-candle. Ali⁴ has shown that retinal adaptation commences below 1 ft-candle and requires about 45 min to reach a maximum. Thus, the changes in the field are in accord with the laboratory findings. With increasing light, retinal changes are evident at intensities above 10^{-2} ft-candle and adaptation is essentially complete at 1 ft-candle. The rapidity of light adaptation⁴ would seem to account for the small differences found in the fish sampled at dawn. Actually, the changes in light intensity in Nature are somewhat more rapid at dawn than at dusk (Fig. 1).

These findings are in accord with the theory that migration of pink salmon is initiated when the retina is only partially adapted to the decreasing illumination. At Jones Creek, where these observations were made, it was found that 80 per cent of the pink migrants entered the trap between 7 p.m. and 9 p.m. (Pacific standard time) on the nights of the study.

During this period the light intensity decreased below 1 ft candle and reached 10^{-4} ft-candle. It is not to be expected that all the fish will be affected at the same time since there are shaded and exposed areas in every stream. These observations, however, support well the theory that, whether the pink salmon is transported or actively swims downstream¹, its nocturnal movement will be initiated when visual contact with its environment is reduced or impaired. This will be associated with the rather specialized behaviour of rising to the surface of the water at low light intensities¹.

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Deoxyribonucleic Acid Formation in Multiplying HeLa Cells

WHILE studying the behaviour of parasyn-
chronously dividing HeLa cells (Gey), Newton and
Wildy¹ have measured the amount of deoxyribo-
nucleic acid as a function of the time interval between
one division and the next. Their results suggest that
the synthesis of deoxyribonucleic acid occurs during
two periods in interphase: one soon after and one
just before cell division. Between these periods in
mid interphase, there exists an interval during which
the amount of deoxyribonucleic acid (DNA) in the
cell remains approximately constant (Fig 1, curve a).

Partial confirmation of this result, using a micro-
spectrophotometric technique, has been obtained in a
further series of experiments made with randomly
dividing cultures. Replicate cultures of HeLa cells
were grown on cover glasses held in 10 ml hard glass
screw capped bottles. These were made by intro-
ducing into each bottle 1.0 ml Gey's saline containing
30 per cent human serum 0.5 per cent lactalbumin
hydrolysate (Nutritional Biochemicals Inc.), 100
units/ml penicillin, 100 mgm/ml streptomycin and
0.003 per cent phenol red in which were suspended
250,000 separated cells. After incubating at 37° C

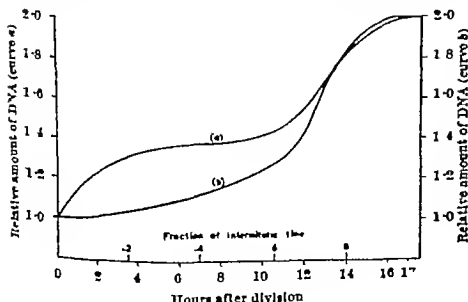


Fig 1

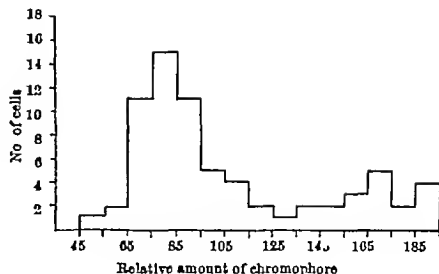


Fig 2

for 36 hr the cultures were fixed in methanol, stained by the Foulgen technique and the amount of chromophore per cell was measured for 70 cells (from two different cultures) by the two wave length technique², using the microspectrophotometer made by M L Mendelsohn³ in the Department of Radiotherapeutics, Cambridge. From these measurements a histogram has been constructed which shows the distribution of the chromophore, and hence the relative amounts of deoxyribonucleic acid, among the individual cells of the culture (Fig 2).

Walker⁴ has shown how the synthesis curve for deoxyribonucleic acid max, with certain restrictions, be constructed from such a histogram. It is believed that the cultures used for the estimation satisfied these conditions. Fig 1, curve b, has therefore been constructed from the histogram of Fig 2.

Comparing the curves in Fig 1, it will be seen that whereas it is not possible to tell from Fig 1b whether the early formation of deoxyribonucleic acid shown in Fig 1 curve a, occurs, there is certainly a rapid synthesis beginning about 5 hr before cell division and continuing up to a comparatively short time before cell division.

The late period of formation of deoxyribonucleic acid agrees with the findings of Walker and Yates⁵ using other kinds of cells and with those of Painter and Drew⁶ using tritiated thymidine on cultures of growing HeLa cells.

It is, however, difficult to explain the failure to detect the earlier rise in deoxyribonucleic acid which was found with parasynchronously dividing cultures though the following two explanations should be considered: (1) that the present method is inadequate for demonstrating such a rise, (2) that the early rise is characteristic only of parasynchronously dividing cells. The latter explanation is thought to be more likely because in such cultures the early rise in deoxyribonucleic acid has never been observed before the first cell division has occurred.

A limit to the end of the synthesis period has been obtained by examining autoradiographs of cultures growing in the presence of tritiated thymidine. After 36 hr growth, tritiated thymidine (Schwarz 3.0 c/mM) was added to the medium to give a concentration of 1 μ c/ml and 30 min later, the culture was fixed in methanol. The cells were afterwards stained with galloxyanin and autoradiographs were prepared. In these although interphase cells were well labelled examination of several hundred cells in all stages of mitosis showed that none of them was labelled. From this it can be deduced that synthesis of deoxyribonucleic acid ends at least 1-1½ hr before the commencement of mitosis, since

the cells were in the thymidine for $\frac{1}{2}$ hr and the duration of mitosis is about 35 min

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Induction of Parthenocarp in *Rosa arvensis* Huds. with Gibberellic Acid

As has been previously reported¹, parthenocarp may be induced in the two non-apomictic species, *R. rugosa* Thunb. and *R. spinosissima* L., by means of α -naphthaleneacetic acid, α -naphthaleneacetamide and 2,4,5-trichlorophenoxyacetic acid. Similar experiments were carried out in an attempt to induce parthenocarpic development in a third non-apomictic species, *R. arvensis*.

The auxin was applied in two ways to the unopened flower-bud, which was emasculated by cutting off the

Since the development of rosaceous fruit after fertilization is characterized by increase in cell size rather than in cell number, the properties demonstrated for gibberellic acid suggested that it might be effective in inducing parthenocarpic development. In February 1958 parthenocarpic hips of *R. rugosa* were produced in the greenhouse by the application of gibberellic acid and shortly afterwards similar results were recorded for *R. spinosissima*¹.

In June 1958, 200 flower buds on a bush of *R. arvensis* were emasculated and 10 per cent gibberellic acid in lanolin was applied. Control groups of normal and emasculated buds were also selected, it had previously been shown that the application of lanolin alone produced no response. Samples from each group were harvested at intervals for determinations of fresh and dry weight, and Fig. 1 shows the development of the different groups of hips in terms of average hip diameter and fresh weight.

The main period of fruit-drop in *R. arvensis* is 3–5 weeks after flowering, 46 days after treatment with gibberellic acid. 107 out of 150 hips were developing parthenocarpically, which represented a fruit-set of 71 per cent compared with 45 per cent for the normal, fertilized hips under these field conditions. None of the emasculated buds developed. Of the 57 parthenocarpic hips allowed to remain until maturity at 14 weeks after treatment, 48 had the appearance of normal, ripe hips while the other nine were smaller and not fully pigmented.

The *Triticum* coleoptile straight-growth test of Luckwill² showed that normal hips appear to contain two acidic, growth-promoting substances having R_F values of 0.1–0.2 and 0.4–0.5 in isopropanol/ammonia/water, and a neutral, growth-promoting substance with an R_F of 0.0–0.1 which is present in small quantities in the bud and flowering stages but which could not be detected 17 days after flowering, or in subsequent assays. None of these three substances was found in either parthenocarpic hips or emasculated controls, but a neutral growth-substance ($R_F = 0.4–0.6$) was present in the emasculated hips and an apparently identical substance was found in the parthenocarpic hips. A consistent growth-inhibitory effect was present in the tests, predominantly in the acid fraction and centred at $R_F 0.8$ in all stages

of normal, emasculated and parthenocarpic hips.

The relationship between achene development and variations in the amount of growth regulators will be reported elsewhere.

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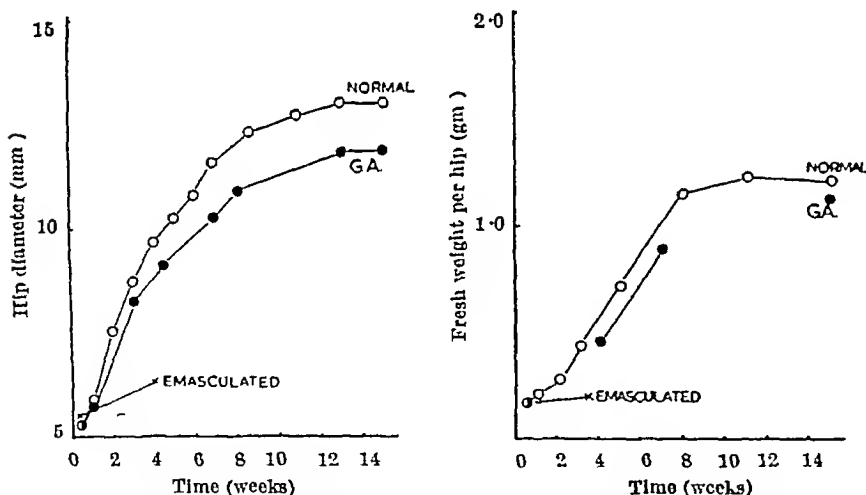


Fig. 1. The growth in terms of average diameter and fresh weight of normal hips, O—O, emasculated flower buds x—x, and emasculated flower buds treated with 10 per cent gibberellic acid in lanolin, ●—●.

'disk' (including the head of stigmas) immediately prior to treatment. In early experiments aqueous solutions of the auxins mentioned above and indoleacetic acid were injected into the cavity of the receptacle in concentrations ranging from 2 to 25 p.p.m. In later work the auxin was applied to the cut surface as a lanolin paste in concentrations of 0.025–1.0 per cent. Since *R. arvensis* differs from the other two species in having a much lower ascorbic acid content³, additional mixtures, including ascorbic acid, were used.

Almost all these experiments produced negative results, the emasculated control hips usually surviving longer than those treated with auxin. Out of a total of about 300 buds treated, only four showed any signs of growth, these had received the lowest concentration of auxins in lanolin and two of them had had ascorbic acid.

HÆMATOLOGY

Anti-A Hæmagglutinins from a Non-Leguminous Plant—*Hyptis suaveolens* Poit

CERTAIN plants, chiefly their seeds, contain agglutinins for the erythrocytes of various species. Whereas most plant agglutinins make no individual distinctions among human erythrocytes, some act selectively on one or other of the following blood group antigens¹ A, A₁, B, H and N. Except for separable anti-H and anti-B agglutinins from the seed capsule of certain species of *Eunymium* of the family Celastraceae, all specific seed agglutinins have hitherto been obtained from Leguminosae¹.

An anti-A agglutinin has now been found in the seeds of *Hyptis suaveolens*, Poit., of the genus Labiatae. The agglutinin works best when a fresh seed extract is tested on a flat tile which is gently and continuously rocked. Although it is not very avid when tested with erythrocytes suspended in isotonic saline solution, it agglutinates A₁ and A₁B cells strongly, A₂ weakly, and fails to agglutinate A₂B cells. Thus *Hyptis suaveolens* seed extract sharply differentiates A₁ and A₁B erythrocytes from those of the weaker subgroups of A and AB; however, it is not as satisfactory for this purpose as *Dolichos biflorus* seed extract², which is far more avid.

The *Hyptis suaveolens* agglutinin acts as strongly at 37° C or 4° C as at room temperature. It does not cross react with B or O cells after 24 hr at 4° C or when erythrocytes are suspended in albumin album, however, potentiates the agglutination of A₁ and A₁B cells. Agglutination is inhibited by A secretor saliva and by AB serum. A full description will be presented elsewhere.

The 'new' agglutinin is of special interest because it is the first seed anti-A (anti-A₁) agglutinin to be found outside the Leguminosae. The current trend is to confine the search for specific seed agglutinins to leguminous plants; wide examination of other plant families might be profitable.

I am grateful to D. S. Das for collecting the seeds and for technical assistance. The seeds were identified by the Botanical Survey of India, Poona.

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Interaction of Erythrocytes and Endotoxins

CONSIDERABLE diversity of opinion exists as to the sensitivity of hæmagglutination tests. The discrepancy in results may to some extent be attributed to technical differences. The factors influencing the reaction, the elution of endotoxin *in vitro* and the uptake by erythrocytes *in vivo* have been examined using a dehydrated endotoxin derived from *S. typhi* (TO-901). This powder consisted of 88.5 per cent ash, 7.8 per cent moisture, 1.6 per cent protein, 2.3 per cent lipids and based on L-rhamnose hydrate as standard, 2.7 per cent rhamnose. If the method of calculation described by Webster *et al.*¹ is adopted the polysaccharide content is 14.3 per cent and the endotoxin approximately 20 per cent. The powder was dissolved in isotonic saline heated to 56° C for

30 min and stored at 4° C for at least 24 hr before use. The solution had a slight buffer action, pH 7.2. Erythrocytes from healthy rabbits were washed and measured with the hæmato-crit. A volume of 0.2 ml packed cells was used in most experiments.

Endotoxin was adsorbed on to the washed and measured erythrocytes at 37° C for 1 hr. The cells were then washed three times in 6-8 volumes of isotonic saline and accurately made up to a 20 per cent suspension. Agglutination was performed on slides, using 0.05 ml of sensitized erythrocytes and an equal volume of a diluted standard TO serum. The slide was agitated regularly and the test read after exactly 10 min.

The amount of endotoxin adsorbed on erythrocytes was dependent on both the absolute quantity of endotoxin available and on its concentration. The speed of the process was proportional to the concentration of endotoxin and related to the temperature, being five to six times faster at 37° C than at 4° C.

Erythrocytes coated with very small amounts of endotoxin were unagglutinable in antiserum, whereas those with greater quantities of endotoxin agglutinated readily. This afforded the basis for the determination of an 'erythrocyte-agglutinating unit', defined as the smallest amount of endotoxin, incubated with 2 ml of 10 per cent erythrocytes for 1 hr at 37° C, which rendered the cells agglutinable in standard serum diluted 1 in 10. One erythrocyte agglutinating unit was found to be equivalent to 0.16 mgm of the dehydrated powder. The quantity of crude endotoxin adsorbed on erythrocytes in these circumstances was 0.12 mgm, thus removing 75 per cent of endotoxin from the supernatant. Assuming the crude powder contains 20 per cent endotoxin it appears that 0.2 ml of agglutinable packed cells under our experimental conditions must be coated with a minimum of 24 µgm. of endotoxin.

Erythrocytes, initially sensitized with sub-agglutinable quantities of endotoxin, became agglutinable on subsequent exposure to endotoxin provided that the sum of the two doses constituted at least one erythrocyte agglutinating unit. Thus the erythrocytes appear to bind the adsorbed endotoxin quite firmly.

Assuming that the endotoxin was not removed or rendered undetectable except by fixation to erythrocytes the reduction in endotoxin content as measured by determination of the erythrocyte agglutinating unit on the supernatant, will be a direct, quantitative expression of adsorption. Experiments along these lines indicated that erythrocytes were capable of binding at least 200 times the minimum amount required for agglutination under standard conditions, that is to say 0.2 ml packed cells could adsorb more than 200 × 24 µgm or 4.8 mgm of endotoxin as calculated, corresponding to 2.2 per cent of their own weight.

Erythrocytes of the same batch, coated with amounts of endotoxin ranging from 1 to 200 erythrocyte agglutinating units, gave final agglutination titres against the standard serum ranging from 1/10 to 1/1,280. Hence, the titre of a given serum will vary according to the quantity of endotoxin adsorbed on to the cells. This may explain, at least partially, the discrepancy and inconsistency in results obtained by hæmagglutination tests, it could be overcome by rigorous standardization for which accurate measurement of endotoxin is essential.

Fluon of endotoxin at our experimental conditions (pH 7.2-7.3) was minimal. Erythrocytes coated with 1/5 times minimum agglutinating dose of endotoxin

were still agglutinable after 12 washings in saline at room temperature. Thus, on the assumption that the stability of an erythrocyte suspension is unaffected by washing, it may be concluded that elution is of a low order. Since this could not be measured in erythrocyte-agglutinating units, a technique for estimating smaller quantities of endotoxin in solution was provided by the construction of a dose-response graph in rabbits. The maximum antibody response, as measured by bacterial agglutination, was directly proportional to doses of crude endotoxin ranging from 0.01 μ gm to 1 mgm. Using the dose-response technique for endotoxin estimation, further studies on elution at room temperature showed that endotoxin was released, but that this did not amount to 1 per cent of the adsorbed endotoxin per equivalent volume of saline. Whether the eluted endotoxin originated from intact or disintegrated erythrocytes has not as yet been established, but it is noteworthy that the washings caused slight haemolysis.

Sensitized, washed cells inoculated intravenously into non-immune rabbits were highly antigenic. A single injection of a suitably adjusted erythrocyte suspension produced, in 7-10 days, agglutination titres up to 1:100,000. The serum of a rabbit previously immunized by endotoxin produced haemagglutination *in vitro* against its own sensitized cells. Haemolysis occurred on the addition of complement. Intravenous inoculation of 20 ml of 50 per cent suspension of these erythrocytes, which agglutinated *in vitro* with the recipient's serum, boosted the antibody production. The animals failed to produce an acute intravascular episode. Nor was there conclusive evidence of a haemolytic process as measured by serum bilirubin estimations and Schumm's test. This tolerance of what is a serologically incompatible transfusion is unexplained.

In vivo sensitization in rabbits was demonstrated by intravenous injection of large doses of endotoxin. The animals were bled 4 hr later and the erythrocytes, washed six times in excess saline, were inoculated intravenously into non-immune rabbits. They responded with a significant antibody production. Which part the adsorption *in vivo* plays in the defence against endotoxins has not as yet been established.

Details of these experiments will be published elsewhere.

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BIOCHEMISTRY

Interaction of Sucrose Stearate with Starch

It is generally agreed that changes in the starch component of flour are responsible for the staling of bread¹. Following a report by Bohn² that the stearates are effective as anti-staling agents, a study of the interaction of starch with sucrose stearate, kindly

provided by Dr. J. H. B. de Vries, was made. Addition of a sucrose stearate solution to a 1 per cent solution of 'AnalaR' starch in 0.1 per cent sodium chloride resulted in the precipitation of some starch. The maximum amount of precipitate (about 20 per cent of the weight of starch) was obtained with concentrations of sucrose stearate above 0.06 per cent.

Extension of the study to undegraded starches (Table 1) showed that the amount of precipitate depended upon the type of starch. Fractionation of the potato starch into amylose and amylopectin³ followed by precipitation with excess sucrose stearate showed that most of the amylose but little of the amylopectin was precipitated (see Table 2). Treatment with excess sucrose stearate of an artificial mixture of amylose and amylopectin in the ratio in which they occur in starch gave a figure intermediate between that of the whole starch and that which would be expected on the basis of the separate amylose and amylopectin precipitations. These results indicate that the amylopectin is precipitated more efficiently in the presence of amylose than in its absence.

Table 1 PRECIPITATION OF STARCHES BY SUCROSE MONOSTEARATE

| Type of starch | Polysaccharide concentration (per cent) | Sucrose monostearate concentration (per cent) | Precipitate (per cent of polysaccharide) |
|-------------------|---|---|--|
| 'AnalaR' starch | 1.0 | 0.1 | 21.6 |
| Potato starch | 1.0 | 0.1 | 70.0 |
| Wheat starch | 1.0 | 0.1 | 92.4 |
| Waxy maize starch | 1.0 | 0.1 | 13.0 |

Table 2 PRECIPITATION OF STARCH FRACTIONS BY SUCROSE MONOSTEARATE

| Type of starch fraction | Polysaccharide concentration (per cent) | Sucrose monostearate concentration (per cent) | Precipitate (per cent of polysaccharide) |
|---|---|---|--|
| Potato starch | 0.4 | 0.04 | 72.7 |
| Potato amylose | 0.4 | 0.04 | 70.0 |
| Potato amylopectin | 0.4 | 0.04 | 11.1 |
| 20 per cent amylose 80 per cent amylopectin | 0.4 | 0.04 | 43.9 |

Controlled acid hydrolysis of potato starch showed that a high molecular weight was important in determining the amount of precipitate formed with sucrose stearate and it is likely that the low yield of precipitate from 'AnalaR' starch could be attributed to this factor.

A study of the change in diameter of wheat starch granules on heating in aqueous suspension in the presence and absence of sucrose stearate showed that the rate of swelling was reduced in the presence of sucrose stearate. From an examination of the change in turbidity on heating wheat starch suspensions (0.1 per cent), it appeared that in the presence of 0.01 per cent sucrose stearate the gelatinization temperature is raised about 10 deg.

As sucrose stearate is firmly bound by starch, it seemed likely that it would interfere with the starch/iodine reaction. This was shown to be so, and that iodine and sucrose stearate compete for the amylose fraction. There was no evidence for any marked interaction between sucrose stearate and amylopectin by this technique. It is possible that the stearate chain of the sucrose stearate mole-

cule occupies a position down the centre of an amylose helix, in the same way that iodine does¹

A complete account of this work will be published elsewhere

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Influence of X-Rays on the Activity of Carbonic Anhydrase in Erythrocytes and on their Haemolytic Resistance

SINCE sickle cell anemia is possibly related to the activity of carbonic anhydrase¹, it is of interest to find some way of inhibiting the enzyme without altering the resistance of the cell membrane. Carbonic anhydrase is very stable² but its activity can easily be changed experimentally by adjusting the pH and temperature, or by adding sulphonamides or certain organic ions. All these factors, however, have a marked influence on hemolysis, whereas erythrocytes seem to be rather resistant to X rays³. We therefore decided to examine whether carbonic anhydrase could be inhibited by a dose of X rays which would have little or no effect on hemolysis.

For the determination of the enzyme activity we designed an improved Warburg technique⁴. This method is based upon measuring the rate of evolution of carbon dioxide when a bicarbonate solution is treated with a buffer and the enzyme. We calculated the unimolecular velocity constant of the reaction, which is also used as an index of activity by Mitchell, Pozzani and Fessenden⁵. The standard error of our measurements was 12 per cent and for the non-catalysed reaction 4 per cent. As a measure of the hemolytic resistance we used the hemolytic index⁶, the highest in conventional experimental conditions⁶, the highest dilution of lysin which produces 100 per cent hemolysis within 2 hr. The standard error of our hemolytic indices was 2.5 per cent. Suspensions of 10⁹ cells/cm³ in physiological saline solution were irradiated in vessels of 2 cm³, dose 100,000 r, instrument Philips 'Compacta', 210 kV, h.v.l. = 4 mm of aluminium, dose rate 6,700/min.

In non irradiated blood we found the following carbonic anhydrase activities, calculated per cubic centimetre of full blood: ox blood, 1.85 Mitchell units; human blood, 1.4; chicken blood 1.2. Irradiations of four samples of ox blood, two samples of human blood and two samples of chicken blood had no effect on the activity. Repeating this dose after 24 hr yielded no inhibition. Solutions of purified enzyme (Schering's 'Cataso', 0.1 per cent) treated in the same way, showed an inactivation of 20 and 50 per cent respectively. The fact that these high doses of X rays do affect erythrocytes in other respects was shown by their hemolytic index.

In our controls this was 13,300 with saponinum album (Morch), after irradiation the index was increased by 10 per cent and after the second dose of 100,000 r the increase was 17 per cent.

Our experiments confirm the great stability of carbonic anhydrase, and indicate that this stability is still greater inside the red blood cell. We found no decrease in activity of the carbonic anhydrase of erythrocytes after irradiation with 200,000 r. The hemolytic resistance of the cells was clearly diminished by this dose, so that it is possible that irradiation by X rays will permit us to modify the structure of the cell membrane without altering its carbonic anhydrase activity.

We wish to thank Prof. R. Ruysen for advice and encouragement and Prof. Van Vaeckenberg, who provided the necessary X ray equipment.

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A Method for distinguishing between α - and β -Glycosides by the use of Plant Haemagglutinins (Lectins)

SEVERAL plant seeds contain proteins that agglutinate red blood cells^{1,2} as do many antibodies. For these proteins the name 'lectins' has been suggested³. They can be as specific as animal antibodies in that they react only with erythrocytes of certain blood groups. The ABO blood group specific lectins—as well as the ABO specific antibodies—are inhibited by some simple sugars, mainly components of blood group polysaccharides^{4,5}. Several 'unspecific' lectins are also inhibited by simple sugars, but these sugars are not necessarily components of blood group polysaccharides^{6,7}. The explanation of this phenomenon is that the sugars the structure of which most closely resembles the specific (sugar) group of the red cell receptor attach themselves to the active site(s) of the lectin molecule thus blocking them.

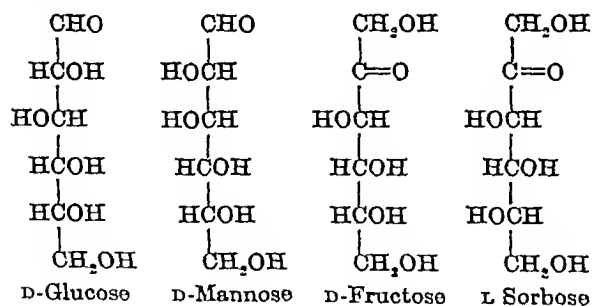
A monosaccharide as a rule retains its inhibiting power even when linked to other sugars through the hydroxyl group of the first (in ketoses the second) carbon atom⁸. The type of link, whether α or β , seems to be significant. In order to throw light on this problem, I made plant agglutinin inhibition tests by a method described in detail elsewhere⁹.

The following sugars were used in all experiments:
D glucose D glucosamine N-acetylglucosamine D

glucuronic acid, D-gluconic acid, D-xyllose, D-mannose, D-fructose, L-sorbose, D-galactose, D-galactosamine, N-acetyl-D-galactosamine, D-fucose, L-arabinose, D-talose, L-galactose, L-fucose, D-arabinose, D-ribose, D-digitoxose, L-rhamnose, maltose, sucrose, turanose, trehalose, cellobiose, gentiobiose, melibiose, raffinose, and lactose

Seeds of *Pisum sativum* L., *Cytisus sessilifolius* L., *Bandeiraea simplicifolia* Benth., and *Crotalaria juncea* L. were used. The lectin solutions were prepared by incubating a mixture of seed powder (1 part) and physiological saline (9 parts) for 2 hr at 37° C. After centrifugation the supernatant was used. 0.05 ml of seed extract containing 2-4 agglutinating doses of lectin and 0.05 ml of sugar solution (pH 7.0) in saline were mixed, and after 30 min incubation at 20° C 0.05 ml of a suspension containing 3 per cent human red cells in saline was added. After 2 hr further incubation at 20° C the tubes were read for agglutination. The quantitative inhibiting power of the sugars was measured by preparing two-fold serial dilutions of them.

The results are shown in Tables 1 and 2. The figures give the final concentration of sugar. Of the sugars tested (see above) only those which inhibit either *Pisum sativum* or *Cytisus sessilifolius* lectin at a concentration of 0.08 M are included in Table 1. The *Pisum* lectin is strongly inhibited by D-glucose, D-mannose, D-fructose and weakly by L-sorbose. The structural differences between the first three sugars are confined to carbon atoms 1 and 2. L-Sorbose differs from D-fructose only with regard to carbon atom 5, but its inhibiting activity is far lower. D-Glucuronic acid and D-gluconic acid are not inhibitory.



It will be seen from the second part of Table 1 that α -glucosides inhibit agglutination by *Pisum* extract as effectively as D-glucose, while β -glucosides are not inhibitory. Sucrose is not only an α -glucoside but a β -fructoside as well, however, the fructose

Table 1

| Sugar | Minimum amount of sugar (m moles/l) inhibiting the action of | |
|--------------------------|--|-------------------------------------|
| | <i>Pisum sativum</i> lectin | <i>Cytisus sessilifolius</i> lectin |
| D-Glucose | 1.25 | >80 |
| D-Glucosamine | 5 | >80 |
| N-Acetyl D-galactosamine | 2.5 | >80 |
| D-Mannose | 0.6 | >80 |
| D-Fructose | 2.5 | >80 |
| L-Sorbose | 40 | >80 |
| (Lactose) | >80 | 40 |
| Maltose | 1.25 | >80 |
| Sucrose | 2.5 | >80 |
| Turanose | 0.6 | >80 |
| Raffinose | 0.6 | >80 |
| Lactose | >80 | 5 |
| | | 40 |

that any of it is so

Table 2

| | Minimum amount of sugar (m moles/l) inhibiting the action of | |
|--------------------------|--|---------------------------------|
| | <i>Bandeiraea simplicifolia</i> lectin | <i>Crotalaria juncea</i> lectin |
| D-Galactose | 0.6 | 5 |
| D-Galactosamine | 5 | >80 |
| N-Acetyl D-galactosamine | 0.4 | |
| D-Lucose | 2.5 | 20 |
| L-Arabinose | 5 | 20 |
| D-Talose | 20 | |
| L-Rhamnose | 40 | >80 |
| α -Galactosides | 0.3 | 5 |
| β -Galactosides | 0.3 | 20 |
| Lactose | 20 | 1.25 |

part is not probably responsible for the inhibition, since another β -fructoside, raffinose, has no effect on *Pisum* lectin. An agglutination by *Cytisus* extract, on the other hand, is inhibited by β -glucosides but not by α -glucosides. The failure of glucose itself to inhibit the *Cytisus* lectin is difficult to explain unless it is due to the hexose molecule being too small.

It seems possible, on the basis of the above results, to ascertain the type of the glycosidic link (α or β) of D-glucose, perhaps also of glucosamine, acetylglucosamine, D-mannose, in disaccharides and other oligosaccharides the structure of which is only partially known.

There are other lectins (*Bandeiraea simplicifolia* and *Crotalaria juncea*) by means of which it seems possible to obtain information of the type of the D-galactosidic (and perhaps D-fucosidic, L-arabinosidic, etc.) link, even though the differences between α - and β -galactosides are less definite (Table 2) than differences between α - and β -glucosides (Table 1). Unfortunately the number of galactosides tested is small.

If need be, the determinations can be made with 0.01-1 mgm of sugar, and the solution need not be pure, many amino-acids and other sugars, for example, do not interfere. There are other methods of studying the nature of the glycosidic link, but the amount of sugar needed for enzymatic or polarimetric studies is greater. The information obtained by chromatographic or infra-red spectrographic studies is limited unless an adequate stock of reference compounds is available.

Of the seeds quoted above only those of *Bandeiraea simplicifolia* may be difficult to get. The rest are obtainable from many seed shops, and can even be replaced by other related species. The *Bandeiraea* lectin is blood group B specific—it can be used with B erythrocytes only, and *Cytisus* lectin is O(H) specific—it should be used with O cells. The other lectins can be used with red cells of any blood group.

The ability of lectins to differentiate between α - and β -glycosides supports J. Lederberg's (personal communication) suggestion that there is some connexion between them and plant glycosidases. Lectins are not, however, likely to be true glycosidases because (a) they are present in ungerminated seeds and their amount does not increase appreciably after germination, (b) there is no correlation in occurrence between lectins and glycosidases in plant species, and (c) several purified lectin preparations have been found not to hydrolyse the disaccharides which inhibit agglutination.

The monosaccharide specificity of lectins seems to be less definite than that of glycosidases, though

glycosidases are not strictly specific, the members of a certain homomorphous sugar series (sugars with an identical pyranose or furanose ring) behave more or less alike as substrates of glycosidases³, but many lectins are inhibited by members of two homomorphous series. These series can differ with regard to the substituents of carbon atom 2. Thus *Phaseolus* lectin is inhibited by D-glucose and D-mannose. *Bandeiraea* lectin by D-galactose, D-fucose, L-arabinose and D-talose (see above) and *Lotus tetragonolobus* lectin by L-galactose, L-fucose, D-arabinose and D-deoxy-L-talose⁴. The substituents in carbon atoms 3 and 4 seem to be of the greatest importance to the capacity of monosaccharides to inhibit lectins, a view which was expressed six years ago by Morgan and Watkins⁵ with regard to *Lotus tetragonolobus* lectin.

I wish to thank Mr E. R. Vaughan, curator, Botanical Garden, University College of Ghana, who kindly sent me several samples of *Bandeiraea simplicifolia* seeds.

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Reactivity and Interrelationship of Intermediates in the Hydrolysis of p-Nitrophenyl Acetate Catalysed by Chymotrypsin

KINETIC studies by Gutfreund and Sturtevant¹ suggest that p-nitrophenyl acetate reacts with chymotrypsin rapidly at a pH greater than 6.5 to

form monoacetyl chymotrypsin (AC-I) and that AC-I is then deacylated slowly. The kinetic observations are consistent with the esterification of a single serine hydroxyl of the enzyme². In contrast, spectroscopic studies³ of the deacylation of monoacetyl chymotrypsin formed at pH 5.0 and isolated according to the procedure of Balls and Wood⁴ (AC-A) show that when AC-A is brought to pH 9.0, a rapid increase in absorption at 245 mμ occurs which is followed by slow decay of the absorption peak. Since both the absorption peak and its rate of decay appeared characteristic for N-acetyl imidazole, Dixon and Nourah⁵ suggested that the deacylation of monoacetyl chymotrypsin proceeds by a rapid intramolecular shift of the acetyl group from a serine oxygen to an imidazole nitrogen of the enzyme (AC-II) and that the rate-limiting step of the enzymatic reaction is the base-catalysed hydrolysis of N-acetyl imidazole. Recently however we have observed⁶ that AC-I and AC-A are deacylated at different rates as measured by the liberation of p-nitrophenol from p-nitrophenyl acetate catalysed by AC-I and AC-A and that AC-I is converted to AC-A under the conditions used in the isolation procedure⁶.

The result of investigations reported below further delineate the differences between AC-A and AC-I and suggest an interrelationship between AC-A, AC-I and AC-II as well as a structure for AC-A. The experiments illustrated in Fig. 1 indicate that AC-A (salt free α-chymotrypsin, recrystallized three times, gift of the Sigma Chemical Co., St. Louis, Missouri) cannot be deacylated via a single intermediate which decomposes with a single rate constant identical with the rate of decay (1.7×10^{-3} sec⁻¹)⁶ of the 245 mμ absorption peak. Curve 1 represents α-chymotrypsin preacylated for 10 min. at pH 5.0 with 100 equivalents of p-nitrophenyl acetate and mixed at zero time with buffer such that the final pH was 8.0. Zero-order steady state liberation of p-nitrophenol is observed within 15 sec. The rate of deacylation (k_d) of this enzyme (AC-I) calculated from the observed rate of liberation of p-nitrophenol is 1.6×10^{-3} sec⁻¹ at 15°C. Curve 2

represents an experiment in which AC-A was mixed at zero time with p-nitrophenyl acetate at pH 8.0. The rate of liberation of p-nitrophenol during the first 30 sec. is only about 70 per cent of the rate observed in curve 1 (AC-I) and essentially the same as AC-I after 300 sec. The deviation from zero-order kinetics observed during the first 300 sec. of the reaction of AC-A with p-nitrophenyl acetate is interpreted as indicative of the rates of reactions involved in the conversion of AC-A to AC-I. These reactions are presumably the deacylation of AC-A and its reacylation at pH 8.0 to form AC-I. However, the rate of conversion of AC-A to AC-I is incompatible with the complete deacylation of AC-A via the imidazole intermediate as can be seen

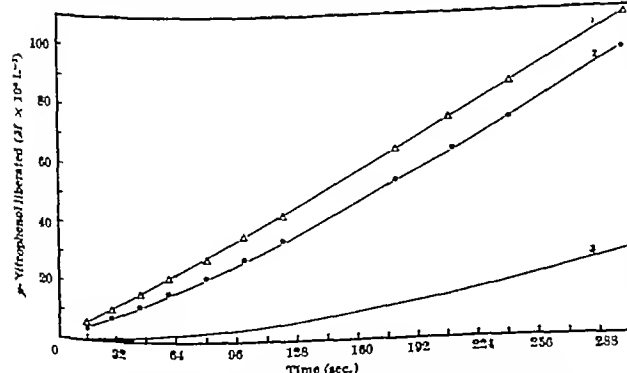


Fig. 1. The liberation of p-nitrophenol in the catalytic hydrolysis of p-nitrophenyl acetate by α-chymotrypsin and monoacetyl-α-chymotrypsin preparations. Curve 1: α-chymotrypsin, 0.12 M, in 0.1 M Tris-(hydroxymethyl)-aminomethane-maleate buffer, pH 8.0 at 15°C. Total ionic strength 0.12 M. $[E]_0 = 2.1 \times 10^{-3}$ M, $[S]_0 = 1.7 \times 10^{-2}$ M. Curve 2: monoacetyl-α-chymotrypsin, 0.12 M, in 0.1 M Tris-(hydroxymethyl)-aminomethane-maleate buffer, pH 8.0 at 15°C. Total ionic strength 0.12 M. Curve 3: α-chymotrypsin, 0.12 M, in 0.1 M Tris-(hydroxymethyl)-aminomethane-maleate buffer, pH 8.0 at 15°C. Total ionic strength 0.12 M. Curve 1: α-chymotrypsin preacylated for 10 min. at pH 5.0 with 100 equivalents of p-nitrophenyl acetate at pH 5.0 and 15°C, and then mixed with buffer at zero time to bring the pH to 8.0. Curve 2: isolated monoacetyl-α-chymotrypsin (ref. 4) (AC-I) curve 3: a calculated curve for the catalysis of p-nitrophenyl acetate by a monoacetyl enzyme which is deacylated with a rate of 1.7×10^{-3} sec⁻¹.

Activation of Staphylococcal-free Coagulase by Purified Human Prothrombin

FREE coagulase¹ is an extracellular protein produced by pathogenic staphylococci², which reacts with coagulase activator³, present in the plasma of certain animal species, to yield an active material capable of clotting any fibrinogen¹. The active material has been called activated coagulase⁴ and has been shown recently, by a study of the kinetics of the reaction between purified free coagulase⁵ and an impure preparation of coagulase activator, to be produced during the enzymic degradation of the former by the latter. This work, however, shed no light on the vexed problem of the nature of coagulase activator²⁻⁵, owing to the inhomogeneity of the coagulase activator preparation employed.

Through the kindness of Dr F Duckert of the Medizinische Universitätsklinik, Zurich, we have been able to repeat some of these experiments, using, as the source of coagulase activator, a highly purified sample of human prothrombin prepared by chromatography on barium sulphate and 'Hyflosupercel' by a slight modification of the method used by Duckert, Koller and Matter¹⁰. This material contained about 1,000 units of prothrombin and 160 units of coagulase activator per mgm protein, and was thus enriched between 600 and 700 times (Dr Duckert, private communication).

Solutions of prothrombin in phosphate buffer (0.07 M disodium hydrogen phosphate-potassium dihydrogen phosphate, pH 6.8) were incubated at 37° C with various concentrations of free coagulase and activated coagulase was assayed in the mixtures as already described⁴. The results, which are summarized in Table 1, are essentially similar to those obtained previously⁴ and demonstrate the instability of activated coagulase under these conditions. The concentration of activated coagulase produced and the length of time before its exhaustion are directly dependent upon the initial concentration of free coagulase in the mixture. These facts, together with the finding that the exhausted mixtures still contain coagulase activator but no free coagulase, confirm that free coagulase is enzymically degraded by coagulase activator.

Table 1 FORMATION AND DESTRUCTION OF ACTIVATED COAGULASE IN MIXTURES CONTAINING A CONSTANT AMOUNT OF PURIFIED HUMAN PROTHROMBIN AND VARIOUS AMOUNTS OF FREE COAGULASE

Values given are for the concentration of activated coagulase (units/ml)

| Incubation time of mixture at 37° C (hr) | Concentration of coagulase (units/ml) added to an equal volume of purified human prothrombin (250 µgm/ml) | | | |
|--|---|-----|------|------|
| | 25 | 10 | 5 | 2 |
| 0 | 3.3 | 1.0 | 1.2 | 0.5 |
| 1 | 4.3 | 2.8 | 1.4 | 0.0 |
| 2 | 4.0 | 2.8 | 1.4 | 0.0 |
| 3 | 4.0 | 2.4 | 1.4 | 0.5 |
| 4 | 3.8 | 2.4 | 0.9 | 0.3 |
| 5 | 4.3 | 1.5 | 0.8 | 0.25 |
| 6 | 4.0 | 1.4 | 0.0 | 0.23 |
| 8 | 3.0 | 0.8 | 0.5 | 0.17 |
| 22 | 1.5 | 0.9 | 0.34 | 0.08 |

After incubation for 22 hr the mixtures were divided into three portions and to (a) was added an equal volume of prothrombin 190 µgm/ml, to (b) an equal volume of coagulase 25 units/ml and to (c) an equal volume of buffer. They were then incubated for 10 min and the activated coagulase content measured as before.

| | a | b | c |
|------|-----|------|------|
| 0.5 | 0.5 | 0.12 | <0.1 |
| 2.7 | 3.1 | 2.7 | <0.1 |
| 0.13 | 0.5 | 0.13 | <0.1 |

In view of the highly purified nature of the human prothrombin used as a source of coagulase activator, it seems likely that the two are identical. This suggestion is supported by the observation that the ratio of prothrombin to coagulase activator in normal human plasma is identical with that in the present highly purified preparation of prothrombin.

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CHEMISTRY

Separation of Polyvinyl Chloride and Polyvinyl Acetate by Chromatographic Methods

THE material used in this work was known to contain at least two co-polymers. A method of separation was sought which would not require a complex chemical procedure. The separation of high polymers by chromatographic means was carried out by Claesson¹, while separations on columns packed with carbon black were attempted by Landler².

It was found that absorption decreased with increased molecular weight. A column of activated charcoal was packed and saturated with methyl iso-butyl ketone. The mixture containing the two co-polymers in this solvent was added to the top of the column and washed with the solvent. After a few minutes, the elutant was giving a positive test for chloride. After 1 hr washing the fractions began to give positive acetate results.

In order to attempt some form of confirmation, a method of separation was devised by paper chromatography.

The mixed co-polymers in solution were spotted on to a strip of Whatman's No. 4 filter paper and air-dried. This strip was then allowed to run at room temperature for 45 min, using once again methyl iso-butyl ketone as a solvent. The strip was then air-dried and sprayed with a solution of one part BDH Universal indicator and one part distilled water. The whole strip was then washed in distilled water and dried. The acetate spot remained stationary, while the chloride moved with the solvent front. *R_F* values were zero for chloride 0.985 and 0.0 for the acetate. Both spots were eluted, yielding positive tests for acetate and chloride, respectively.

To determine the accuracy of the separation, two pure polymers of acetate and chloride were mixed in the solvent. These were then spotted on to a No. 4 filter paper and run as a control. Identical results were obtained as with the mixed co-polymers.

This method is not suggested as an analytical procedure but as a rapid means of separating mixed polymers.

Further details of this work will be published elsewhere

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A New Method for working up Processing Mixtures containing Anhydrous Aluminium Chloride

On working up the mixture in order to isolate the products of reactions catalysed by anhydrous aluminium chloride, the first step is usually decomposition with an ice acid mixture¹. However, difficulties are often encountered in the separation of the aqueous phase containing the aluminium salts, due to the formation of stable emulsions. This makes the repeated washing of the organic phase necessary to ensure complete extraction of the aluminium salts, a rather tedious operation.

In our experiments we found that a solution of sodium fluoride could be used with advantage at this stage, and also to eliminate interference during later stages. The favourable effect is due to the formation of the complex Na_2AlF_6 , which is soluble in water. The advantages of the method may be summarized as follows:

1 The aqueous solution, when it contains sodium aluminium fluoride, is readily and quickly separable from the organic phase, in our experiments, nitrobenzene.

2 When the second step of working up the reaction mixture is steam distillation of an alkaline solution no separation of the aqueous phase is necessary. Further as the aqueous phase is already alkaline, no addition of alkali is required to secure the alkaline reaction of the medium.

3 When a neutral solution is wanted during processing, a slightly acidified solution of sodium fluoride can be used. The exact amount of hydrochloric acid necessary can be determined by blank tests on a solution of anhydrous aluminium chloride at the same concentration as the reaction mixture. These blanks are of great importance as the quantity of acid required depends on the quality of the sodium fluoride.

4 Since the method facilitates the working up and analysis of very small quantities, it is particularly suitable for micropreparation and kinetic studies. Although stoichiometrically 6 moles of sodium fluoride are required for each mole of aluminium chloride, we find it best to use at least 7 moles of the reagent.

As an example, part of an unpublished kinetic study will be given here, where a quantitative determination of the ketone was carried out on the mixture obtained by the Fries rearrangement of thymyl acetate in nitrobenzene in the presence of aluminium chloride.

Preparation of thymyl methyl ketone 2.4031 gm (12.4 mmoles) of 99.14 per cent thymyl acetate was treated with a solution of 4.17 gm (31.3 mmoles) of anhydrous aluminium chloride (B.D.H.) in nitro-

benzene, and the mixture was made up to 20 ml with nitrobenzene. The mixture was allowed to stand for 5 hr in a thermostat of 40° C, and then an aliquot of 2 ml was transferred by pipette into an equal volume of ethanol. This mixture was refluxed for 30 min with 30 ml of a solution of sodium fluoride (containing 35 gm sodium fluoride) 3 ml of 1 N sodium hydroxide and 24 ml of ethanol. After cooling the solution was made up at room temperature to 100 ml with water and allowed to stand overnight in a glass cylinder, 2.5 cm in diameter when nitrobenzene separated. A portion of 50 ml was withdrawn from the clear supernatant with a pipette treated with 3 ml of 1 N hydrochloric acid and distilled until the temperature of vapour reached 98° C (approximately 5 min.). The residue was allowed to stand for 2 hr in an ice box, then the precipitated crystals were filtered through a glass filter, dried at 110° C for an hour and weighed together with the filter. Thymyl methyl ketone was then separated from inorganic contaminants by treating the filter with 3-5 ml of hot ethanol. After drying the filter for 20 min. at 110° C, it was again weighed. The difference was 0.0881 gm. The almost white crystalline product obtained by evaporating the ethanolic solution had a melting point of 122.5-125° C. For $\text{C}_{11}\text{H}_{18}\text{O}_2$, molecular weight 192.25, calculated (per cent): C 74.07, H 8.39, found (per cent): C 74.95, H 8.07.

The ketone obtained by the classical Rosenmund method² was nearly black, m.p. 116-122° C.

The correction for the solubility of the ketone gives a gross yield of 0.092 gm., thus by the Fries rearrangement a yield of 94.6 per cent was obtained. With suitable modifications the quantity of unconverted ester can also be determined by titration³.

We wish to thank the Hungarian Academy of Sciences for a grant and the Microanalytical Laboratory of the Institute of Organic Chemistry of the University of Szeged for carrying out the microanalyses.

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PHYSICAL SCIENCES

Calculation of a 'Cosmic Ray Age' for the Iron Meteorite 'Carbo'

THE potassium of the iron meteorite 'Carbo' compared with ordinary potassium is substantially enriched in the isotopes potassium-40 and 41 as shown in the recent isotopic analysis by Voshage and Hintenberger¹. At least 15 per cent of these isotopes in their sample of Carbo appear to have been produced through the action of cosmic rays. Stoener and Zähringer² found that the concentration of potassium may vary considerably within an iron meteorite. Their analyses were based on the detection of potassium 41 and the β ion that the potassium had the same level as terrestrial potassium of 0.031 p.p.m.

of potassium from one sample is typical of 'Carbo' and is corrected to 0.012 p.p.m. in order to fit the new isotopic analysis, the potassium produced by spallation is at least 4.6×10^{-11} mole/gm. The total ion beam in the Voshage and Hintenberger analysis indicated that the concentration of potassium-40 alone is even greater than 1.8×10^{-12} mole/gm. The amount of potassium produced by spallation is probably about 10^{-11} mole/gm. This figure is quite compatible with that of 1.1×10^{-10} mole/gm for the helium-3 content² because the cross-section for the formation of potassium, including the contribution from argon-39 and calcium-41, seems to be³ about 40 mb, and the measured cross-section for the production of helium-3 (with hydrogen-3) by means of 3 BeV. protons on iron is approximately⁴ 340 mb. The neon also formed by spallation has a concentration⁵ of 5.8×10^{-12} mole/gm, which is comparable with that indicated for the potassium.

Radioactive species formed by spallation have been used to estimate the production rate of stable isotopes by cosmic rays. Radiation ages have been calculated in this way for meteorites from their helium-3 and argon-38 contents⁶. The combination of stable isotopes of potassium with the relatively long-lived potassium-40 may also be used to calculate a 'cosmic ray age', Δt in the following equation

$$\frac{1 - e^{-\lambda \Delta t}}{\Delta t} = \frac{\lambda K_m^{40} (\sigma_{39} - R\sigma_{41})}{\sigma_{40}(K_m^{39} - RK_m^{41})}$$

The relative abundances of the potassium isotopes used are $K_m^{39} = 0.795$, $K_m^{40} = 0.048$, and $K_m^{41} = 0.157$, as reported by Voshage and Hintenberger¹ for the meteorite 'Carbo'. The total decay constant, λ , is taken as $0.529 \times 10^{-9} \text{ yr}^{-1}$. R is the ratio of K^{39}/K^{40} in ordinary potassium.

In addition to the usual assumption regarding a constant cosmic ray flux, some knowledge of the cross-sections for the formation of the potassium isotopes is required. The cross-section versus mass curves for argon formed by high-energy protons on iron and copper are well defined experimentally (refs 3 and 4 and Bieri, R. H., personal communication). The curves are similar and are skewed towards the side of the neutron-rich isotopes. The known isotopes of potassium suggest that the spallation curve of this element is similarly asymmetrical and that the production cross-sections for potassium-40 and -41 are rather large and approximately the same.

Barr³ has estimated the approximate production cross-sections for the isotopes potassium-39, -40 and -41 for 5.7 BeV protons on copper. These cross-sections are 5.2, 9.4 and 9.2 mb, respectively. He inferred them from his measurements of the yields of more than fifty radioactive isotopes produced by the spallation of copper. The observed cross-sections for potassium-42 and -43 were 5.4 and 1.1 mb, respectively. Other spallation products such as argon-39 and calcium-41 contribute significantly to the formation of potassium. The cross-sections for the formation of potassium estimated from Barr's work then become $\sigma_{39} = 14.8$, $\sigma_{40} = 9.4$, and $\sigma_{41} = 14.7$ mb.

The radiation age calculated from the preceding values is $0.6 \times 10^9 \text{ yr}$. It is obvious in the above equation that the value for σ_{39} is comparatively insignificant. This figure may be incorrect by a factor of 2 without influencing the value of the right side of the equation by more than 10 per cent. The relative values for σ_{40} and σ_{41} are important. A

difference of even 20 per cent in their ratio affects the radiation age by 1×10^9 years. This seems to be approximately the uncertainty in this radiation age of 'Carbo', but the relative ages of iron meteorites may be determined with much greater precision. For the radiation age from the potassium to be 4.6×10^9 years, or the same as the lead-lead age^{7,8} and the rubidium-strontium age^{9,10} of stone meteorites, σ_{41} would have to be about one-half the value for σ_{40} . It should be noted that contamination will have a negligible effect on the radiation age as long as the observed abundance of potassium-40 is much greater than the potassium-40 in ordinary potassium.

The cosmic ray age calculated here for 'Carbo' is essentially the same as its estimated cosmic ray helium age of 0.85×10^9 years¹¹. The potassium-argon ages of several stone meteorites are also quite similar. The chondrites 'Kunashak' (grey variety) and 'Pervomaiskii Poselok' (grey variety) have ages of 0.70×10^9 and 0.64×10^9 years, respectively¹². The two shergotites 'Padvarninka' and 'Shergotty' have ages of 1.0×10^9 years¹³ and 0.56×10^9 years¹⁴, respectively. It seems that the stone meteorites belong to two groups, one with radiogenic helium ages of 4×10^9 years, the other with ages of about 0.5×10^9 to 1×10^9 years¹⁴. Helium probably has been lost from the meteorites of the latter group. The potassium-argon ages for the same meteorites clearly indicate some loss of argon¹⁴.

The accuracy of the cosmic ray age calculated from the potassium produced by spallation depends principally upon how well the ratio of the formation cross-sections for potassium-40 and -41 is known and the constancy of the cosmic ray flux. Nevertheless, this age of 0.6×10^9 years agrees remarkably well with independent age determinations for this meteorite and for other meteorites. Evidence is rapidly accumulating for the break-up of solid bodies and for the presumably related heating of at least some of the meteorites between 0.5 to 1.0×10^9 years ago. The comparison of potassium analyses from other iron meteorites may help to answer the question of whether these processes occurred throughout approximately half a thousand million years or during a much shorter interval.

I wish to thank Dr. R. H. Bieri and Dr. J. Geiss of this Institute for many discussions. This study was supported by a grant from the U.S. National Science Foundation.

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Refraction of Very High Frequency Radio Signals at Ionospheric Heights

PEOPLE engaged in radio tracking of space vehicles are well aware of the fact that the Earth's atmosphere may cause serious refractive errors in the elevation angle determination. It is also generally accepted that refractive errors rapidly decrease with an increase in the elevation angle, and become virtually negligible above 10 or 15 degrees. In the case of radio astronomy, this is quite true. However, in the case of space-vehicles which travel in the immediate vicinity of the Earth, this is not the case. The refractive errors due to the troposphere rapidly decrease with the elevation angle, while those due to the ionosphere initially increase with the elevation angle, and then gradually fall off. This behaviour of ionospheric refraction is a necessary consequence of the spherical geometry. The value of the elevation angle at which the maximum ionospheric refractive error occurs lies typically between 100 and 200 milliradians. The exact expressions are rather involved, but it can be shown that the value of this angle is roughly proportional to the square root of the height of the layer. The maximum value of the ionospheric refractive error is about 10-15 per cent higher than its value for a tangentially departing ray.

Fig 1 shows a plot of the elevation angle error δ for realistic models of the ionosphere and troposphere. The tropospheric calculations were based on radio sonde data. The ionospheric calculations were based on a model of electron density profile which was parabolic below the region of the maximum density

and was represented by the hyperbolic secant above the maximum. The constants of the hyperbolic secant were adjusted so that the profile and its derivative were continuous everywhere, and the total electron content above the maximum was three times as large as below it. This is in accord with experimental data based on Faraday rotation measurements.¹ Details of the computational techniques are described elsewhere.²

For the purpose of the accompanying illustration, the ionospheric constants were adjusted as follows: height of the base 200 km, half thickness 100 km, critical frequency 14 mc, signal frequencies 50 and 100 mc. The target height for which the refractive errors were computed was 300 nautical miles.

Examination of Fig 1 shows that at very low angles of elevation α_0 , the tropospheric refraction contributes appreciably to the refractive error while at higher angles, the ionospheric factors predominate. The peculiar behaviour of the ionospheric refraction manifests itself by the presence of the shoulder which is especially prominent at 50 mc, and also by the fact that the refractive error decreases more slowly with the elevation angle than might have been expected from the study of the refraction of radio stars.

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Near Infra-Red System of Nitrogen

In the course of studying the molecular spectrum of nitrogen under various excitation conditions Carroll and Savers¹ discovered a new triplet transition in the near infra red. Only one band was observed as the spectral region of interest was dominated by bands of the first positive system. A spectrogram of the new band was given together with measurements of the four strongest heads at 8265.5, 8283.8, 8293.3 and 8310.6 Å. The structure of the band was obviously complex, and it was suggested by Carroll and Savers that the transition might be $\pi^1 - \pi^2$.

More recently Kistiakowsky and Warneck² have reported bands of nitrogen in the infra red, and these observations have been extended by LeBlanc, Tanaka and Jursa³, who studied the emission from afterglows in argon-nitrogen mixtures at low temperature. They also made a preliminary vibrational analysis and showed that the lower state was most probably $B^2 \Sigma^-$.

There is no doubt that the new system is the same transition as that reported by Carroll and Savers. This is proved by (a) the close similarity in structure between the 8265.5 Å band on Carroll and Savers's spectrogram and the bands in the spectrogram given by LeBlanc, Tanaka and Jursa, and (b) the agreement between the measurements of corresponding heads in the 8265.5 Å band and the $(n+1) - 1$ band of LeBlanc, Tanaka and Jursa.

As the new system is of both theoretical⁴ and astrophysical⁵ interest the 8265.5 Å band has recently been investigated in the large dispersion. It was

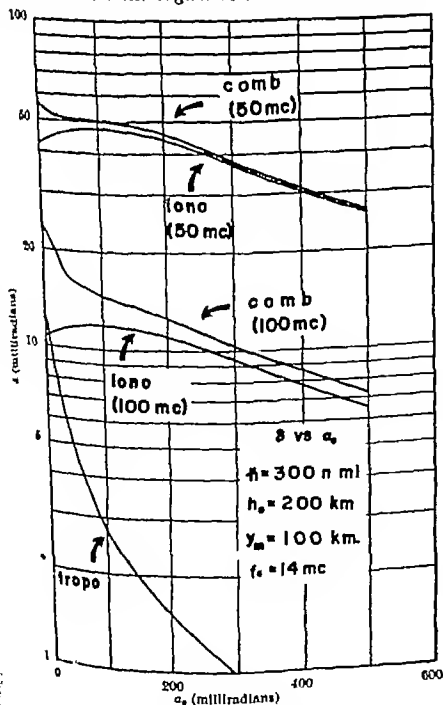


Fig 1

photographed in the second order of the 21-ft grating in the Physics Department of University College, Dublin, and despite the weakness of the band and the presence of the first positive system, a rotational analysis proved possible. Three components were found, each consisting of a fairly strong P , Q and R branch together with a number of weaker satellite branches. A detailed examination of the results shows unambiguously that the upper state is of species $^3\Sigma_u^-$. A preliminary value of B_{n+1} determined from the Q branches alone gives 1.38_6 cm^{-1} . The analysis also verified beyond doubt that the lower state of the 8265.5 Å band is the level $v = 1$ of $B^3\Pi_g$. This is shown by the excellent agreement between the combination differences derived from the present analysis and those formed from the data on the 1-0 band of the first positive system⁶.

The vibrational numbering of the levels in the $^3\Sigma_u^-$ state is not known with certainty at present. However, one can say that the $v = 0$ level cannot lie above about $71,700 \text{ cm}^{-1}$ and that it very probably lies within a few vibrational quanta of this value. Now Mulliken⁴, in his theoretical work on nitrogen, has predicted that a $^3\Sigma_u^-$ state, with a B value of approximately 1.47 cm^{-1} , should occur at about $70,700 \text{ cm}^{-1}$. It is seen that the results of the present work are in satisfactory agreement with Mulliken's theoretical predictions.

A full account of the above work will be published elsewhere in the near future.

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Luminous Spots on Electrodes in Insulating Oil Gaps

IN 1955 we reported the observation of luminous spots on electrodes in transformer oil¹. The spots were detected by a photographic plate in the oil between the electrodes with application of a c and d c voltage stresses for 2-30 min. The oil was usually degassed but not filtered. The luminous spots occurred at random on the surface of a plane electrode and were more concentrated at sharp edges. One of the electrode systems used was an American Society for Testing Materials oil-breakdown test-cup. The threshold average electric stress seemed to be of the order of 50 kV/cm minimum. At the time of those experiments it was not known whether these luminous spots were due to discharges in tiny bubbles or to another cause.

Since those preliminary experiments, more refined and efficient techniques have been used in the investigation of these luminous spots, whereby the electrodes are observed face on through a glass window coated with transparent semiconducting tin oxide. Microscopic examination has shown that, while bubbles do occur sometimes at high voltages under low hydro-

static pressures, or with fibres present, bubbles are not responsible for the luminous spots observed on electrodes in well-filtered, degassed oil. The luminous spots have been shown to occur only at the negative electrode with d c stresses and are therefore attributed to fluorescence of the oil molecules excited by field-emitted electrons from points of high localized electric stress on the electrodes. They have been detected by 10-min exposures with Ansco Super Hypan Film (ASA 500) in a camera having an $f/2$ lens opening at a distance of about 5 in. It is believed that these luminous spots are similar to the luminosity reported seen by Darveniza² at 600 kV/cm, but detected here at much lower average electric stresses. The threshold voltage stress seems to be of the order of 50-250 kV/cm, depending on the degree of polish of the electrodes and filtering of the oil. The local electric stress is very likely 10 or more times higher.

M. Wachtel (Westinghouse Research Laboratories, private communication) and Llewellyn-Jones³ have reported electron field emission into a vacuum or low-pressure gas at average electric stresses of the same order as used here.

The occurrence of luminous spots is not significantly affected by applied hydrostatic pressure from 10 mm mercury to 2 atmospheres. They also occur with a c voltages between glass surfaces, indicating that field emission occurs from glass surfaces. The luminosity is not affected by an efficient additive, benzil, reported by Basseches and McLean⁴ to prevent gassing.

It is believed that observation of these luminous spots assists in explaining the statistical effect of electrode area (and volume) on breakdown, particularly in commercial tests, and the dependence of long time a c electric strength on time of voltage application. It also suggests the origin of the development of gas (hydrogen) in stressed oils, since the electrons exciting fluorescence (requiring about 3 eV) may also have or gain by acceleration sufficient energy to decompose the hydrocarbon oil molecules (requiring about 4 eV).

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Compaction of Briquettes

WHEN a powder is compacted by a simple application of pressure, the density and strength of the compact so formed (measured after the pressure has been released) are determined by the pressure used, but ultimately they approach limiting values which are not exceeded by further increasing the pressure. The limiting density of the compact falls short of the density of the material of the powder by an appreciable margin, say 4-20 per cent, depending on the material used (Fig. 1).

This failure to achieve complete compaction arises in two ways. First, as the briquetting pressure is applied it is opposed by forces set up in the powder

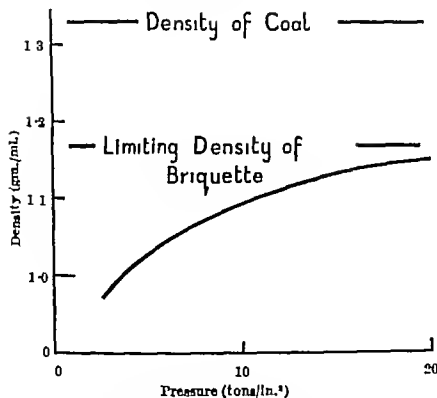


Fig. 1 Betteshanger coal relationship between briquetting pressure and density of briquette

and upon the walls of the mould, which resist the movement of the particles and which resist the deformation of individual particles, these forces prevent intimate contact between the particle surfaces. Secondly, as the external pressure is removed the deformed particles recover their shape elastically in part at least, and the compact expands and the voids within it increase. A large elastic recovery is associated with a weak compact.

It has been found that if the powder compact, while still under load, is subjected to shear strain, (as for example in a rotary shearbox as sketched in Fig. 2) there is a further compaction without any further increase in pressure being required. Also, the elastic recovery of the compact when constraints are removed is reduced. The compact made in this way is stronger than one made by simple pressing at the same pressure, and may possess greater density and strength than the limiting values obtained by simple pressing. Whether the compact is made by simple pressing or by introducing additional shear

strain under load, the strengths and densities are still related by the same single curve. The gain in strength may be substantial, and with coal powders a five fold increase has been attained. The full benefit is obtained only if the shear strain is introduced under maximum load (Fig. 3).

The response to the introduction of additional shear strain under load varies with the material. In a material such as Plasticene, which deforms plastically very readily and which has negligible elastic recovery, the process offers no advantage. Natural graphite powder also compacts readily, and reduces to a compact of about 4 per cent porosity by simple pressing, here again there is little advantage in applying extra shear strain which may do more harm by disrupting the briquette than good by compacting it. At the other extreme anthracite powder which shows an elastic recovery of 30 per cent while still in the die in which it has been pressed forms no compact at all with or without extra shear strain. The advantage of the process is found with materials lying between these extremes. The coal, the properties of which are illustrated in Fig. 3, is an example, the introduction of extra shear strain improves the compaction of the final briquette by about 10 per cent porosity and the strength by a factor of 3-5.

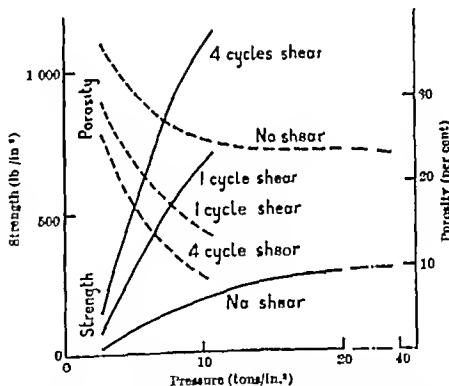


Fig. 3 Sherwood coal relationship between briquetting pressure, shear strain, strength and porosity (shear strain introduced in cycles of amplitude 6°)

The adhesion of particles in these non metallic compacts is not yet fully understood nor is the action understood whereby shear strain improves the adhesion. The fact that a single strength-density relationship applies to all compacts made from a given powder, with or without extra shear suggests that no new mechanism of adhesion is introduced by shearing.

The work described in this paper was carried out as part of the research programme of the Scientific Department of the National Coal Board and is published by permission of the Director General of Research.

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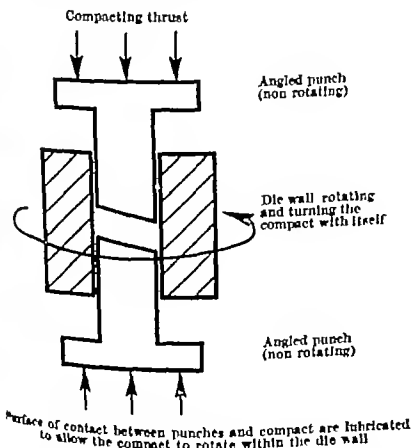


Fig. 2. Action of a rotary shearbox

BIOLOGY

Association between Colour of the Iris of the Eye and Reaction to Dental Pain

AN association has been found to exist, in Australians of European stock, between the colour of the eyes and the reaction to pain resulting from dental cavity preparation.

At the present stage of this study, examination has been made of 403 consecutive subjects whose teeth were being prepared for filling, the cavities being cut by means of the Borden high-speed air-rotor apparatus. Their ages ranged from three years to more than fifty years.

The pain reaction of each subject was assessed, four classes being used: subjects that showed (a) no pain reaction during the preparation of the cavity, (b) a slight reaction, (c) a marked reaction and (d) those whose reaction was so great as to require the injection of a local analgesic. After having recorded the pain reaction of a subject, the colour of the iris was observed, nine categories, ranging from blue to dark brown, being recorded. The pain-reaction classes were given arbitrary values of 0-3, and the colours of the iris, values of 1-9.

The association between these factors is highly significant, but, of course, is considered to be due to their joint association with other factors. The accompanying graph (Fig. 1) of mean values displays the association between pain reaction and colour of iris.

Each point of the graph is based on more than 40 observations, with the exception of the last three, for only 11 subjects were seen with light brown eyes, 23 with brown and 28 whose irises were dark brown.

Judgement of the reaction to pain is based on 12 months use of this new apparatus (Borden high-speed air-rotor), and on more than twenty years' clinical experience, nevertheless, it is acknowledged that both types of observation are open to criticism owing to their subjective nature. However, a test to establish the reproducibility of the results was satisfactory, for out of 136 subjects that were re-assessed between one and four weeks after the original examination, the same values were obtained for the colour of the eyes in 115 cases, and for the pain reaction in 114 subjects. Both for colour of iris and for pain reaction, the mean of the discrepancies between each pair of results was non-significant, the mean discrepancies were, pain reaction 0.02, iris colour 0.04.

Approximately 13 per cent of the total number of subjects required the injection of a local analgesic for cavity preparation, a similar percentage being found

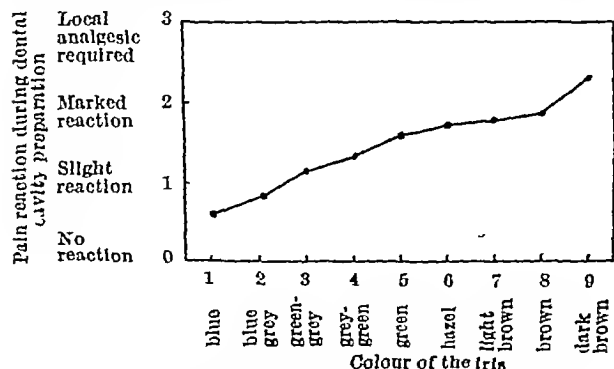


Fig. 1 Association between the colour of the iris and the reaction to pain resulting from dental cavity preparation

in the group of subjects formed by adding the results of those whose eyes were greyish-green, green or hazel. However, this aid was not required by any blue-eyed subjects, and was used for only 2 per cent of those with greyish-blue or greenish-grey eyes, but it was required by 30 per cent of the subjects with light brown or brown eyes, and by more than 53 per cent of those whose eyes were dark brown.

My thanks are due to Sir Arthur Amies, and to the University of Melbourne Research Fund.

PHILIP R. N. SUTTON

Dental School,
University of Melbourne
March 16

Development of the Aplacophorous Mollusc *Neomenia carinata* Tullberg

PRESENT-DAY authorities agree that, within the Mollusca, the chitons (or Polyplacophora) are closely related to the solenogastres (or Aplacophora). An important item influencing this view is the description, by Pruvot¹, of the development of seven overlapping, dorsal, plate-like spicules in the metamorphosing larva of the solenogastre, *Nematomenia banyulensis*. The appearance of these spicules has been considered to be a reminiscence of a chiton-like ancestor and, no doubt, has influenced many authors in coming to the conclusion that the solenogastres are degenerate chitons. Pruvot's description was based on observations on a single larva, but nonetheless the figure he gave of this developmental stage has been widely reproduced in general works.

The purpose of the present communication is to describe some observations on the development of *Neomenia carinata* Tullberg 1875, together with the work of Baba² on *Epimenia verrucosa*, they show clearly that, while the larva of *Nematomenia* may develop overlapping dorsal plates in the manner described by Pruvot, this is by no means the rule in the Aplacophora.

The embryos of *Neomenia carinata* hatch three days after oviposition (at 10° C) as trochophores with the blastopore still open abapically, but with no stomodaeum yet developed (Fig. 1A). These larvae swim over the bottom of the culture vessel, propelled by the strong cilia of the prototroch. As the larvae proceed, they spiral in the same direction as the metachronal waves travel around the prototroch (clockwise when viewed from the anterior). At 7-8 days metamorphosis begins, a caudal bud begins to protrude through what was formerly the blastopore (Fig. 1B). The tip of this bud bears a minute pore, the anus, and is ciliated. The rest of the bud, as it grows out, is unciliated but bears large numbers of pointed spicules (Fig. 1C). The 'trochophore' part of the larva remains ciliated, but becomes reduced in size, while the prototroch and apical tuft degenerate. The caudal bud comes to form by far the greater proportion of the larva (Fig. 1D). The last remains of the ciliated trochophore-mass are ingested through the mouth as the larva completes metamorphosis (Fig. 1E and F) and abandons pelagic life. At no time is there any trace of segmentation, nor of any dorsal shell-plates. When metamorphosis is complete the external surface of the body (except perhaps for the pedal groove) is unciliated, and the form is like that of the adult *Neomenia*.

This description is based on observations on large numbers of larvae of *Neomenia carinata* reared through metamorphosis in the laboratory, and the

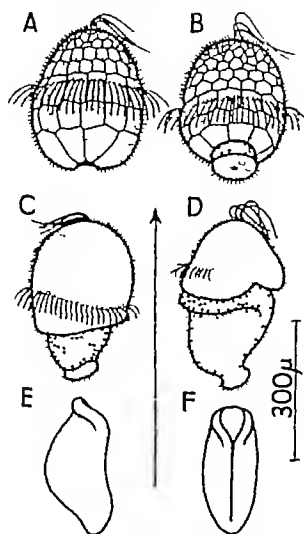


Fig. 1. Metamorphosis of *Neomenia carinata* (camera lucida drawings of live larvae). A. Trochophore at 3 days, ventral aspect. B. Trochophore at 3 days, right lateral aspect. C. Trochophore at 10 days, right lateral aspect. D. Trochophore at 11 days, right lateral aspect. E. Newly metamorphosed stage (12 days), right lateral aspect. F. The same, ventral aspect. In E and F the spicules are not illustrated. The arrow shows the antero-posterior axis of the animals.

results so far obtained plainly show the need for a re-investigation of the development of *Neomenia*. At present, the indications are that the nearest relatives of the Aplousophora within the Mollusca may be found in the primitive Lamellibranchia rather than in the Polyplacophora. The resemblances in development between the solenogastres and members of the Brachopoda, Archannelida and Nemertea (to which various authors have directed attention) are probably without profound significance. The work on *Neomenia* is being continued and is financed by a grant from the Leverhulme Trust.

T. E. THOMSON

Marine Biological Station,
Port Erin, Isle of Man
April 8

¹ Favos G. C.R. Acad. Sci. Paris 3 680 (1890)

² Ede, K. J. Dept. Agric. Kyushu Univ. 6 21 (1938)

Dagger Nematodes associated with a Clover Sickness

Dagger nematodes (*Xiphinema* spp.) are now recognized as important crop pests in many North American states^{1,2} and occur widely in tropical countries³ in close association with plant roots. Because of their migratory ectoparasitic habit they are seldom observed feeding on the host plant, and where they appear to be associated with crop damage pathogenicity is difficult to prove.

Examination in early February of sickly white clover (*Trifolium repens* L.) plants from a clover ley near Crewkerne, Somerset showed no pathogenic organisms, but large numbers of dagger nematodes were recovered from the soil around the roots. The roots themselves bore minute lesions compatible with nematode feeding and many young rootlets

were brown and shrivelled at the tip. The field, a sandy loam, had been sown to grass and clover leys in sown out of the past ten years and had a similar early history.

The area was again sampled at the end of April, by which time the clover was dying off in patches. Many dagger nematodes were again recovered but fungal damage was also evident and small sclerotia believed to be those of *Sclerotinia trifoliorum* Erikss. were seen the stem eelworm *Ditylenchus dipsaci* Kuhn also occurred in numbers sufficient to constitute a possible cause of disease.

The exact role of dagger nematodes in this complex is thus uncertain, this is the first record of the genus *Xiphinema* in Great Britain, and observations and measurements suggest that the specimens recovered represent a new species, which will be described elsewhere.

F. C. PEACOCK

Imperial Chemical Industries Ltd
Jancott's Hill Research Station,
Bracknell, Berks
April 28

¹ Christie J. R. *Phytopathology* 43 295 (1953)

² Adams R. E. *Phytopathology* 45 477 (1955)

³ Schneider A. F. *Nematologica* 8 28 (1957)

⁴ Lordello L. E. O. *Proc. Ind. Soc. Wash.* 22 16 (1955)

⁵ Luc M. *Nematologica* 8 57 (1958)

Pollen of *Acacia* from Tufaceous Limestone near Udaipur

I HAVE undertaken the investigation of fossil microflora from a tufaceous limestone near Udaipur. This fossiliferous locality is about three quarters of a mile north west of the tenth milestone on the Udaipur-Gogunda Road. It was first described by Murti¹, who had suggested a tertiary age to these beds.

A few pieces of fossil were macerated with Schultz's solution and clear dehydrated mounts were prepared by passing the material through various grades of alcohol and mounting in Canada balsam. Some of the preparations were stained with safranin. The



Fig. 1. *Acacia* pollen grain (x 415)

slides so prepared showed many angiospermic pollen grains, some of which belong to the Leguminosae and the Gramineae. Also a few pteridophytic spores were observed.

One well-preserved pollen grain resembles very closely that of *Acacia longifolia*. It is a smooth compound 16-celled grain, eight cells are centrally placed, forming a sort of cubical block with the others arranged in a rectangular fashion. The central group is surrounded by eight peripheral cells all in a plane at right angles to, and bisecting, the central group. The peripheral cells are so placed that their eight contacts with each other are alternately opposite and midway between the four contacts of the central group. The group as a whole is flattened, with a more or less rounded outline, and the intersecting lines between the individual grains cross each other at right angles.

The exine is thick and its corners are rounded. The individual grains measure about 24.5μ in diameter and the whole compound grain is 69.5μ in diameter.

It is significant to note that fossil pollen grains of the *Acacia* type have been recently described from the Victorian Tertiary deposits, Australia, by Cookson².

I thank Dr. Chitley for her guidance in this work.
T. TRIVEDI

Government College of Science,
Nagpur

¹ Murty T. V., Proc. Forty-second Ind. Sci. Congr. Assoc. (1955).

² Cookson, C. I., *Austral. J. Bot.*, 2 (1), 52 (1954).

ARCHAEOLOGY

Stone Implements from Western Nigeria

RECENTLY a number of stone implements have been uncovered by labourers in sand quarries at Green Springs near Ibadan, Western Nigeria. These implements are associated with deposits of river sand and clay. The workmen wash the sand, discarding the clay and stones, usually placing the latter in heaps or scattering them about the ground. Thus it has not been possible to determine the level at which they were lying before excavation. Generally, however, the layers containing stone are between one and seven feet below the main surface-level.

Table 1 lists the definite artefacts found. The material is mainly quartz from the basement complex.

Polished stone axes are common in Nigeria, where they are often used as protective charms against thieves and thunder, in the belief that they are fallen thunderbolts. Flaked and tanged implements, however, have not previously been recorded from the Western Region of Nigeria, although flaked implements which have been compared to the Chelles-Le Moustier epoch in Europe are found in Northern Nigeria¹, and other flaked implements have been reported from the Eastern Region and the Cameroons². Typologically, the Green Springs

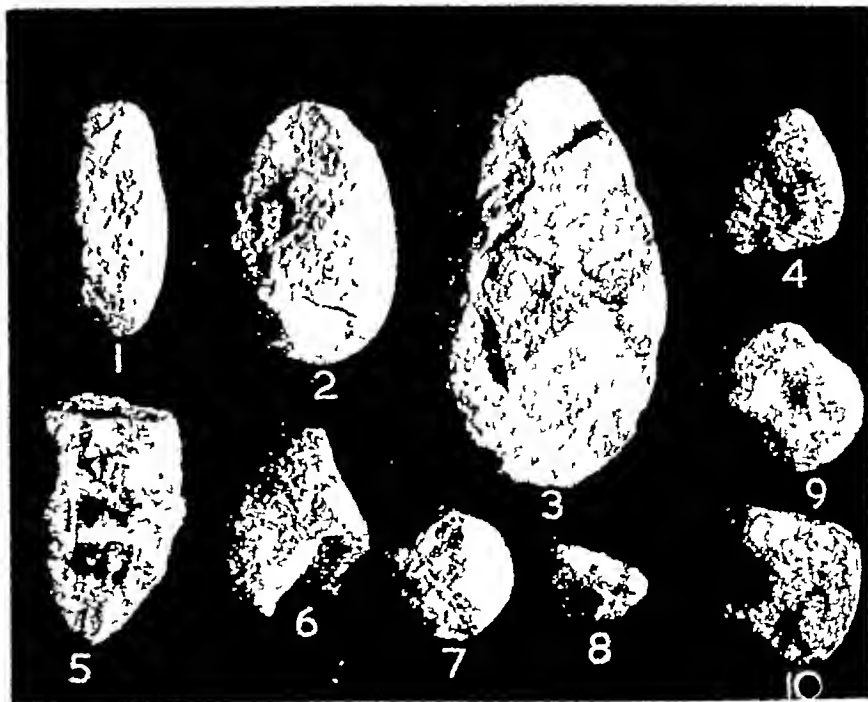


Table 1

| Description | Dimensions | No. |
|--|--|-----|
| Polished hand axes, Fig. 1 | Approx. $12 \times 6 \times 2\frac{1}{2}$ cm | 5 |
| Fragments | Average width 6 cm | 10 |
| Well-formed bifaced hand axe, Fig. 2 | $14 \times 0\frac{1}{2} \times 5$ cm | 1 |
| Unifaced hand axe, Fig. 3 | $23 \times 12\frac{1}{2} \times 4\frac{1}{2}$ cm | 1 |
| Polished cleaver-like stone, Fig. 4 | $7\frac{1}{2} \times 7 \times 3\frac{1}{2}$ cm | 1 |
| 'Points', Fig. 5 | Approx. $13 \times 0 \times 2\frac{1}{2}$ cm | 2 |
| Tanged unifaced blade, Fig. 6 | $11 \times 0 \times 2$ cm | 1 |
| Hand held polishing or grinding stones, Fig. 7 | Approx. $7 \times 6 \times 6$ cm | 3 |
| Bifacial discoid stones (scrappers?), Fig. 8 | Approx. $4 \times 0 \times 2$ cm | 2 |
| Anvil stones indented both surfaces, Fig. 9 | Approx. $0 \times 7 \times 4$ cm | 4 |
| Balls | 5-8 cm dia | 15 |
| Eccentrically perforated stone, Fig. 10 | Width, 8 cm, perf., 2 cm | 1 |
| Fractured stone cylinder | 6 cm dia | 1 |

implements fall into two groups: (a) neolithic types, represented by stone balls, polished axes, anvils and grinding stones, and (b) palaeolithic types, represented by the points, the flaked axes and the tanged blade. The latter are suggestive of the Aterian cultures of North Africa^{3,4}.

We are of the opinion that systematic excavation in the area may be of advantage to pre-history. We wish to acknowledge the kind help of Mr. R. Hockey, geologist, Geological Survey Department, Federal Government of Nigeria.

E. L. KOSTICK
C. N. WILLIAMS
S. A. WILLIAMS

University College,
Ibadan
March 31

¹ Braunholtz, H. J., "Stone Implements of Palaeolithic and of Neolithic Types from Nigeria", Geological Survey of Nigeria, Occasional Paper No. 4 (1920).

² Jeffreys, M. D. W., Pan-African Congress on Pre-History, Livingstone, 1955, edit. Clark, J. D., 202 (1957).

³ Caton-Thompson, G., *J. Roy. Anthrop. Inst.*, 76, 87 (1946).

⁴ Allmen, H., *The Prehistory of Africa*, English trans., Chapter 7, 234 (1957).

FORTHCOMING EVENTS

Monday, August 31—Saturday, September 5

10TH CONGRESS OF THE INTERNATIONAL ASTRONAUTICAL FEDERATION (at Church House Westminster London S W 1)

Wednesday, September 2—Wednesday, September 9

BRITISH ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE (at York)—Annual Meeting

Wednesday September 2

At 8 p.m.—Sir James Gray O.B.E. M.C., F.R.S. "The Proper Study of Mankind is Man" (Presidential Address)

Thursday September 3

At 10 a.m.—Prof. L. P. Bates, F.R.S. "The Visualization of Magnetic Processes" (Presidential Address Section A)

At 10 a.m.—Prof. M. Stacey, F.R.S. "Medical Applications of Complex Carbohydrates" (Presidential Address Section D)

At 10 a.m.—Dr L. Harrison Matthews, F.R.S. "Man and the World Fauna" (Presidential Address Section D)

At 10 a.m.—The late Dr W. R. G. Atkins F.R.S. "Plants on Land and in the Oceans" (Presidential Address Section K read by Dr G. P. Spencer)

At 10 a.m.—Dr H. G. Sanders "Balance in British Farming" (Presidential Address Section M)

At 11.15 a.m.—Mr W. B. Day "The Influence of Pathogenic Factors within the Rooting system on the Development of Even-aged Plantations" (Chairman's Address Section K*)

At 11.30 a.m.—Sir Ewart Smith, F.R.S. "The Critical Importance of Communication and Transport" (Presidential Address Section G)

At 2.30 p.m.—The Countess of Albemarle "Living with Science" (Presidential Address Section X)

Friday September 4

At 10 a.m.—Prof. K. G. Edwards "Trends in Urban Expansion" (Presidential Address Section E)

At 10 a.m.—Prof. John Jewkes "How Much Science?" (Presidential Address Section F)

At 10 a.m.—Sir James J. Robertson "What Are Our Schools For?" (Presidential Address Section L)

At 11.30 a.m.—Prof. Magdalen Vernooy "Perception Attention and Consciousness" (Presidential Address Section J)

At 8 p.m.—Prof. M. Swann "The Uneaten Pattern of Growth" (Evening Discourse)

Sunday September 6

At 10.30 a.m.—Official Service at York Minster Preacher: The Most Reverend The Lord Archbishop of York.

Monday September 7

At 10 a.m.—Prof. G. M. B. Balman F.R.S. "Recent Developments and Trends in Palaeontology" (Presidential Address Section C)

At 10 a.m.—Prof. Ian A. Richmond "The Nature and Scope of Archaeology" (Presidential Address Section H)

At 10 a.m.—Prof. A. Homology "Artificial Organs—Biological Applications" (Presidential Address Section I)

At 8 p.m.—Sir William Hildred "International Air Transport Problems" (Evening Discourse)

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned

ANALYST (qualified for general inorganic analysis) to the Houldsworth School of Applied Science mainly for work on silicates—The Registrar The University of Leeds (2 August 59)

LECTURER IN MATHEMATICS—SENIOR TUTORS (2) IN GEOGRAPHY and LECTURERS (2) IN EDUCATION at Palmerston North University College (Victoria University of Wellington), New Zealand—The Secretary Association of Universities of the British Commonwealth 36 Gordon Square London W.C.1 (New Zealand August 31)

LECTURER (preferably with experience in solid state or low level physics or ultrasonics) IN PHYSICS—The Registrar Queen Mary College, Mile End Road, London E.1 (August 31)

ASSISTANT LECTURER (preferably with interests in plant physiology and plant ecology) IN BOTANY—The Principal Royal Holloway College (University of London) Englefield Green Surrey (September 1)

SENIOR LECTURER AND DIRECTOR (with high academic qualifications and experience of high-speed digital computers) OF THE DEPARTMENT OF COMPUTATION—The Secretary and Registrar The University of Southampton (September 1)

ASSISTANT LECTURER OR LECTURER IN THE DEPARTMENT OF AGRICULTURAL ECONOMICS—The Registrar University College of Wales Aberystwyth (September 1)

LABORATORY ASSISTANT IN THE DEPARTMENT OF BOTANY—The Registrar University College Singleton Park Swansea (September 8)

LECTURER IN ZOOLOGY to the University of Queensland Australia—The Secretary Association of Universities of the British Commonwealth 36 Gordon Square London W.C.1 (Australia September 11)

ASSISTANT LECTURER IN DARTING—The Registrar University College of Wales Aberystwyth (September 12)

LECTURER IN PURE MATHEMATICS SENIOR TUTORS (2) IN PURE MATHEMATICS and a SENIOR LECTURER IN PHYSICAL METALLURGY at the University of Sydney Australia—The Secretary Association of Universities of the British Commonwealth 36 Gordon Square London W.C.1 (Australia September 19)

LECTURERS (2) IN ASTRONOMY in St. Salvator's College University of St. Andrews—Joint Clerk to the University Court College Gate St. Andrews (September 19)

LECTURER IN EDUCATION at the University of Otago Dunedin New Zealand—The Secretary Association of Universities of the British Commonwealth 36 Gordon Square London W.C.1 (New Zealand September 20)

SENIOR TUTOR DEMONSTRATORS (2) IN ZOOLOGY at the University of Sydney Australia—The Secretary Association of Universities of the British Commonwealth 36 Gordon Square London W.C.1 (Australia September 26)

LECTURER IN MATHEMATICS at the University of New England Australia—The Secretary Association of Universities of the British Commonwealth 36 Gordon Square London W.C.1 (Australia September 28)

LECTURER IN GEOGRAPHY at the University of Sydney Australia—The Secretary Association of Universities of the British Commonwealth 36 Gordon Square London W.C.1 (Australia October 1)

MYCOLOGIST (with a good honours degree in botany with mycology as a special subject) a knowledge of the more fundamental aspects of animal and human mycoses and preferably a knowledge of Latin and other languages) at the Commonwealth Mycological Institute Kew—The Secretary Commonwealth Agricultural Bureaux Farnham House Farnham Royal Bucks (November 30)

JUNIOR PLANT BREEDER (male with a good honours degree in botany with postgraduate experience in the technique of plant improvement) at the West African Cocoa Research Institute (serving initially at Tafo Ghana) to carry out research on plant breeding problems relating to cocoa—The Director of Recruitment Colonial Office London W 4 W 1 quoting BOD 197/200/98/T

LECTURER IN PHYSICS and an ASSISTANT LECTURER IN PHYSICS (Grade B*)—The Clerk to the Governors Northern Polytechnic Holloway London N 7

SENIOR LECTURER IN ZOOLOGY—The Registrar Bradford Institute of Technology Bradford 7

TECHNICIAN IN THE ZOOLOGY DEPARTMENT—The Secretary Royal Holloway College Englefield Green Surrey

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

Abstracts of Dissertations approved for the Ph.D. M.Sc. and M. Litt. Degrees to the University of Cambridge during the Academic Year 1958-59. Pp. xviii+267. Titles of Dissertations approved for the Ph.D. M.Sc. and M. Litt. Degrees in the University of Cambridge during the Academic Year 1957-1958. Pp. iv+25. (Cambridge Board of Research Studies The University 1958.) 1144

British Electrical and Allied Industries Research Association Technical Report E/T65 The Low Temperature Liquid Phase Oxidation of Hydrocarbons: A Literature Survey. By Prof. Frank Morton. Pp. 35+8 figures. 21s. Technical Report L/T365 Ultra-High Frequency Oscillations between Rogowski Electrodes. By W. A. Prowse and J. L. Clark. Pp. 15+25 figures. 15s. Technical Report L/T368 Effects of Coulomb Forces on the Conduction Properties of Semi-Conductors. By S. Doniach. Pp. 37. 18s. Technical Report L/T371 The Calculation of Inager's Reaction Field for a Particular Model. By B. V. Paranjape. Pp. 5+2 figures. 7s. 6d. Technical Report Z/T117 Evolution of Extra-Galactic Nebulae and the Origin of Metagalactic Radio Noise. By Dr C. E. R. Bruce. Pp. 7. 3s. (Leatherhead British Electrical and Allied Industries Research Association 1958, 1957 and 1958.) 1144

Polish Cultural Institute London Selective Quarterly Guide to Polish Periodical Literature, Vol. 4 1958 Pp. 1+76. (London Polish Cultural Institute 1958.) 1144

Federation of British Industries Forty-second Annual Report 1958 Pp. vi+42. (London Federation of British Industries 1958.) 1144

Royal Research Institute Collected Papers Vol. 15 Reviews Nos. 1-63. Collected Papers—Summary and Subject Reviews Vol. 15. Pp. 60. (Inchbourn Royal Research Institute 1958.) 1174

Capital Investment in the Coal, Electricity and Gas Industries Pp. 8. (Oxford 715) (London H.M. Stationery Office 1958.) 1164

Ministry of Power Reports of H.M. Inspectors of Mines and Quarries under the Mines and Quarries Act 1954 for 1958. North Eastern Division. By H. J. Morris. Pp. iii+40+4 plates. (London H.M. Stationery Office 1959.) 1174

New Developments in Tralots Five Studies to the Efficient Communication of Skills Edited by Frank A. Heller (New Development Series No. 3) Pp. 80 (London Polytechnic Management Association Ltd 1958.) 1174

Isles No. 63 Reprinted from the Journal of Ecology Pp. 167-221 (Oxford Blackwell Scientific Publications 1959) 1174

Imperial Cancer Research Fund Fifty-sixth Annual Report 1957-1958 Pp. 1+100. (London Imperial Cancer Research Fund 1958.) 1174

Anti Locust I of the Desert The Colour Pattern of the Desert Locust. By J. H. Law. Pp. 11+4 plates. (London H.M. Stationery Office 1959.) 1174

Ministry of Home Affairs of the Standing T. (London H.M. Stationery Office 1959.) 1174

government and the public. All that he writes, however, about the futility of the pathological secretiveness of the British Government, matched in Europe only in Spain and Portugal, applies even more forcefully where science is concerned. These attempts at secrecy merely hinder scientific or technical advance without promoting security and, more serious, impede the informed public discussion and understanding of what both science and Government are doing which is essential if science is to be wisely used.

This is even more important now that we stand at the cross-roads, as Sir Solly reminds us. Hitherto, we could claim that the applications of science have increased the sum total of human happiness. The process of applying scientific knowledge is as endless as is the prospect of getting new knowledge, and we can be reasonably certain that neither the backward and under-developed nor the rich nations will allow the process of applying the fruits of scientific knowledge to stop, either in the national or the international framework. In this process, however, means become ends, because as new ways of doing things are discovered, they transform the things done, and so their purpose. In fact, weapons may end by determining strategy and even the purpose behind the strategy.

Here, in Sir Solly's view, arises the real clash to-day between the scientist and the humanist, and this form of scientific application could indeed constrain our democratic liberties and even, if we ceased to be vigilant, the liberty of science itself. That would seem to imply a special responsibility for the scientist, though Sir Solly does not agree that such a responsibility means more than that the scientist is better able to appreciate scientific facts. It is not reasonable, he points out, to expect the scientist as such, who is not responsible for the application, to accept the responsibility for predicting some vast social transformation which might result from a seemingly innocent observation.

Nor is that all, for it has to be remembered that the process of government involves much more than taking account of scientific and technical factors and their implications. Even if the problem is essentially a scientific one, the statesman or minister who has to take a decision and formulate a policy must have regard to public acceptability, and accordingly to the public understanding. Normally there will be many other factors to be considered, and it is the corollaries of the application of science that are of importance, since they are most readily appreciated and most relevant politically.

In this connexion Sir Solly reaches the same conclusion as to the importance of the views of Dr Chapman and the recent book by Mr C H

constituting to-day an essential part of an education in the humanities. An understanding of social and political purpose can no longer be realized through the liberal arts, unless their scope is widened to embrace a proper understanding of the scientific knowledge the application of which is so rapidly transforming our intellectual and material environment.

It is with realism and not arrogance that Sir Solly places science, technology and humanism in that order of importance in determining our affairs, and in the same spirit that he suggests that, to continue as a potent educational discipline, the humanities must encompass an understanding of the social forces which arise from the application of the natural sciences. Nor does he suggest that higher education necessarily guarantees higher virtue or higher political wisdom, rather we are likely to avoid bad decisions if we realize that decisions taken in major scientific matters to day may determine the course of the future. Dr Chapman comments that no other European country has emphasized to the same extent as Britain the strange division between science and the humanities, with the result that the common difficulty of finding adequate numbers of Civil servants with sufficient specialized training is accentuated, nevertheless, he recognizes that all branches of the public service, ministries as well as industrial public enterprises, need a proper balance between administrator, manager and technician, and that ministries often lack technical competence in scientific, industrial and economic fields.

Apart, however, from referring to the way in which France has been able to meet some 90 per cent of her requirements for first-class engineers and technologists with administrative experience, Dr Chapman does not discuss the place of the scientist or technologist in administration. He stresses the importance of education and recognizes that this means the education of the general public as well as of the administrator, and the politician and minister. He makes the significant comment that a menial mind should not be a qualification for high administrative office, but his constructive criticism is rather on the structure of the Civil Service itself, where it points to the fresh thinking that is required in order that the public services may be able to fulfil the needs of the modern State.

Nor are his suggestions for the Civil servant or the minister alone. They are no less worthy of the attention of professional organizations, for they point to ways in which not merely could the public services be absorbed more effectively into the structure of the modern State, but also, and no less important, the professional scientist or technologist could serve the State under conditions less likely to constrain professional ideas and tradition. Mr C H

in "The Spirit of British Administration", is as to the possibility of a general education. He believes just as firmly as Sir Dr Chapman that the survival of general education is of parliamentary

government or indeed of any government based on a discussion, with this goes the survival of administrators who are not daunted by specialists take it for granted that the practical implications of all their work can be explored and explained in a sufficiently agile lay mind

The defence of freedom is a central problem of our age, and it is not simply one of defence against aggression from totalitarian systems outside. Sir Lionel Zuckerman shows clearly how it arises from the nature of science itself, and from the impact of science on society. Any scientist or technologist who is concerned about these changes and how they can be best avoided or minimized will be led inevitably to think not simply about the association of scientist and technologist with government but about the process of government itself. To such thinking both the books mentioned above offer some contribution in different ways: they can assist in the understanding of the nature of administration and the limitations within which the administrator works; they indicate also the mind of the administrator and how it is trained or formed, and they point to some of the ways in which reform or developments are required if the task of government is to be discharged adequately to-day. But, like Sir Lionel Zuckerman's volumes, they are primarily a challenge to the scientist or technologist to accept such responsibility to-day, and a stimulus to the creative thought by which alone that responsibility can be discharged.

THE NEED FOR MARINE RESEARCH

Living Resources of the Sea

Opportunities for Research and Expansion. By Dr Lionel A. Walford (A Conservation Foundation Study). Pp xv+321 (New York: The Ronald Press Company, 1958). 6 dollars.

It is more than sixty years since the foundation of the International Council for the Exploration of the Sea, the avowed purpose of which is the accumulation of knowledge necessary for the rational exploitation of marine resources in northern waters. There are now a dozen or more councils or commissions covering other areas of the world, including commissions limited to certain animals, such as halibut, salmon, tuna and whales. The fear of over fishing, which has been the spur to the activity of the International Council for the Halibut Commission and other more recently formed organizations, has always been well to the fore in the minds of those concerned with the science of the sea. The necessary research has been concentrated on the main northern fisheries, but now the demand to feed the under-nourished millions has focused attention on the sea as a whole as a possible source of protein.

At the request of the Conservation Foundation, Dr Lionel A. Walford, chief of the Biology Branch of the U.S. Fish and Wildlife Service, was asked to explore the question "What scientific researches, apart from those which are in progress, would contribute significantly toward learning how to enlarge the yield of food from the sea in answer to human needs?" This has resulted in a useful book in which

Dr Walford considers the problem from human and biological angles. The major conclusion is that research must be extended into those areas where the need is greatest, and where there is the most possibility of increasing the food supply where it is most lacking. A number of interesting charts are included indicating the existing intensity of fishing and research in different parts of the world, those areas of the sea which might be expected to be productive, and those on land where the need for food is greatest. This survey impresses on us that where the fisheries are at present most developed and exploited there lies the major effort of research. The number of pertinent marine laboratories is now about 240. Nearly 90 per cent of these are in the northern hemisphere and 85 per cent north of latitude 20° N. Thus, those areas in which the need for research is now greatest have least facilities to do so both in material equipment and trained personnel. The problem is one both of research and development, and it is not easy to do the former without the latter unless exploration for fishing grounds is subsidized by governments.

It is thus both humanely and politically advisable that the countries most advanced in marine research should do their utmost to help the under-developed areas. Since the Second World War fisheries research under the auspices of Her Majesty's Colonial Office has added significantly to knowledge in certain areas, the U.S. Fish and Wildlife Service has extended its investigations into the oceanic pelagic fisheries, and the United Nations Food and Agriculture Organization has helped in supplying experts and supervising training. But this effort should if possible be much increased, and every encouragement given to those who wish to do research that will add to our knowledge of conditions in tropical seas.

Dr Walford's book is not a text-book; it attempts to show where be the gaps in knowledge, and these are both large and numerous. As a single example of what we know of the probably enormous food potentialities available in pelagic cephalopods which now constitute 60 per cent of the Japanese fisheries?

Marine resources are also not necessarily all of value as food; some may have medical value. On our own planet there lies a whole world which we have only recently begun to study extensively. It is to be hoped that Dr Walford's book may stimulate us to greater efforts.

F. S. RUSSELL

ANOTHER DEBT TO DARWIN

Index Kewensis

Plantarum Phanerogamarum Supplementum Duo decimum Nomina et Synonyma Ornium Generum et Specierum ab Initio Anni MDCCCLXI usque ad Finem Anni MDCCCLV. Nonnulla etiam antea Edita Complectens Ductu et Consilio Georgii Taylor confecerunt Herbarii Horti Regii Botanici Kewensis Curatores. Pp iii+157 (Oxonii: E. Pello Clarendon domano 1959). 75s net.

IN this centenary year of the publication of the "Origin of Species" biologists owe very much in mind the debt that they owe to Charles Darwin. It is probable, nevertheless, that many of them do not remember that the inception of "Index Kewensis" was due not only to Darwin's perception of the necessity for such a work but also to his generosity in providing the funds.

We might at this moment remember that the work was started under the supervision of Darwin's great friend, J. D. Hooker, and has since been supervised by subsequent directors of Kew and carried out by numerous able, but often anonymous, helpers.

"Index Kewensis" is taken so much for granted by plant taxonomists working with angiosperms that it is often not fully appreciated. To anyone who has struggled, even briefly, with taxonomic and nomenclatural problems in groups such as algae, where no such index exists, the lack of it is keenly felt and the value of a catalogue of names with places of publication is soon fully realized. It is interesting to note in this connexion that an "Index Muscorum" is due to be published shortly—another descendant of the original Darwinian idea.

"Index Kewensis", the twelfth quinquennial supplement to which has now been published under the direction of Dr. G. Taylor, supplies far more information about flowering plants and papers concerning them than might at first sight appear.

For example, in the five-year period between 1951 and 1955 approximately 12,000 species of flowering plants have been described. This, after more than two centuries of taxonomic work in the post-Linnean period, is a staggering total and gives some measure of the imperfection of our knowledge of the dominant group of plants.

It is also easy to obtain from these Supplements references to important monographs and information about the geographical areas and the plant groups which have been the subject of special attention in the recent past, as well as the names of the workers concerned.

In conclusion, I may perhaps be allowed to repeat what has so often been said before: "Index Kewensis" is indispensable. T. G. TUTIN

OPTICS: CLASSICAL AND MODERN

Concepts of Classical Optics

By Dr. John Strong. Pp. xxii + 692. (San Francisco: W. H. Freeman and Company, London: Bailey Bros. and Swinfen, Ltd., 1958.) 9.50 dollars, 80s.

THIS is a very good book, and one of its best features is the care taken by the author to ensure that the student understands what is going on. Mathematical treatment is kept to a minimum, but where it is necessary we are not left to flounder; the author explains what he is doing by means of a sort of running commentary, and even reassures us that although the solution we are after is buried in complication at the moment it is going to emerge safely in a minute. The only criticism here is that some simplification of the symbols used would lead to even greater clarity; for example, why was it necessary to use the symbol λ for mass early in Chapter 1, only to announce, a few pages later, that "we now abandon this for its customary use, symbolizing wavelength"?

The author also takes the trouble to expose and explain theoretical difficulties which are too often ignored. A good example of this is the section on "No Diffraction, by Cornu's Spiral", in which the limitations of this construction are pointed out, with the conclusion that "it affords the student an example of a typical theory in physics which has an impressive neatness, inspiring awe, which makes

necessary compromises, requiring prudence, while is blennished by a lack of complete validity, requiring understanding."

At first glance the most distinctive feature of the book is the character of the illustrations. These at once in the style one associates with the author's well-known book on laboratory practice. They have a freehand appearance, are pleasant to look at and are extremely clear; for example, the drawings in the section on double refraction, which is inherently a difficult subject to illustrate, are models of clarity. What is even more important is that the drawings showing apparatus give one a good idea as to how it is actually constructed—too often one's first sight of the actual equipment comes as a shock after having seen only text-book illustrations. It is only in some of the attempts to reproduce optical images by means of sketches that actual photographs might have been better.

The book is described in the preface as being intended for an intermediate course in optics, taking one or two terms. This is a considerable understatement of the ground covered and the book should be valuable for much more advanced students and also for general reference purposes. It in fact covers most of the physical optics required for an honours degree in physics.

The only real adverse criticism of this book concerns the price—£4—which is surely at least twice as much as most students would willingly pay for a single book. This is to some extent offset by the seventeen so-called appendices, which occupy nearly half the book and are in effect a series of short monographs by specialists. To quote the preface: "these are intended to give the student the flavour of current activities and interests in our field." The topics covered in this way include, among other things, interferometer apodization, Fourier transformations and interferometric spectroscopy, radiation detectors, micro-wave optics, wave theory of image formation, lens design, fibre optics and filters. One of the appendices supplies some of the mathematical background assumed in the rest of the book. This is well done, and includes frequent attempts to make the student think—both by formal examples and by interjected questions such as "(why?)" or "(how do we know?)" after mathematical steps in the text. J. E. GEAKE

BLOOD GROUP METHODS AND TECHNIQUES

Practical Blood Grouping

By Dr. F. Stratton and Dr. P. H. Renton. Pp. xxiv + 331 + 16 plates. (Oxford: Blackwell Scientific Publications, Springfield, Ill.: Charles C. Thomas Publisher, 1958.) 42s. net.

OVER the past fifteen years mass grouping of blood donors and ante-natal cases has grown enormously, and of necessity special methods and techniques have been evolved to meet an entirely new situation.

The authors of this book, faced with the alternative of describing a multiplicity of methods, or confining themselves to those known and well tried in their own laboratory, have wisely chosen the latter.

Not all would agree that the paper slide test offers substantial advantages over existing (and equally well-tried) techniques, for example, tube testing. Even if some small advantage could be

demonstrated, the disorganization which would follow a drastic change to a new technique would carry inherent dangers, probably outweighing any benefits likely to result.

Nevertheless it is always of value to study methods which have proved satisfactory over a number of years, and many pathologists engaged in this work will be most interested in a method which has satisfied such critical observers as the writers.

In the section dealing with ante natal grouping, the possible alternative to the current practice of ABO and Rh(D) screening with the customary follow up of the Rh(D) negatives is attractive from the point of view of economy in laboratory working. It might, however, be difficult to convince clinicians, and particularly obstetricians, that this economy at the expense of their advance knowledge of their patients' groups would be justified. It is certain that they would argue as is foreseen by the authors, that obstetric emergencies would not be so well covered.

It would seem that the writers themselves have not adopted this possible alternative in their own practice, having doubtless explored the possibilities and the difficulties which it would entail.

An interesting and informative chapter on cross matching difficulties encountered in their own laboratory (p. 337) was found to be slightly confusing. For example, of the 2,967 cases involved the donor's blood was not of the ABO group as stated on the bottle in two cases.

Without knowing the total number from which the 2,967 are selected the two wrongly labelled bottles may or may not represent a much higher proportion of error than is considered unavoidable in an earlier chapter.

In any event some explanation of how these two bottles escaped the rigid checks and cross-checks, described in detail in Chapter 7 where the combined manipulative and serological sources of error are calculated at 1 in 43,000, would be helpful.

Two mistakes of this nature, picked up on cross match might represent a total of four such errors in the series, since bottles wrongly labelled O would escape detection by this final cross matching check.

Minor points, such as these, and the confusion in the description of the anti U antibody (p. 381) must not be allowed to detract from the value of this book. The subsequent editions, which will assuredly be demanded, will provide opportunity for elucidation and correction.

The bibliography is comprehensive and indicates the degree of care that has been taken in providing a manual which should appeal to pathologists, technicians and indeed to all engaged in blood transfusion work.

R. A. ZEITLIN

SCIENCE AND THE HUMANITIES

History and Philosophy of Science

An Introduction By L. W. H. Hull Pp xi+340+16 plates (London and New York Longmans, Green and Co., Ltd., 1958) 25s net

THIS is not a detailed history of science. It tries to bridge the gap between science and the humanities by considering scientific ideas in a context of history and philosophy. In these words the author describes the object of his work. Few will deny the existence of the gap, or the need to bridge it and a book of this nature should be welcomed, on

one hand by those whose training and background have led to an emphasis on technology and on the other, by students of the humanities who seek to understand the vital contribution of science to human thought. The general reader also will find the author's approach both interesting and stimulating. He anticipates the criticism that "most readers will, no doubt, find too little about some topics and too much about others". He points out that before the spread of evolutionary ideas the influence of biology seems scarcely comparable with that of mathematics and the physical sciences.

The book opens with a review of ancient science covering three periods: the first from the beginnings of science until the rise of Athens after the Persian wars, the second until the Macedonian conquests of the fourth century B.C., the third period takes the Alexandrians as its theme. This review is comprehensive in relation to the hundred pages allotted to it, and makes interesting and instructive reading. Chapter 4 carries the story through the period of the Middle Ages with some reference to Arabic contributions.

In the two following chapters celestial geometry and celestial mechanics are very adequately surveyed from the time of Copernicus to that of Newton. With such fundamental changes in ideas concerning the universe it is appropriate that a chapter is devoted to Changes of Outlook and Method and this constitutes one of the most valuable parts of the book. A separate chapter deals with other scientific developments in the sixteenth and seventeenth centuries, such as the phenomenon of light and attention is directed to the philosophical thought of Berkeley and Hume.

The chapter 'The Nineteenth Century and Evolution' introduces the reader not only to Darwinian theory and its implications but also to its significance in the development of thought. In an 'Epilogue' which includes the theme of twentieth century trends the author gives a warning which it is to be hoped in the interests of both science and the humanities will not fall on deaf ears. 'It is urgently necessary to restore the unity of intellectual life. Unless we do so we shall soon lose what is best in Western civilization.'

H. D. ANTTONI

INDIAN PREHISTORY

The Pre-historic Background of Indian Culture

By D. H. Gordon (Sponsored by Bhulabhai Memorial Institute) Pp xi+190+32 plates (Bombay M. D. Desai 1958) Distributed by N. M. Tripathi (Private) Ltd., 1958) Rs 20

UNTIL recent years the study of the archaeology of the Indian peninsula has woefully lagged behind that of some other parts of the world. Especially is this so in the case of its prehistory. It is true that isolated finds of stone implements have been made from time to time during the past one hundred years—and in this connexion the name of Bruce Foote in Madras has an honoured place—but it is only recently that it has become possible to piece together an overall picture of the successive cultural phases in India and even now the gaps in our knowledge are more than numerous. The subject is complicated since India seldom presented a uniform picture. Even in very early times the Madras area formed part of the vast Chellean-Acheulean complex

while the northern regions belonged to another and distinct province which included the early stone-age cultures of Burma and south-east Asia. Most of the worthwhile investigations have, until recently, been undertaken by non-Indians, but nowadays highly trained investigators like Dr Sankalia and his colleagues have come into the field and are making important explorations. But there is so much to be done in the field that there is little opportunity for these investigators to stand back, as it were, and give a general report of what has so far been pieced together of the ancient history of their fascinating land. It is here that Colonel Gordon steps in.

Gordon has served, travelled and explored in India for thirty-two years and himself has undertaken not a few investigations, and he knows as much about the rock-shelter paintings of the Central Provinces as any man alive. But in the volume under review he has set himself the task of attempting to see the archaeology of India as a whole and to make available for students the latest ideas on the subject. Geographically, India is a large and varied country, and just as the cultures are not, and never have been, uniform throughout, so the climate differs in different areas and has differed greatly in past ages. A brief study of climate changes must necessarily be considered first, and then the earliest stone age cultures can come under review. The later stone age cultures are next dealt with, and here it must not be forgotten that in some regions these seem to have continued until quite a late date, indeed some of the Megalithic tombs and polished stone axes have been dated as late as the third century B.C. A chapter on the peasant potters of Makran, Baluchistan and Sind follows, and this naturally leads on to a discussion of the civilization of the Indus valley. Thanks to Sir John Marshall's work and the excavations at Mohenjo-Daro and other sites, a great deal has come to light of recent years, and this fascinating civilization has become comparatively well known. The period of invasions and the rock paintings and engravings are then dealt with, and in conclusion there are chapters on the 'Dark Age' stone and copper cultures, leading to a chapter which carries on the story to the threshold of history and to the use of iron.

Colonel Gordon has done his job well. It must not be expected that in one small volume the student will find detailed studies of the archaeology of the whole of India. But the selections made are judicious and the result does give a connected picture of the past. There are a number of full-page illustrations at the end of the volume and plenty of maps, tables and text figures.

M. C. BURKITT

FLUID SYSTEMS

Chemical Engineering Practice

Edited by Herbert W. Cremer and Trevor Davies
Vol. 6 Fluid Systems II Pp. vii + 600 + xx
(London: Butterworths Scientific Publications,
New York: Academic Press, Inc., 1958) 95s,
13 30 dollars

THE latest volume in this series covers a very wide range of chemical engineering operations, although for convenience the editors have labelled the volume "Fluid Systems II". There are fifteen chapters covering gas absorption, fluidization, liquefaction and fractionation of gases, adsorption, leaching, crystallization, colloids, filtration, sublimation and the practice of evaporation. Dr Norman and his

colleagues from Manchester have written two chapters on the principles of gas absorption and the characteristics of packed-column absorption towers. The first chapter is excellent, not only for these in universities and technical colleges but also for all who are concerned with gas absorption. The second chapter, though good, lacks a little of the practical touch one would have liked. The chapter on evaporation practice by Mr Watkins from King's College, London, assisted by Mr Macmurray from Scott and Son and Mr Forker from the Dupont Company, is very readable and covers the usual types of units. More attention might have been given to the actual size of units and some of the practical problems associated with operating evaporators would have been appreciated.

The chapters on fluidization by Dr Botterell from Birmingham and Mr Turner from British Petroleum are excellent, and will be looked at very much as indicating the position with this relatively new technique, which offers so much promise of further development. In the same way the chapters by Dr Gardner of British Oxygen Co., Ltd., and by Mr Pasteur of J. and E. Hall are welcomed as showing the real problems and successes of low-temperature technology. Low-temperature gas separation is still a new technique but most challenging as a technical process.

Prof. Donald has given an interesting account of leaching, including one or two references to history which are lacking from the other chapters. One is left with the idea that operations of such long standing are not yet carried out with very elegant equipment and there must be room for improvement here. The chapter on the principles of filtration is also written by Prof. Donald.

Dr Mullin from University College, London, has written the chapters on crystallization, centrifuges, and colloid science. These are all difficult subjects and one would certainly have liked more on the practical difficulties of continuous crystallizers. We cannot learn from these chapters the physical size of units for definite capacities and there are many unresolved problems in the production of true regular crystals.

Mr Salter, from Dorr-Oliver, and Mr Hosking, from L. A. Mitchell, have given a clear statement of the variety of filters and the method of selection of equipment. Their section on accessories such as pumps and blowers for vacuum filters is a real attempt to size up these important auxiliaries. One cannot help feeling that some of these units have had their day and are a bit crude, some pruning of variety might have been suggested by these specialized authors.

This book enables one to see the range of processing problems which are now regarded as the province of the chemical engineer. It is not surprising that in his relatively short history there are many untidy edges to his work. Apart from selecting the right type of unit there is a definite degree of uncertainty as to the ability of the engineer to scale-up such plant satisfactorily.

The book will be welcomed particularly as it provides a discussion of the work in quite a number of fields which have not been adequately covered before in the British literature.

Mr Cremer has written a foreword to the volume in which he refers to the untimely death of the former managing editor, Mr Trevor Davies. Mr S. B. Watkins, head of the Chemical Engineering Department at King's College, London, has taken up the work.

J. M. COULSON

Basic Electricity

(A Course of Training Developed for the United States Navy by Van Valkenburgh, Noogor and Novillo, Inc. Adapted to British and Commonwealth Usage by a Special Electronics Training Investigation Team of the Royal Electrical and Mechanical Engineers) Part 1: Pp vi+127 Part 2 Pp vi+121 Part 3 Pp vi+122 Part 4 Pp vi+104 Part 5 Pp vi+117 (New York: The Boleat Press, London: Technical Press, Ltd., 1959) 12s 6d net per part 55s not the set

THIS five part course, aimed at training technicians rather than electrical engineers is distinguished by the simple language of its text and its concentration on essentials. It is illustrated to an extent that makes it (or at least the first two parts of it) qualify as a visual aid as well as a text-book. The cartoon like artistry is a little florid—the sort of thing one might associate with 'Jane' but not with 'Fighting Ships' and the going seems slow, by ordinary teaching standards, in the early stages. It soon becomes evident what the authors are up to—using the same technique as the creators of the La'l Abnors and the purveyors of branded goods, to set up an image and attract a loyalty to it, the image being that of the electron. I have no doubt that the early parts would be highly successful in bringing people who would not normally gain a great deal from the printed word to a really sound understanding of the fundamental principles, and simple circuits and meters. The last three parts use the artist in a much more quantitative kind of way. The usual work on alternating current, a.c. circuits and electrical machinery is done with the minimum of algebra; but every important result is explained and illustrated with the help of vector diagrams and graphs. These parts, in fact are a very well-conceived textbook of the orthodox type, and contain some new ideas for expounding the more difficult points, which are never skirted. Instructions for experiments are given, with a list of apparatus needed to work through them. The really exacting part of instruction at this level is in making the initial contact with the pupil. The originality and skill that have been lavished on the early stages of the course should ensure for it a very high contact potential. G. R. NOAKES

The Strategy of Chemotherapy

Eighth Symposium of the Society for General Microbiology, held at the Royal Institution, London April, 1958. Edited by S. T. Cowan and E. Rowatt. Pp ix+360 (Cambridge: At the University Press, 1958. Published for the Society for General Microbiology) 35s net

THIS symposium shows what a complex field of research has developed from Ehrlich's pioneer work on the use of specific substances to attack micro-organisms in the tissues without damage to the host. The organizer invited contributors to suggest fresh methods of attack and the result was a series of papers of extreme diversity in approach, techniques and objectives. They were given by the micro-biologist, the pharmacologist, the biochemist and physical chemist, and include such fundamental conceptions as membrane penetration, bacterial cell wall synthesis and energy supplying reactions wherein the research worker is endeavouring to discover some subtle difference in the components of host and parasite which may be exploited to the detriment of the latter. At the other end of the scale

are the frankly empirical mass methods used so successfully in the production of the antibiotics and other synthetic drugs, but without any fundamental explanation. These random methods still offer probably the greatest chance for further production of new compounds and therefore have their place in the field of chemotherapy, but the symposium does emphasize the necessity for the combined operations of each type of research worker if chemotherapy is to have a logical basis of development and not be, as one worker defined it, dependent upon intelligent guesswork. H. BERNY

The Native Pinewoods of Scotland

By Prof. H. M. Stoven and A. Carlisle. Pp xvi+368+20 plates (Edinburgh and London: Oliver and Boyd, Ltd., 1959) 63s net

THIS beautifully produced book will be a welcome occupant of the bookshelves of many students of Scottish history and natural history. The subject-matter is both broader and narrower than the title might suggest—broader in so far as the authors discuss much relating to the general history of Scottish forests and to the relationships of pinewoods to woodland of other species, narrower in so far as some features of the pinewoods receive particularly detailed treatment.

The authors trace the history of Scottish woodlands from the Pleistocene period onward through historic times, collating and summarizing an immense amount of evidence from geological, palynological and archaeo-logical sources which has never before been brought together. They pass on via a very general ecological account of the pinewoods to a systematic description of all the known surviving examples of woods which are with reasonable certainty composed of naturally regenerated indigenous pine. Carefully prepared maps accompany the descriptions, and show the exact distribution of pine and of other species of trees in the neighbourhood of the pinewoods. This portion of the book is noteworthy for copious historical information which has been gathered together from estate records, early maps, accounts by travellers, etc. An account of Dr Carlisle's study of the morphological variation of pine in Scotland concludes the book.

A fine series of photographs illustrate the book. I have noticed only one trivial misprint. The book should form a valuable foundation for further ecological work in our western outposts of the European boreal conifer forest which have so long attracted British naturalists. E. W. JONES

South African Animal Life

Results of the Lund University Expedition in 1950-1951, Vol. 5. Edited by Bertil Hünström, Per Brännö and Gustaf Rudebeck. Pp 520 (Stockholm: Almqvist and Wiksell 1958) 75 Sw kr

VOLUME 5 of this series of publications contains accounts on Porifera, Crustacea, Diplopoda, Diptera, Homoptera and Coleoptera. Six chapters each on the Homoptera and Coleoptera make up the bulk of this volume. As in earlier volumes the taxonomic treatment is amplified by zoogeographical accounts, and frequently the general accounts are not restricted to the description of the Lund collections, but bring them into relationship with other material. For an assessment of the scope and general merit of this series the reader is referred to an earlier article in this journal (*Nature* 180, 56, 1957).

Inside the Living Cell

Some Secrets of Life By Dr J A V Butler Pp 174+16 plates (London George Allen and Unwin, Ltd, 1959) 21s net

DR J A V BUTLER'S former book, "Man is a Microcosm", was reviewed enthusiastically in these pages some years ago. The scope of the present work is much wider, quite apart from the fact that many parts of the subject have advanced radically in the past few years.

The author describes in straightforward language many of the great advances which have been made during the past ten years in our knowledge of the mechanisms which operate within living cells. These include not only the ways in which food materials are taken and transformed into proteins, nucleic acids and other constituents, but also the way in which the ability to make all these is transmitted from generation to generation. In these processes we come very near to the basic mechanisms of life itself. In addition to his excellent account of the normal behaviour of cells the author discusses neoplasms and other abnormalities caused by ionizing radiations, those which seem to occur spontaneously and those which are caused by chemical carcinogens.

Later in the book some abilities of specialized cells, such as those which form muscles and nerves, are dealt with, and an account is given of the immense structures which living cells achieve in the higher animals and finally in man.

Altogether the reader is given some idea of what life has achieved, first, in reaching the level of the cell, and secondly, in elaborating great assemblies of cells in the higher forms of life. Finally, the author discusses the causes and significances of ageing and death, and the meaning of life in the world of atoms.

Throughout, the work is informed by the original work and thought of the author. The book is beautifully produced in every way. The illustrations are particularly good and include photomicrographs such as those by D A Sholl of nerve cells in the visual cortex, and by R W G Wyckoff of bacteriophage. The book can be recommended warmly to many classes of reader. Most of it should appeal to the educated adult and it will be invaluable for the general reading of a good science sixth former, or university undergraduate.

W L SUMNER

Organic Syntheses

An Annual publication of Satisfactory Methods for the Preparation of Organic Chemicals, Vol 37, 1957 Edited by James Cason Pp vii + 109 Vol 38, 1958 Edited by John C Sheehan Pp vii + 120 (New York John Wiley and Sons, Inc, London Chapman and Hall, Ltd) Each 32s net

AMONG the 32 compounds for which preparative methods are described in Vol 37 are benzofurazan oxide, *trans*-2-dodecenoic acid, glutaric acid and glutarimide, norbornylene, parabanic acid, and *ar*-tetrahydro- α -naphthol, and the 31 preparations of Vol 38 include diphenylacetaldehyde, hendecanedioic acid and several related compounds, monobenzal and monobromo-pentaerythritol, monovinylacetylene, *trans*-stilbene oxide, and 2-vinylthiophene. Each volume has a cumulative index extending back to Vol 30. Four enclosed leaflets direct attention to explosions that have been experienced in preparing ethyl azodicarboxylate, methoxyacetylene, and *o*-toluamide, and in storing *p*-tolylsulphonylmethyl-nitrosamide.

JOHN READ

Trends in Birth Rates in the United States since 1870

By Bernard Okun (The Johns Hopkins University Studies in Historical and Political Science, Series 76, No 1) Pp 203 (Baltimore, Md The Johns Hopkins Press, London Oxford University Press, 1958) 3 50 dollars, 28s

THIS monograph consists of three essays. The first two discuss the secular trend of the declining birth-rate in the White and Negro population of the United States, respectively. The method used is an analysis of fertility indices (the ratio of children to the total population, and the ratio of children to women of reproductive age) in different States of the U S A. The discussion will be of interest mainly to the specialist in demography, and adds little to what is already available in the monograph by Grabill, Kiser and Whelpton, who have surveyed the material in much greater detail. The third essay, however, is of more general interest. Here Dr Okun surveys the hypotheses and approaches used in explaining birth-rate trends, and attempts a classification and an assessment of the methods that can be used to test the hypotheses. No very definite conclusions emerge, but the essay is a useful summary.

The Structure of Glass

Proceedings of a Conference held at Leningrad, November 23-27, 1953 Translated from the Russian by E B Uvarov Pp ii+295. (New York Consultants Bureau, Inc, 1958) 20 dollars

THIS translation was sponsored by the Glass Division of the American Ceramic Society and the National Science Foundation with the expressed object of providing a general look at the status of glass science in the U S S R, and admirably does it fulfil its purpose. The fact that this conference was attended by more than 500 delegates from twenty-eight towns of the Soviet Union is itself impressive, and conveys immediately an idea of the large scale on which research in this field is being conducted.

As a report of a conference the volume is excellent, the printed discussion is particularly lively, and occupies 70 pages, 42 papers were communicated to the conference and these account for 228 pages of the volume. Remembering that the conference took place five years ago it would appear that at that time there was no great difference between the topics being discussed in the U S S R and in Western circles.

It would be easy to dismiss the discussion as being concerned too much with semantics and to criticize some of the ideas put forward. However, examples of similar ideas and arguments are well sprinkled through the literature. The great argument of the conference was on the rival merits of the 'random network' theory of glass structure and the 'crystallite' theory. The proponents of the crystallite theory attacked their opponents on the ground that the randomness was not complete, while their own definition of 'crystallite' was hedged by sufficient qualifications to make it clear that the majority of them did not mean that term to imply anything that could properly be described as a crystal.

Perhaps the fairest summing-up is that here there is realization that the network theory of glass is only a first approximation—a view which is receiving increasing emphasis at the present time.

The translation was well worth while, and all interested in the physics and chemistry of glasses will enjoy reading the book.

R W DOUGLAS

LIBERTY IN AN AGE OF SCIENCE*

By SIR SOLLY ZUCKERMAN, C.B., F.R.S.

Department of Anatomy University of Birmingham Medical School Birmingham

IF, two or three decades ago, one had spoken of science and liberty in the same breath, the emphasis would have been different from my present theme. That period was the era in which the social function of science was a central issue of debate and it culminated in the almost total mobilization of the scientific forces of our two countries during the Second World War. This War was the turning point. Where previously scientists were seen according to the interests of the observer either as dedicated scholars, or as the source of invention or as the technical guardians of the social services on which an urban civilization depends to-day they also appear in a number of new guises—as the backbone of national defence, as pioneers of outer space, and even as the counsellors of presidents and prime ministers.

The world has come not only to recognize but also to insist that science has a social function, but, not all the world. There have always been those who have questioned whether the democratic way of life, and a life of liberty can survive the stresses of rapid economic growth, and as the hazards of our century mount, their numbers are being reinforced by others who are fearful lest all society becomes a victim of the forces that have been unleashed in our present scientific age. "The scientists think they are God" one exclaims "they want to remake the universe and we pay the price for their mad ambition."

This is no lonely voice, and it is one that has been heard before. Long before the days of artificial Earth satellites, long before the era of nuclear weapons. George Gissing wrote "I hate and fear science because of my conviction that for a long time to come if not for ever it will be the remorseless enemy of mankind. I see it bringing a time of vast conflicts, which will pale into insignificance the thousand wars of old and as likely as not, will overwhelm all the laborious advances of mankind in blood-drenched chaos."

But what science is thus that is the enemy of mankind? Surely not the pure thought or theory which enhances man's understanding? It is well to consider out of what confusion it is that science presents this ominous look.

The cultivation of science, by which we mean the quest for new natural knowledge through controlled and reproducible observation, can be treated as an endeavour which is either personal and private, or social and public. But however pure or personal may be the object of acquiring a scientific understanding of the universe in which we have our being, science inevitably becomes social or public not only because there can be no awareness of the existence of a new scientific idea until it is communicated from one person to another, but also because pure science frequently turns out to be basic to some practical development—to some piece of applied science—or to some convention of thought which then starts

transforming the environment within which it was distilled. So it is that pure science and applied science have progressed hand in hand over the years, the pure fertilizing the applied with ideas and the applied often providing the pure with the physical apparatus to help in the next intellectual leap forward.

This process has been a major factor in the progressive replacement of superstition by rational theory. And as Condorcet—that great French scientist of the latter half of the eighteenth century who was so powerful a protagonist of human dignity and freedom—wrote "The progress of the sciences ennobles the progress of the art of education which in turn advances that of the sciences"—a reciprocal operation which he did not exaggerate by describing "as one of the most powerful and active causes working for the perfection of mankind."

Man's evolution has also meant the continuous transformation of his social institutions through the directed application of pure scientific knowledge. We talk to-day of living in a new age of science of a world in the throes of a new scientific revolution but there is nothing new about this revolution except its speed and its greater hazards. Science has always revolutionized society ever since some basic discoveries in animal husbandry and crop cultivation made it possible for nomadic life to give way—to ten to twenty thousand years ago—to permanent village settlements, and so to the diversification of labour and the beginning of trade.

The transformation of society by scientific discovery and application has continued ever since, sometimes so slowly that decades pass before the historical record reveals much change, sometimes as at present with ever mounting force. While it could be argued that the technical advances of the past ten to twenty years transcend those of the rest of human history, that the speed with which new discoveries are disseminated and applied is now unprecedented, that the political and economic consequences of all this scientific activity will prove far more profound than those which resulted from past epochs of discovery, there is nevertheless no immediate reason to suppose that the social process which is involved in to-day's scientific revolution is different in kind from what was entailed in previous phases of rapid change.

If we are to understand the confused position in which the layman and the scientist now stand in relation to each other, we need therefore to examine certain features which characterize the growth of scientific knowledge, and also some which relate to its present impact on social affairs.

What, first do we mean by the need for scientific freedom as it applies to the pure scientist? One means not only the freedom to investigate those problems which one seeks ~~oneself~~, the fact that significant advances in ~~not be ordered by dogma~~, requires its special

* Substance of the address delivered at the Sixty-fifth Commencement Exercises of the California Institute of Technology on June 12.

thermodynamics, of relativity, or of natural selection, undoubtedly had their antecedent relations, no one could have predicted, before it actually occurred, if, and how, and when any of these major advances in our scientific understanding was to have taken place. Nor would it be possible to force a scientist to make this or that specified discovery. For example, genius though he was, no one could have prevailed upon Charles Darwin, say, in 1830 when he was twenty years old, to anticipate the basic genetic law revealed by Gregor Mendel thirty-five years later. One can employ special measures to encourage this or that branch of science. One can provide the conditions in which pure science flourishes, by multiplying the opportunities which make it possible—the universities, the laboratories, the freedom from other responsibilities. But having done these things, one can only then wait to see what emerges. One cannot in advance specify the shape and content, or determine the possible impact of what is not yet known.

Being unpredictable, it follows that the untrammelled emergence of new scientific ideas is not compatible with any restraint on the liberty of the scientist to roam where his fancy leads. Indeed, once the growth of any set of scientific ideas becomes constrained, it stands in danger of becoming obstructive dogma. A valid scientific hypothesis is never more than the best statement which, for the moment, can be made of the relations of the matters to which it refers, and should be swept away as soon as a better one emerges.

The growth of science thus necessitates freedom, even the freedom to be revolutionary. How then is stability to be achieved in a world in which science has so great an impact? How does science become, as it has often been described, the servant and the handmaiden of freedom?

One's immediate answer is that since economic and military power are to-day proportional to the degree with which scientific knowledge is exploited, science is the defender of the ideal of freedom on which Western democracy rests. In a more particular sense, as many have pointed out before, the applications of science have also provided the apparatus which has made central government powerful.

But surely science is in these respects no more the servant of the democracies than of the authoritarian regimes poised against them, and of the philosophical and political concepts on which they, in turn, are based. In a world of conflicting power, science is both the arsenal and instrument of power—but science *qua* science is always a neutral arsenal and a neutral instrument.

We cannot invest pure scientific knowledge with any inherent moral direction. That is imparted by the way science is used, and we can be certain, therefore, that all sides in the present world struggle will use science and technology in the achievement of their respective national aims, and also in whatever efforts they may make to narrow the over-widening gap between the developed and under-developed territories of the world.

My first main point, therefore, is that while the growth of fundamental scientific knowledge necessitates complete freedom from restraint, science is not uniquely associated with the preservation of freedom either in the personal or social sphere.

But there is a deeper issue underlying the relation of science and freedom. Let me first define the sense that I propose attaching to the concept of freedom

on liberty, which both in isolation, and as the ideal which annunates democracy, has always been a major concern of philosophical discussion.

By freedom I mean here the liberty an individual enjoys after the infinite number of degrees of freedom which are open to him in the abstract have been reduced by, say, the give-and-take of social life, still leaving a vast area of choice within which he could either engage in, or desist from, any particular activity. It was essentially in this sense that the great utilitarians of the industrial revolution—Bentham, John Stuart Mill and others who joined them in the battle for justice—conceived of freedom in the ideal society—a society which is governed by common consent for the common good, in which the greatest number enjoy the greatest happiness, in which there is equality of suffrage, and in theory, at least, in educational and economic opportunity, and in which laws and institutions, regulating the behaviour of individuals, are there because the unlimited exercise of one man's liberty would inevitably impose restrictions on that of his fellows.

It is essentially in this social sense, however 'negative' it may be, that liberty is implied in the proposition that science is its handmaiden. Science may, of course, well be the handmaiden of equality in the economic sphere, given, of course, the right political institutions. But is the proposition true in the philosophical sense of the term 'liberty', whether in relation to the concept to which I am directing my observations or to any other idea of liberty which philosophers have examined? Can it be true of the actual environment within which we exercise our freedom—an environment which is not some unreal stratosphere peopled either by abstract shadows of human beings or of social groups? Surely our social environment is a real one which is constantly being transformed by new scientific ideas, and by the application and practical development of these ideas. This transformation constitutes more than a process whereby men are conditioned in their thoughts and actions. Whenever some major development is pursued, for example, the development of machines based on steam, it means that some other path that potentially might have been followed was not followed. A material civilization of motor cars, of radio, of synthetic fibres, of nuclear power is not necessarily the only form a material civilization might have taken. But now that it has taken that shape, it helps define for us the content and boundaries of the area within which we exercise our freedom.

Liberty, in the sense I am using the term (and I believe to most political philosophers), means the power to act freely within the compass of the institutions which a people may set up in the exercise of their sovereign power, which implies their right to act as they think best as a collective body and which, according to legal theory, "is not restrained in any way except by the limitations inherent in human nature". It is irrelevant here that the exercise of democracy may not infrequently depart from its ideals, or that the institutions which had to be set up to preserve the hard-won freedom of modern times may themselves have eroded the principles they were meant to preserve. The point I wish to make is that science, through its practical impact, is to an increasing extent, almost to a dominant extent, determining the way the presumed uninhibited sovereign power expresses itself. Because of its achievements in eliminating disease and alleviating pain, through

the food and wealth it has brought, most people to-day prefer to regulate their lives in accordance with scientific discovery rather than in any other way. In that sense they are prepared to constrain their abstract liberties in accordance with what science unfolds and the riches it brings. Is the choice, we may ask, conscious? Can we know for what it is we are opting? Hobbes, like other philosophers, found liberty consistent with necessity. Is liberty truly consistent with necessity, when necessity is determined by science? Is the sovereign power consciously deciding to develop thus or that scientific discovery, and so to determine social development in this or that direction? Or is it merely adapting itself as best it can to what comes out of Pandora's scientific box?

The answer to any of these questions is inevitably bound up both with the constraints and unpredictability of any new major scientific advance. Of course, there are always certain fields of science which are more popular and better supported than others. Scientific knowledge never develops evenly over the whole potential field of knowledge. But in so far as scientific activity is in general confined by past discovery to certain areas, so is our abstract liberty, in effect, constrained. Furthermore in any field of science several alternative courses of action might be pursued in search for a solution to a problem. In choosing any one of them the research worker may deny himself, and others the opportunity of pursuing another. There is also the increasing complexity of the scientific knowledge which is now being transformed into new remedies, new chemicals, weapons systems, and so on. The facts which these days transform our lives become more and more difficult to comprehend and on occasion are still not fully decided when they are applied. If this were not so would there still be debate—I choose the most urgent example of all—about the hazards associated with radioactive fall-out?

Above all is the fact that the nature and magnitude of potential discovery cannot be defined in advance any more than can its impact on our social lives. As de Toqueville wrote: 'We entrust ourselves to the future, an enlightened and impartial judge—but one who sits, alas, always too late.'

Faraday, Hertz, Curie—what could they have known of the ultimate uses to which their discoveries would be put in the field of electric power, radio and nuclear energy, or of the social and political consequences of their uses? We ourselves, years later, cannot tell what these consequences will be. Can we to refer to just one more vital question out of many now once this scientific age is generating, commit ourselves now to more than arbitrary views of the possible political consequences of the elimination of disease and of its complementary change, the explosive growth of population in so many areas of the globe?

Science has created wealth, it has helped in the struggle for freedom from economic exploitation, it has redistributed power. But in doing these things as it widens the area of material choice, it circumscribes and determines the environment in which we exercise our abstract liberties. That is my second point. Itself demanding freedom and revolutionary in its ways, science is now determining in an increasingly unpredictable way, the main issues about which we as citizens, exercise our freedom of choice. Can there be much more than a fictional verity to the abstract idea that an area exists within which

man can enjoy the capacity of unconditioned or untrammelled choice?

Democracy was man's answer to tyranny and exploitation. The only form of exploitation it will never help overcome is the coercion of new knowledge, which by guiding our social lives into certain channels, limits advance in other directions, the new knowledge which focuses the interests of humanity on goals which cannot be properly charted until they have been achieved. To the philosopher, as I have said, ultimate limitations on the freedom of the individual are set by the inexorable laws of Nature. To the scientist, the limitations are set by the particular laws of Nature man himself discovers, out of a potential infinity of such laws and from the use to which he puts these laws.

Up to now we have been able to claim that the applications of science have increased the sum total of human happiness. But to-day we stand at a cross road. The process of applying scientific knowledge is as endless as is the prospect of gathering new knowledge, and the basic scientist is responsible for only the beginning of the cycle of activity which creates a demand for the application of his discoveries. Industrialization has established itself as the one cure for poverty in a world the bulk of the population of which still lives by subsistence farming and history as yet gives no example of any but small communities which have voluntarily turned their backs on higher material standards of living. Instead a uniformity of desire and demand is generated for the so-called good things of life as the one world discovers how the other lives and what it itself lacks. Obviously we cannot say that the economic history of the West will be recapitulated as industrialization spreads and as the chains of the past are broken in distant parts of the world. But we can be all but certain that neither the needy nor the rich will allow the process of applying the fruits of scientific knowledge to stop, either in the national or the international frame. In this process means become ends, because as new ways of doing things are discovered they transform the things being done and so their purpose. In these days it is only in theory that one chooses weapons and tactics to achieve a strategy. In fact weapons often end by determining strategy—and sometimes the purpose behind the strategy.

In my view it is against this force of scientific application that the Gensings of to-day rail—not against science as such and it is this force which could construe our democratic liberties and which, if we ceased being vigilant, could even constrain the liberty of pure and basic science—and by so doing paradoxically destroy itself.

Ideally we think that democracy to-day means government by the representatives of the people by consent of the people. But many to-day also feel that the sovereign power, the people, has through a process of negative democracy, abdicated its rights to a power elite, to a bureaucracy to what you will which is consciously determining the directions we follow. This it seems to me, is again too simple. The element of the unknown in government increases with every step we are now taking to apply the fruits of science. If sovereign power is being abdicated it is less to some governing body, however formed, and more and more to a process of applying scientific knowledge without any real possibility of determining its final consequences. Neither the voice of the majority, nor those through which it is expressed, can proclaim the precise lines of the future.

Where do scientists stand, as ordinary citizens, in this process whereby the application of the fruits of their discoveries can become a potential prison for our abstract liberties? It is argued that because of their special knowledge scientists can be aware of the danger and promise arising from their discoveries, and that therefore they have a special responsibility in relation to the most pressing problems of our time. I should agree with this, if it meant no more than that scientists are better able to appreciate the scientific facts. For how can the scientist as such, who is not responsible for its application, accept the responsibility for predicting some vast social transformation that might result from what seems an innocent observation at the time it is made?

But I should agree all the more if one coupled with this view of the scientist's responsibility the thought that in the problem of preserving our liberties lies the most important reason for regarding an education in science as constituting to-day an essential part of an education in the humanities. For if an understanding of social and political purpose is one of the aims of the liberal arts, then that aim cannot be realized until their scope is widened to embrace a proper understanding of the scientific knowledge the application of which is now so rapidly transforming our intellectual and material environment.

Science, technology and humanism seem to have assumed that order of importance in the determination of our affairs. I do not know how it is in the United States, but over the post-war years the changes which the tacit application of science and technology have occasioned in Great Britain seem far more profound than any that have been brought about through the overt discussion of social values or social goals. If this kind of thing is happening, can the humanities continue as a potent educational discipline without encompassing an understanding of the social forces which derive from the application of the natural sciences? Scientific literacy, we are told in a recently issued report on education, will need to be far more widespread than it is "if we are to solve the problems of this age". Undoubtedly this is needed, but alone it is not a sufficient condition to ensure the solution of our problems—for here I agree with Aldous Huxley that "higher education is not necessarily a guarantee of higher virtue or higher political wisdom". What we most need to learn is that in the major scientific matters which now affect human destiny, one cannot safely take decisions for to-day unless we realize that those same decisions determine the future. This realization may not lead to the right decisions, but it might help obviate some of the worse.

SATELLITE OBSERVATIONS OF SOLAR COSMIC RAYS

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ON three occasions during August 1958, large increases in the intensity of charged particles outside the Van Allen radiation zones were detected by the *Explorer IV* satellite 1958 epsilon, at high magnetic latitudes and rather low satellite altitudes (270–650 km), where the Geiger tubes carried in the satellite normally count only cosmic rays. Figs 1, 2 and 3 show that the charged particle intensity in both counters increased sharply with magnetic latitude, above about 60°, on August 16–17, August 23–24 and August 26–27. (We have defined 'magnetic latitude', λ_{dip} from the magnetic dip angle δ at the point of observation, through the dipole relation $2 \tan \lambda_{\text{dip}} = \tan \delta$.) Different symbols have been used for each satellite pass on any one day, recorded at the microlock station in Van Buren, Maine, in the geographical longitude range (95° W–45° W). The

time-interval for each pass (usually about 5 min duration) is given, and each point has been characterized by the altitude in kilometres at which the observation was made. The charged particle detectors in the satellite have been described in detail elsewhere by Van Allen *et al.*¹ The two Geiger counters (one shielded with 1.6 gm/cm² lead, and the other unshielded except by the satellite hull) could detect protons of energies greater than 40 MeV and 30 MeV, respectively, and electrons of energies greater than about 5 MeV and 3 MeV. The omnidirectional geometric factors ranged from 0.140 cm² to 0.823 cm² in the shielded counter, and from 0.140 cm² to 0.705 cm² in the unshielded counter. Table 1 gives the upper and lower limits to the omnidirectional fluxes of particles which would produce the highest observed counting rates in (a) the unshielded counter

Table 1

| Date August 1958 | Time of satellite pass (UT) | (a) Flux through unshielded Geiger counter (particles/cm ² /sec) | (b) Flux through shielded counter (particles/cm ² /sec) | (c) Ratio of counting rates unshielded/ shielded | (d) <i>E</i> _{min} (MeV) | (e) <i>E</i> _{max} (MeV) | (f) Elapsed time after 3 + solar flares (hr) |
|---------------------|-----------------------------------|---|---|--|---|---|--|
| 16 | 11 17–11 19 | 86 > <i>J</i> _{su} > 17 | 78 > <i>J</i> _{st} > 13 | 1.1 ± 0.3 | ~ 90 | ~ 200 | 6.8 |
| 16 | 13 11–13 15 | 193 > <i>J</i> _{su} > 38 | 179 > <i>J</i> _{st} > 30 | 1.1 ± 0.2 | ~ 90 | ~ 200 | 8.7 |
| 17 | 11 01–11 06 | 240 > <i>J</i> _{su} > 48 | 86 > <i>J</i> _{st} > 14 | 2.8 ± 0.3 | ~ 90 | ~ 200 | 30.5 |
| 17 | 12 50–13 00 | 121 > <i>J</i> _{su} > 24 | 43 > <i>J</i> _{st} > 7 | 2.8 ± 0.5 | ~ 60 | ~ 200 | 32.4 |
| 23 | 09 22–09 30 | 577 > <i>J</i> _{su} > 115 | 193 > <i>J</i> _{st} > 33 | 3.0 ± 0.2 | ~ 90 | ~ 250 | 19.1 |
| 23 | 11 14–11 23 | 445 > <i>J</i> _{su} > 88 | 150 > <i>J</i> _{st} > 25 | 2.9 ± 0.2 | ~ 35 | ~ 250 | 21.0 |
| 24 | 10 50–11 05 | 140 > <i>J</i> _{su} > 28 | 37 > <i>J</i> _{st} > 6 | 3.8 ± 0.5 | ~ 35 | ~ 250 | 43.8 |
| 26 | 08 26–08 34 | 1,010 > <i>J</i> _{su} > 200 | 405 > <i>J</i> _{st} > 79 | 2.2 ± 0.1 | ~ 85 | ~ 350 | 8.4 |
| 26 | 10 22–10 28 | 1,300 > <i>J</i> _{su} > 265 | 515 > <i>J</i> _{st} > 83 | 2.5 ± 0.1 | ~ 55 | ~ 350 | 10.3 |
| 27 | 08 06–08 15 | 143 > <i>J</i> _{su} > 28 | 46 > <i>J</i> _{st} > 7 | 3.1 ± 0.5 | ~ 85 | — | 32.0 |
| 27 | 10 04–10 08 | 132 > <i>J</i> _{su} > 26 | 50 > <i>J</i> _{st} > 8 | 2.6 ± 0.5 | ~ 55 | ~ 350 | 34.0 |

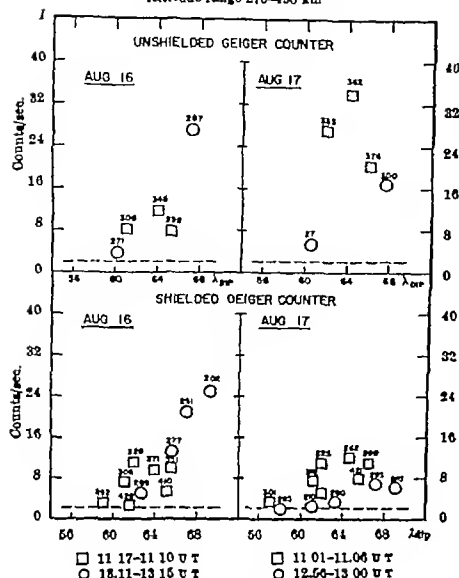
Intensity versus magnetic latitude
Altitude range 270-450 km

Fig 1

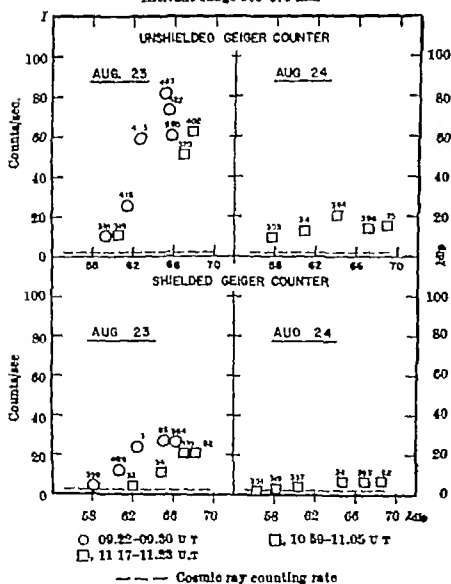
Intensity versus magnetic latitude
Altitude range 500-670 km.

Fig 2

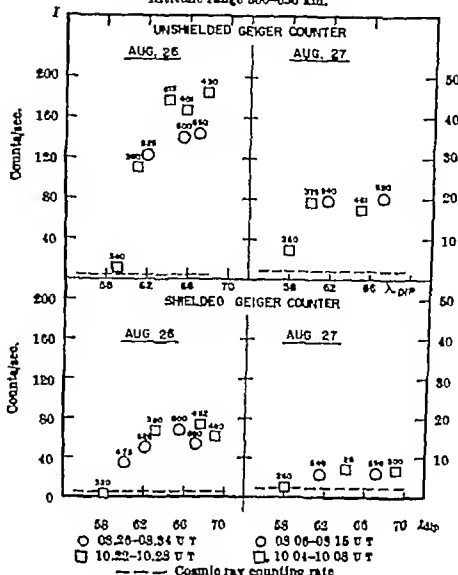
Intensity versus magnetic latitude
Altitude range 800-650 km.

Fig 3

(J_{eq}), (b) the shielded counter (J_{sh}), and (c) the ratio of these counting rates (unshielded/shielded) at each satellite pass on which an increase in intensity was observed. The cut off energies for protons, at (d) the highest magnetic latitude on each pass (E_{min}) and (e) the lowest latitude at which counting rates in excess of the cosmic ray rate were recorded (E_{max}), are estimated from the local values of the Earth's magnetic field.

The particle fluxes are at least one or two orders of magnitude greater than the normal cosmic ray flux. It seems unlikely that these intensity increases are due to soft particles from the outer Van Allen radiation zone, because

(a) *Explorer IV* cuts through the outer zone (as observed with the Geiger counters) at about 56° magnetic latitude, that is, farther south than the intensity increases reported here.

(b) The ratio of counting rates between the unshielded and shielded Geiger counters in the outer zone is typically, about 30 or 40 to one, in contrast to the comparable counting rates observed in both counters at the higher latitudes.

The ratios unshielded/shielded are reasonably consistent with the hypothesis that the charged particles are protons the energies of which lie between E_{min} and E_{max} . The wide limits placed on the estimated fluxes are due to the uncertainty in the absolute geometric factor for the counters in the proton energy range 30-100 MeV.

We suggest that the intensity increases are in fact due to solar protons, associated with the large solar flares which occurred at 0432 UT on August 16, 1417 UT on August 22 and 0005 UT on August 26. Strong support for this suggestion is provided by measurements made from balloons and with rocket motors during this period.

(1) Anderson⁴ and Winckler *et al*⁵ measured an increase in charged particle intensity at balloon altitudes above Churchill, Canada (magnetic latitude 77°), and Fairbanks, Alaska (magnetic latitude 64°), on August 22 and 23, and have identified the particles as solar protons of energies up to a few hundred MeV. It is almost certain that the satellite has recorded the same event. (The increased intensity was not observed until August 23 because there was no pass over Van Buren after 1100 UT on August 22.) Anderson *et al*⁵ deduce a differential number energy spectrum $n(E)dE = K(t)E^{-(5 \pm 0.2)}dE$ (where t is the elapsed time after the solar flare) for the solar protons in the energy-range 100–400 MeV. At 1115 UT on August 23 they estimate that the flux of particles with energies greater than 100 MeV was about $1.5/\text{cm}^2/\text{sec}$. Intensities observed from the satellite at that time suggest that a spectrum of this form may well extend down to about 30 MeV.

(2) Leinbach and Reid⁷ have suggested recently that the absorption of cosmic radio noise, measured with riometers following large solar flares, is due to ionization of the upper atmosphere by solar protons. H. Leinbach (private communication) and Hultquist and Ortners⁸ have observed three such events, commencing August 16, August 22 and August 26, in the riometers at Thule (Greenland), Fairbanks (Alaska) and Kiruna (Sweden). Absorption effects of this type occurred on twelve other occasions, between July 1, 1957, and September 30, 1958 (H. Leinbach, private communication).

During the period August 16–27 no increase in intensity was observed in the Canadian cosmic-ray neutron monitors at Resolute, Churchill, Sulphur Mountain and Deep River⁹ at magnetic latitudes of 88°, 77°, 61° and 62°, respectively, but it is not surprising that protons with a steep number-energy spectrum and maximum energies of a few hundred MeV produced no detectable effects near sea-level.

The ratio of the maximum counting rates in the two counters increased significantly during each event. This suggests that either (a) the shape of the energy spectrum of the solar protons changes, and relatively more low-energy particles arrive at later times, or (b) that some particles with energies below the usual magnetic cut-off energy can arrive at a given location later in the event.

Freier *et al*¹⁰ have, in fact, reported that protons with energies below the usual measured cut-off were found at balloon altitudes over Minnesota on March 26, 1958, three days after a large solar flare, and at the time of a magnetic storm. When the Earth's field is disturbed, some charged particles can probably be admitted to regions normally 'forbidden' to them, and particles with energies below the normal cut-off may arrive at a given latitude during, and perhaps for some time after, the disturbance. During the period August 16–27 'sudden commencements' occurred at 0622 August 17, 0228 August 22, 0140 August 24, and 0303 August 27.¹¹ The lowest ratios unshielded/shielded occurred on August 16 before this period of magnetic activity.

There is now evidence from several sources which strongly suggests that solar protons with energies up to a few hundred MeV quite frequently bombard the upper atmosphere at high latitudes for some days following a large solar flare. The five widely observed, extraordinary increases in cosmic-ray intensity near sea-level which have occurred during the past twenty years of continuous observation are probably unusually energetic examples of a common solar phenomenon, namely, the acceleration and ejection of protons with energies approaching those of galactic cosmic-ray particles.

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A BORE-HOLE TO THE EARTH'S MANTLE: AMSOC'S MOHOLE

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MAN'S knowledge of the interior of the Earth has been largely obtained by indirect methods, and although a great deal is now known about the qualities that subterranean materials must possess, numerous uncertainties remain. There is now a project under way, sponsored by the AMSOC Committee of the U.S. National Academy of Sciences to obtain corroborative evidence about the nature of the interior of the Earth by the direct method of drilling a hole completely through the oceanic crust to obtain samples of the mantle. Since the boundary between the crust and mantle is known as the 'Moho'

(after Prof. A. Mohorovičić of Yugoslavia, who first described the seismic discontinuity there) it seemed reasonable to contract the project name to 'Mohole'.

The American Miscellaneous Society, founded in 1952 as a whimsical reproof of scientific societies which are sometimes too specific for their own good, uses its cable address, AMSOC, in the alphabetical world of Washington. It has no formal members, officers, by-laws or publications, and there is a bent towards geophysics.

On the subject of drilling through the crust of the Earth, however, the AMSOC group has been formally

organized so that it can receive funds from the US National Science Foundation. The original members of the Committee were Gordon Lill (chairman), Prof Maurice Ewing, Dr William Heroy, Prof Harry Hess, Dr Harry Ladd, Dr Arthur Maxwell, Prof Walter Munk, Prof Roger Revelle, Dr William Rubey, Dr Joshua Tracy and Willard Bascom (technical director).

The Mohole project in more or less its present form was born at a breakfast at Prof Munk's house in California, at which he led the conversation on the need for a geophysical analogue for the space exploration programme. The suggestion of Dr Frank Eastabrook, made in *Science* (October 1956) for the digging of a "Geophysical research shaft", had set forth the principal scientific advantages of direct sampling. But AMSOC, unaware at the time of that suggestion, proposed a deep drilling project.

The following September in Toronto, at the meeting of the International Union of Geodesy and Geophysics, a resolution was passed "urging the nations of the world to study the feasibility and cost of an attempt to drill to the Mohorovičić discontinuity at a place where it approaches the surface". A hole 10-15 km deep on an oceanic island was suggested. The sponsors were Harry Hess, Roger Revelle and T F Gaskell.

The question of the structure and material of the interior of the Earth is a puzzle which has long challenged the mind of man. In all major aspects the most acceptable present hypothesis holds together very well. This is remarkable, for it requires that there be reasonable agreement between at least eight sub-sciences, all of which make indirect measurements. Studies of astronomy, meteorites, volcanoes, geological structure, gravity, seismic waves, the magnetic field, and heat flow each contribute to the total knowledge.

If one assumes that meteorites are the wreckage of a planet similar to the Earth and that the rocks spewed out by volcanoes (the volcanic precursors of which begin well below the Mohorovičić discontinuity) contain samples of mantle material, then we already have samples of the deep rocks. Moreover, Harry Hess believes that mantle rock actually outcrops (at St Paul's Rocks in the mid Atlantic, in Japan and in California). Astronomical observations give the total mass, the average density and the moment of inertia of the Earth.

But in the main, evidence about the interior of the Earth has come from earthquake waves. By the combination of tedious computation and great skill, seismologists have worked out characteristics of the planet which keep within the limits set by the other evidence.

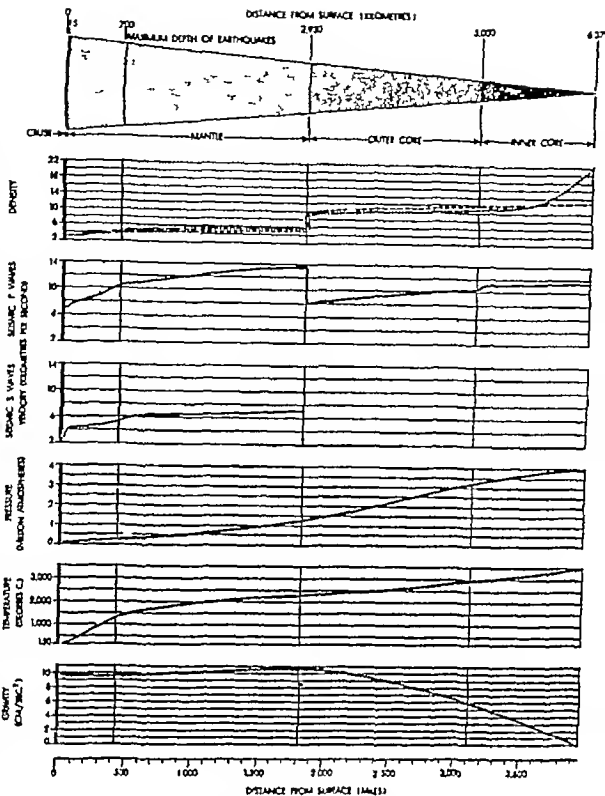


Fig 1 The Interior of the Earth

The hypothesis of inner and outer cores surrounded by a thick mantle and capped with a thin crust has stood the tests of many years. Now the problem is to refine the information and to obtain evidence which cannot come from further advances in seismology. The composition of the mantle, which represents about 85 per cent of the volume of the Earth, is the principal problem of geophysics to-day, for although a lot is known about it, uncertainties remain (Fig 1).

The exact mineralogical and rock composition, the density, strength, temperature, the amount of radio activity, the thermal and electrical conductivity—all these will contribute immeasurably to the understanding of the Earth and its origin. Moreover they will serve to enhance the value of the indirect geophysical measurements. Finally some new and entirely unexpected piece of evidence may be unearthed that will cause science to revise substantially its concept of the Earth.

The crust is closer and easier to study than the interior, but even so it is more controversial. Generally it is agreed that continents represent relatively thick blocks of andesitic rocks, and that ocean basins are composed of much thinner basaltic rocks—the average thicknesses being about 30 km.

AMSOC believes that this series of holes which will eventually sample the mantle of the Earth is likely to produce the greatest advances in man's knowledge of the Earth in our time

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ASYMMETRICAL DELIVERY IN RABBITS

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The Rockefeller Institute, New York, 21

THE experiments of Corner and Allen¹ and Allen and Reynolds², performed on rabbits, premised an understanding of the mechanism by which pregnancy is maintained and terminated in mammals. They also provided us with a key substance which controls these processes, the ovarian steroid progesterone.

The thirty years which followed these discoveries, however, brought disappointments. The different consequences in different species of ovariectomy or oxytocin infusion upon pregnancy, the lack of correlation between uterine activity and the concentration of progestational compounds in body fluids, and the lack of success in predicting effective progesterone therapy in women led many investigators to believe that either progestational compounds do not have a key role in the control of the pregnant uterus, or else a variety of mechanisms operate in different species.

These conclusions are challenged by a striking experiment of Nature which strongly implies that the maintenance of pregnancy is more a local than a systemic affair, thus allowing an explanation of the

differences cited above. When a woman who has a duplex or bicornate uterus bears twins, one in each horn, the infants may be born several weeks apart, showing that in the same woman at the same instant conditions can be appropriate for the maintenance, as well as for the termination, of pregnancy³.

Classical endocrinology limits our thinking to a systemic hormonal control of the uterus by which the glandular product is distributed uniformly in the target organs. This simple experiment of Nature, however, suggests to us that such a systemic control may not operate in all instances. A 'local' effect may be considered instead, when the organ of secretion and its target are in direct contact, allowing diffusion of an active compound from one cell to the next. Thus the local effect of placental progesterone has been postulated and described⁴ as an alternate mechanism.

The existence of such a local mechanism could explain present controversial issues concerning the mechanism of the maintenance of pregnancy. Species differences could be looked upon not as differences in basic principles, but, for example, as differences in timing and in magnitude of the shift from ovarian (systemic) to placental (local) progesterone effect, or

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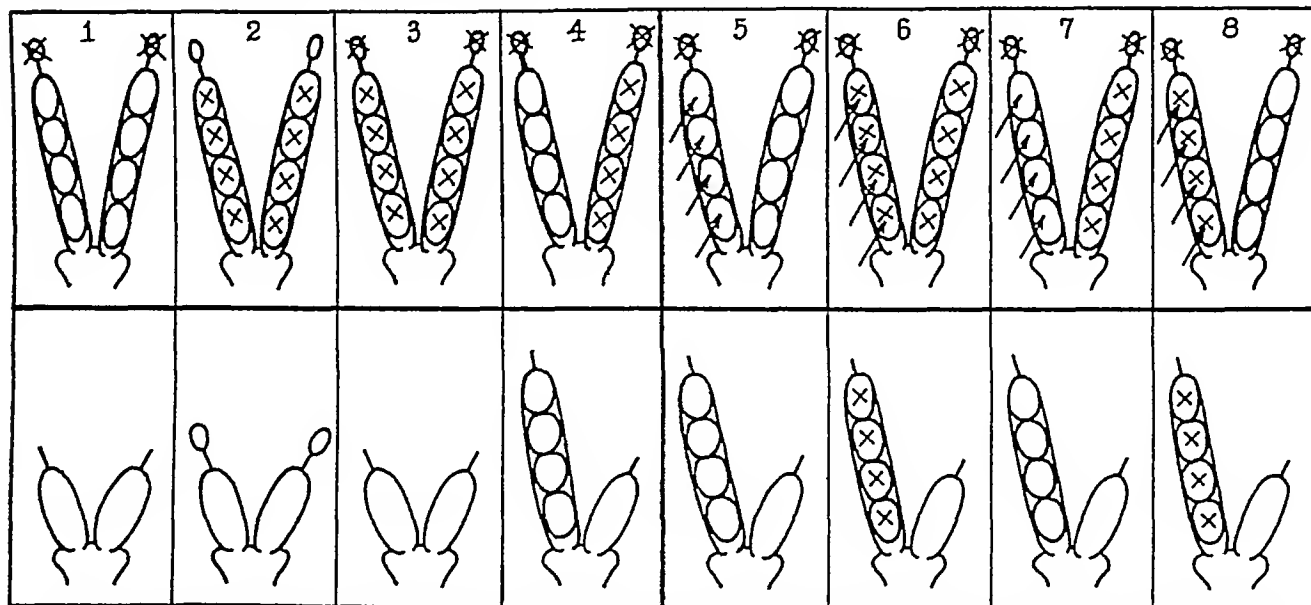
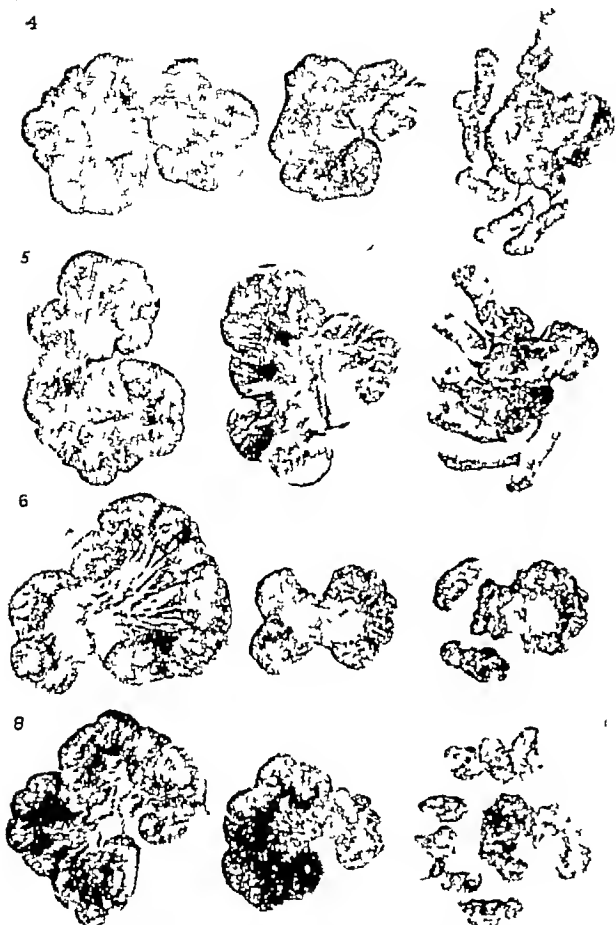


Fig 1 Schematic illustration of the type of operations used in the present study (upper row). Crosses over the ovaries represent ovariectomy, crosses over the conceptuses, placental dislocation. Arrows indicate intraamniotic injection of 2 mgm progesterone in 0.04 ml oil. The lower row represents the effect on delivery of the operation or treatment.



[Fig. 2. Asymmetrical delivery in rabbits induced on the twenty-fifth day of pregnancy. The numbers on the left represent the type of operation as illustrated schematically in Fig. 1. The first picture on the left is taken immediately after the operation, the second is made on repeated laparotomy after delivery is completed in one horn and the third after the undelivered horn is opened and the fetuses and placentas examined.]

as differences in the metabolism and elimination of progesterone, dependent on the exposure of progestational compounds to the systemic circulation, prior to their uptake by target organs. The concentration of progestational compounds and their changes in concentration in body fluids would not be expected to reflect quantitatively the endocrine condition of the uterus because much higher concentrations than occur in the blood or in the urine could be present in key positions at the myometrial cell, in fact, body fluids may contain only the 'leakage' of a local arrangement or what is left from destructive and eliminating processes. The lack of conclusive evidence for the effective use of progesterone in therapy would become a challenge than this appointment because an effect

placental progesterone could be therapeutically initiated only by a similar local application, or by forms of progesterone not subject to systemic destruction.

To demonstrate a local effect of placental progesterone on the myometrium, we studied thirty-five pregnant rabbits in the present experiments. It is generally believed that pregnancy in rabbits is entirely maintained by ovarian progesterone not supported by placental contribution. We suspected, however, that even in rabbits there may be progesterone production or effective metabolism, in the placenta in late pregnancy^{4,5,6}. In women on the other hand, during the last six months of pregnancy the placenta seems to substitute completely for the endocrine function of the ovaries⁷.

In our colony of New Zealand white rabbits labour can be induced with 1 i.v. Pitocin (Parke Davis), intramuscularly, in 94 per cent of the animals 31 days after mating. Only 7 per cent of the animals deliver after similar treatment (even if repeatedly applied) if the animal is less than 30 days pregnant.

We ovariectomized rabbits bilaterally (op No 1) on the twenty-fifth day of gestation (duration of pregnancy = 32 days) and found that 13 hr after the operation 1 i.v. of 'Pitocin' successfully induced delivery.

If the ovaries were not removed (op No 2), but all the placentas in both uterine horns were dislocated (by gently pressing the uterine horn at the placental implantation site) placental function ceased and delivery was successfully induced by 'Pitocin' 20 hr later. Thus is evidence that the rabbit placenta is indispensable for the maintenance of pregnancy.

If the two procedures ovariectomy and placental dislocation, are combined (op No 3) labour can be induced 9 hr later. These observations suggest that in the rabbit both the ovaries and the placentas contribute to the maintenance of pregnancy. When both these possible sources of progestational compounds are removed the myometrium has enough stored material to defend pregnancy for 9 hr against the labour inducing effect of 1 i.v. 'Pitocin'. The placentas can prolong this period for four additional hours and the ovaries for 11 hr. This suggests that the ovarian contribution is three times as great as the placental.

If after any of these operations 'Pitocin' is not administered, spontaneous delivery ultimately occurs but the time between operation and delivery, as well as the time needed for delivery, is greatly prolonged. Also, the mother may destroy or partly eat the

uterine contents, which makes accurate timing and observations difficult. For this reason we induced labour with 'Pitocin'.

It may be argued that the rabbit placenta only stores, but does not produce, an active progestational compound. The following experiment, however, suggests that the placental contribution is not only storage, but also synthesis or effective metabolism. If ovariectomy is combined with the dislocation of one set of placentas, in one horn only (op No 4), this horn alone delivers 9 hr later on 'Pitocin' administration, whereas pregnancy is maintained in the other horn. Thus asymmetrical delivery, resulting from the presence of a set of functional and another set of non-functional placentas in two horns, respectively, is indication of the production of an active compound as well as evidence of the local effect of the placenta.

It might be said, however, that the active compound of the placenta is not like progesterone, but is an entirely different compound. This is unlikely, since the local effect of the dislocated placentas can be substituted for by the injection of 1-2 mgm progesterone into the amniotic sac. If only one horn is treated with progesterone in the ovariectomized animal, delivery is always asymmetrical. The untreated horn delivers first, irrespective of whether the placentas in one horn are dislocated or not (op Nos 5-8). The time when delivery occurs reflects a functional or non-functional set of placentas, but the phenomenon is the same, that is, delivery is asymmetrical if the distribution of progesterone is asymmetrical. Whether the litter is alive or not does not alter the picture, nor does the mechanical

irritation of the uterine horn during the operation.

These observations are best explained as follows. Pregnancy in rabbits is maintained by a joint contribution of an active progestational compound by the ovaries (systemic) and placentas (local). The placental contribution is less than that of the ovaries, but both organs are needed to maintain an effective concentration of the active compound in the myometrial cell. When the defence is effective, labour cannot be induced by 'Pitocin', if it becomes ineffective, labour can be induced. When the systemic effect of the ovaries is suspended by ovariectomy the local effect of the placenta controls the uterus and if this local effect is asymmetrical, labour is asymmetrical.

In women, an early and complete shift from ovarian to placental hormone production could result in a dominant local progesterone effect early in pregnancy. This would lead to an 'endocrine asymmetry', resulting in asymmetrical function. Such an asymmetry is exaggerated in a bicornate uterus when endocrine function in one placenta fails earlier than in the other. Functional asymmetry of the human uterus offers attractive explanations of puzzling problems concerning normal and abnormal pregnancy and delivery.

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WARREN SPRING LABORATORY, STEVENAGE

IN setting up Warren Spring Laboratory at Stevenage "to carry out process research and development over a wide field not limited to particular areas of technology", the Research Council for the Department of Scientific and Industrial Research expressed its conviction that, when necessary, the Department's research stations should change in function and objective to meet the needs of changing situations. The Council considered that the Fuel Research Station had largely fulfilled the aims in view when it was set up, and that current needs were satisfactorily catered for by researches going on elsewhere, it decided, therefore, to close down the Fuel Research Station, and to transfer the staff to a new Laboratory in Stevenage, with new programmes. To ensure that there should be no likelihood of an impression being gained that the Fuel Research Station was being continued at Stevenage, or that the title of the new Laboratory might appear to restrict the field of activity, it is named after a lane which used to run across the site.

Of the work carried out at the Fuel Research Station only two programmes have been transferred to the new Station, namely, research on the abatement of atmospheric pollution, and on the synthesis of oils and chemicals by the Fischer-Tropsch process.

There had been a number of substantial indications of need for research in the field of mineral processing, and it was decided that this should form one of the new projects to be undertaken, there had also been indications of need for work on a pilot scale in various fields which the Department had not been able to meet. With these pointers, it was decided to build a laboratory in a modern industrial style, to be as flexible as possible, to house in the first place a staff about the size of that of the Fuel Research Station, and with facilities for both laboratory research and pilot-scale work.

The main three-story laboratory building is 372 ft long and 37 ft 6 in wide (Fig 1). It is based on a 4-ft module, which is expressed elevationally by vertical posts supporting floors and roof, and by internal posts centrally along the length. The main spine corridor is set to one side of the central supports. The only solid internal walls are those of the corridor and the secondary staircases, all other partitioning is of light, demountable, prefabricated construction, which can be placed in any desired position between the outer walls and the inner corridor walls, subject only to the basic 4-ft module.

Gas, water, electricity, compressed air are available at every third module (12 ft) along a perimeter distribution system.

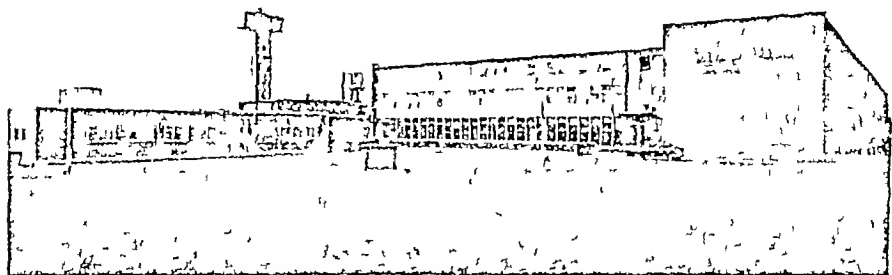


Fig 1 The Warren Spring Laboratory Department of Scientific and Industrial Research

The building is heated by panel type radiators; made-up dummy panels matching them are inserted between the radiators to give the appearance of a continuous radiator panel along each wall between the concrete columns at 12 ft centres. The radiators and the dummy panels conceal the services which run around the perimeter of the building. The dummy panels can be readily removed when service connections are required. Fume cupboards are ranged along the inner, corridor walls, each cupboard having its own extract duct which discharges at roof level.

The finishes are simple, self-coloured, fair faced brickwork being used throughout, except in laboratories with special functions. With the exception of laboratories which are adapted for wet processes, floor finishes are in linoleum.

A three-story administration block runs at right angles to the main laboratory building, it is similar in construction and design except that there is a lower ceiling height.

There are three pilot-scale buildings, each 90 ft long by 55 ft wide by 37 ft 6 in maximum height. In two of them, a 20 ft wide section is 20 ft high only. These buildings are linked to the main laboratory block by a corridor with small scale laboratory units on each side. The buildings have folding doors to the side bays to permit the introduction of heavy plant at any point. The structure is carried by precast concrete posts. Vertical cladding above a brick protective walling, consists of asbestos-cement sheeting and patent glazing, the roofs are of asbestos-cement decking overlaid with bituminous felt.

The workshops and engineering stores occupy a large steel framed building comprising six east light bays each 60 ft by 30 ft minimum headroom.

Steam is required night and day for process purposes, two fully automatic, oil fired, high efficiency boilers are used with a nominal pressure of 120 lb/sq in. One is rated at 10,000 lb and one at 5,000 lb of steam per hour. The front of the boiler house is fully glazed with a patent system permitting removal in sections when boiler tube replacements are necessary, so that it is possible to reduce the dimensions from front to rear. A high level water reservoir, in reinforced concrete, has been designed integrally with the boiler flue (see Fig 1).

Service mains run in open, splay sided trenches to avoid the expense of underground ducts or the unsightliness of overhead gables.

The total cost of the establishment including buildings services fixed, laboratory fittings library bookshelves, and all site works was approximately £620,000.

Research Programmes

Atmospheric pollution Purely by coincidence the closing of the Fuel Research Station occurred simultaneously with the introduction of the Clean Air Act, it was therefore particularly apposite to review the programme in starting at the new station. The work now being undertaken follows naturally from that begun at the Fuel Research Station and is designed to meet the requirements of the Ministry of Housing and Local Government.

The principles of smoke elimination that have proved successful in reducing smoke from hand fired boilers on land are being applied to marine boilers. The possibility of developing after burners to burn smoke in various situations is being investigated.

The properties of smokes from different sources are being examined with special reference to the constituents that might be injurious to health. The occurrence of oxides of nitrogen in the atmosphere under different conditions is being studied.

In the new investigations of air pollution there is a need for greater accuracy than has been possible in some of the measurements made in the past. As a matter of urgency a review is being made of the principal instruments at present in use. This work is being undertaken by the Scottish Branch of the Laboratory at Thorntonhall.

Micro-surveys are in progress to examine the concentration of various types of pollution at different types of site in a limited area. The results of such investigations will be important, for example in helping to determine the value of smoke-control areas, and in assisting those responsible for deciding the height of siting of large industrial chimneys.

Process development Synthesis of oils and chemicals from carbon monoxide and hydrogen is being studied as part of a project to develop, if possible, an econ-

omic process for producing oil from coal. The development of oils from coal is a two-stage process: the first stage involves the complete gasification of the coal to yield a mixture of carbon monoxide and hydrogen, and the second the catalytic conversion of the gas mixture into the desired end-products. The work at Warren Spring Laboratory is concerned only with the second of these stages. Economic considerations indicate that the most promising version of the Fischer-Tropsch process for use under British conditions is the slurry process, in which the gas mixture is passed through a suspension of powdered catalyst in molten wax at temperatures of 250–300° C., and at pressures between 5 and 30 atmospheres.

The objectives of the programme are (1) to develop an iron catalyst of longer life and higher activity than those at present available and one that will yield a high proportion of desired end-products, (2) to select operating conditions (gas composition, temperature, pressure) to combine a high reaction velocity with a given distribution of end-products, (3) to obtain data necessary to design a full-scale reaction vessel.

Synthesis gas is produced on the site at a rate of 4,500 std cu ft per hr in a standard, water-gas generator operated by the Engineering Services Division. There are arrangements for feeding carbon dioxide with the steam so as to vary the hydrogen-carbon monoxide ratio between 1.15 and 0.6. The gas is purified from hydrogen sulphide in Gastechnik towers and washed with caustic soda to control the carbon dioxide content. It is then compressed to 15 atmospheres pressure in the first two stages of a four-stage compressor, passed through the active carbon scrubbers to remove organic sulphur compounds, and then further compressed in the third and fourth stages to a pressure of 120 atmospheres.

The study of catalysis, which has been proceeding over a number of years at the Fuel Research Station, has brought to the team concerned considerable experience which should prove of value in some of the new programmes which it is hoped to undertake in the future.

Mineral processing research and development. Dr M. G. Fleming, of the Bessemer Laboratory of the Royal School of Mines, has been appointed consultant to this Division.

It seems probable that for some time a fair proportion of the effort of this Division will be engaged on sponsored work on particular ores, but it is hoped that basic investigations will include (1) a study of grinding in the presence of additives such as surface-active agents, (2) the kinetics of bubble attachments to mineral surfaces, as a contribution to the knowledge in the field of froth flotation, and (3) a study of the behaviour of mineral particles in a high-tension field, and the modification of this behaviour by various surface treatments.

The laboratories are equipped to handle most laboratory-scale mineral-dressing operations such as flotation, jigging, tabling, heavy-media separation, wet and dry magnetic separation, and high-voltage separation. In the hydrometallurgical field, facilities are available for atmospheric and pressure leaching, for fluidized-bed roasting, chlorine metallurgy, and solvent extraction. Pilot-plant facilities enable primary crushing operations to be carried out on a scale up to 2½ tons per hour, and flotation plant is available for treating up to 1,000 lb per hr. It is possible to carry out full-scale tests with radioactive tracers. The Division has a Mineralogical Section,

but relies on the Physical and Chemical Services Division for its analytical work.

Many of the problems on which work is likely to be necessary concern overseas deposits. Already a number of requests for investigations have been received from overseas territories, and an Overseas Mineral Processing Advisory Committee has been set up to advise on the selection and priorities of the programmes of interest to these territories.

Chemical engineering. It will be apparent that chemical engineering must play a large part in practically all the major activities of the Laboratory, and the decision of the Research Council to transfer "the work on Chemical Engineering . . . carried out at the National Chemical Laboratory to Warren Spring Laboratory" will readily be understood.

The Division has three functions: (1) to carry out research on physical operations which play an important part both in processes which are under development in the Laboratory, and those in more general use in industry; (2) to undertake research in the field of chemical engineering sponsored by industry or by Government departments; (3) as a result of these functions to accumulate basic information in chemical engineering for use by other sections of the Laboratory and industry.

Bearing in mind work that is already going on elsewhere in the Department on heat transfer and on fluid flow, it is proposed in the first instance to concentrate on the field of mass-transfer, and in particular to obtain results which will permit more accurate prediction of the performance of gas-liquid contacting equipment, and thus to facilitate the design of distillation columns, gas-absorption towers and reactors of the liquid-phase type, of which the Fischer-Tropsch slurry reactor is a particular example.

Four main lines of study are being followed, namely, bubble dynamics, gas-liquid mass transfer rates, fluid mixing, and specific problems in gas absorption with chemical reaction.

The National Engineering Laboratory of the Department has sponsored work at Queen Mary College, London, on the synthesis of organic compounds for use as drop-wise condensation promoters and has evaluated their effectiveness. The proposed work at the Warren Spring Laboratory is being planned in consultation with the National Engineering Laboratory and is intended as a study of the mode of action of these promoters in order to facilitate the development of compounds which will be effective for prolonged periods with a wide range of metal surfaces. It is proposed to study the mechanism of attachment of synthetic promoters to metal surfaces by methods of radiochemical labelling and to observe the subsequent history of these substances under conditions of use in heat exchangers.

Physical and Chemical Services Division. This provides a comprehensive central service in the fields of analysis, both by chemical and physical methods, instrument development, physical measurement, and photography. Special equipment includes gas chromatography, quartz and infra-red spectrometers, and equipment for X-ray diffraction and fluorescence spectrometry.

Engineering Services. This Division has a drawing office which undertakes design of pilot-scale plant for the Laboratory; it has an industrial staff of approximately 120, and well-equipped workshops.

Intelligence. In addition to the library and editorial services which are essential to any research estab-

ishment, the Intelligence Division is setting out to provide an information and project appraisal service. A start has been made, for example, in building up a centre of information in mineral processing, by assembling data from a wide variety of sources in such a way that they can be used in research and industry.

From what has been described it will be apparent that there is a wide choice of field before Warren Spring Laboratory, and that at the moment the main problem is that of selection and of allocation of priorities. In addition to the factors which govern the work of other laboratories of the Department of Scientific and Industrial Research, there is the task

of undertaking sponsored work to a greater extent and on a larger scale. Such work may be carried out for Government departments or for industry, and it may be on a fully confidential basis. The special facilities of the Laboratory will also be available for use, in certain circumstances, by teams from industry, which can work in collaboration with the research staff of the Laboratory.

The programme is regularly considered by a Steering Committee, appointed by the Research Council, the present members of which are Sir Harry Jeppeott (chairman), Sir Harry Melville, Dr R. Holroyd, Mr D. A. Oliver and Mr S. H. Clarke.

OBITUARIES

Mr T. L. Eckersley FRS

THE death of T. L. Eckersley on February 16 removed another of the rapidly dwindling band of pioneers in the field of radio research, among whom he was notable both for his theoretical and practical work. His interest in electromagnetic waves was aroused while he was still at school at Bedales, but it was during the First World War, after studying at University College, London, and Trinity College, Cambridge, with some years at the National Physical Laboratory in between, that he made his first big contributions to radio wave propagation. These were his explanation of 'night-effect' in direction finding observed in Egypt and Salonika, in which he invoked the existence of an upper ionized layer giving rise to a reflected wave with variable polarization characteristics, and his observation of coastal refraction which he sought to account for in terms of the properties of Zenneck surface waves.

He was thus among the first to obtain evidence of the presence of the ionosphere by the reflexion of radio waves and so began a life-long interest in the magneto ionic theory of propagation. His first work, however, on joining the Marconi Co. after the War was a classical research into the properties of earth screens for increasing the radiation efficiency of long wave aërials, followed by his analysis of the results of observations made on very long wave transmitters by K. V. Tremellon and C. M. Allnutt during a round-the-world expedition. For more than twenty years Tremellon was Eckersley's personal assistant, and his patient observational work formed the basis of the succession of papers which Eckersley wrote on short-wave radio transmission.

The last of these was on scattering from 'clouds' in the ionosphere, a subject which has since become of great practical importance in the development of the ionospheric 'forward scatter' communication system. Not only did all this work lay the foundation of much of our knowledge of the part played by the ionosphere in long-distance propagation, but it also led to many advances in technique, for example, in the field of accurate direction finding and in the measurement of field strength and polarization characteristics.

Although he would not have claimed to be a pure mathematician, he had a consummate ability to apply mathematics to physical problems. Indeed many of his experimental researches were preceded or sup-

ported by elegant analysis. He had a great interest in modern physics, especially in its quantum and relativistic aspects, and it was the knowledge so acquired that inspired some of his finest work in radio. It was the phase integral treatment of potential barriers in atomic theory that led him to his brilliant applications to ionospheric and ground wave propagation, while in the scattering of α particles he found an analogy for the scattering of radio waves as a function of wave-length, cloud size and scattering angle.

Eckersley had something of the absent-mindedness associated with genius, which was reflected in the style of his writing and made some of his papers difficult for others to read. He was thus not as well known in the world at large as he deserved to be, but in due course full recognition among scientists came with his election to fellowship of the Royal Society in 1938 and the award of the Faraday Medal of the Institution of Electrical Engineers in 1951. He was also a well known figure at international radio conferences especially at the CCIR and U.R.S.I. assemblies.

He was proud of the fact that he was a grandson of T. H. Huxley, and he was most happy in his family life, his wife being Eva, the daughter of Barry Pain, the Victorian novelist, who survives him with a son and two daughters. She is an able pianist and composer, and their home at Danbury, Essex, was often visited by distinguished musical friends. He was a delightful host, for he combined great courtesy with a delicate sense of humour, and though he did not play himself he had a great love of music.

At the time he died he had become almost completely helpless from multiple sclerosis, the first symptoms of which had appeared more than twenty years ago. In spite of increasing disability, he remained at work throughout the Second World War as scientific adviser to the Inter Services Ionosphere Bureau at the Marconi Research Laboratories, and after his retirement in 1946 he continued to work at home for several more years.

During this period he published a number of papers, his devoted wife acting as his amanuensis. There is no doubt that it was her amazing courage and cheerfulness that maintained his life for so long, and indeed it was to pneumonia during the influenza epidemic that he finally succumbed. The loving care which surrounded him during these last years was a source of inspiration to all who witnessed it.

G. M. L. STONER

Prof A O R Windaus

ON June 9 it was reported from Göttingen that Adolf Windaus had died in his eighty-third year. He had retired as professor and director of the University Chemical Laboratory at Göttingen in 1938, and was made emeritus professor and director in 1944.

Windaus was born in Berlin in 1876, educated at the Universities of Berlin and Freiburg-im-Breisgau and became *Privatdozent* in 1903. After a short period at Innsbruck, he was elected to Göttingen in 1915. He was awarded the Nobel Prize for Chemistry in 1928, and also received the Baeyer, Pasteur and Goethe Medals.

To those interested in steroids, Windaus's name will stand with that of the late Heinrich Wieland as the greatest in the period of German pre-eminence in discovery about the chemistry and physiology of these substances. Most of his publications between 1903 and 1928 were about cholesterol and described, *inter alia*, the preparation of complexes with digitonin, solanin, etc. (1909, 1918), the nature of the side-chain (1913) and the relationship to coprosterol (1916) and to the bile acids (1919). Papers also appeared on stigmaterol (1906, 1924), sitosterol (1918, 1924), hydrodeoxycholeic acid (1923, 1926), chenodeoxycholeic acid (1924, 1925, 1926) and on 'β'-phocæcholic acid (1928). All this work and much more, including some on heart poisons and saponins, was done without modern knowledge of steroid formulæ, yet Windaus's fundamental discoveries stand largely unchallenged to-day. His work on scymnol (with W. Bergmann and G. König, *Hoppe Seyl Z.*, 189, 148, 1930) was the first on the chemistry of this substance. The paper with Alfred Hess, of Columbia University, New York, entitled "Sterine und antirachitisches Vitamin" and published at the session of the Gesellschaft der Wissenschaften zu Göttingen on January 28, 1927, clearly recognized that both ergosterol and an impurity separable from cholesterol acquired antirachitic activity on irradiation with ultra-violet light. Parallel work had already begun in England (for example, I. M. Heilbron, E. D. Kamm and R. A. Morton, O. Rosenheim and T. A. Webster, *Chem. and Indust.*, 45, 932, 1926), it was energetically pursued there, and also by Windaus and his colleagues until, in 1931, success in isolating a pure vitamin D was announced almost simultaneously from Göttingen and Hampstead, London. From irradiated ergosterol, F. A. Askew, H. M. Bruce, R. K. Callow, J. St. L. Philpot and T. A. Webster (*Nature*, 128, 758, 1931) obtained calciferol, and Windaus and O. Linsert (*Liebigs Ann.*, 489, 269, 1931) vitamin D₂; these substances were later found to be identical, although the separate names were retained.

'Vitamin D₁', originally reported as pure by the German workers (*Liebigs Ann.*, 489, 252, 1931), was later proved (*ibid.*, 493, 259, 1932) to be a molecular compound of vitamin D₂ and lumisterol.

For Windaus, this was by no means the end of the vitamin D problem. Doubts as to the identity of calciferol (vitamin D₂) and the antirachitic vitamin of fish-liver oils persisted, and C. E. Bills (*Physiol. Rev.*, 15, 1, 1935) summarized evidence that the antirachitic vitamin in irradiated (impure) cholesterol and in cod liver oil (as measured in 'rat units') is more potent for chicks than the vitamin (calciferol) in irradiated ergosterol.

Windaus brilliantly recalled that J. Mauthner and W. Suda in 1896 (*Mh. Chem.*, 17, 579) had oxidized

cholesterol with chromic acid to 7-ketocholesterol, and, with H. Lottré and Fr. Schenck (*Liebigs Ann.*, 520, 98, 1935), he reported the conversion of this substance into 7-dehydrocholesterol. Irradiation of this gave a mixture from which was isolated (Windaus, Fr. Schenck and F. von Wörder, *Hoppe Seyl Z.*, 241, 100, 1936) vitamin D₃, identical with the natural vitamin obtained from tunny liver oil by H. Brockmann (*Hoppe Seyl Z.*, 241, 104, 1936) at Göttingen. Windaus's later papers were about the chemical nature of natural forms of vitamin D and the chemistry of irradiation products of ergosterol and 7-dehydrocholesterol.

Windaus's publications, which ceased in 1944, remain as an inspiring example of what a great intellect can still accomplish in scientific discovery.

G. A. D. HASLEWOOD

Dr F Busemann

DR FELIX BUSEMANN, who died on April 30 at the untimely age of fifty-one, was an outstanding authority in his chosen subject, electrical transmission, as is his brother, Adolf Busemann, one of the leading German aerodynamicists now in America. Trained at the Institute of Technology, Darmstadt, he became later assistant to the professor of electrical machine design there, and in 1934 joined the firm of Siemens Schuckert in Berlin, becoming one of a team concerned with future developments in electrical transmission. This team had as one of its assignments that of high-voltage direct current transmission. Starting with a pilot scheme between Charlottenburg and Moabit, it followed by planning the Siemens Schuckert half of the major Elbe-Berlin project. After the Second World War, Dr Busemann was chosen by the Darwin Panel and came to Britain in 1946 to report on the German work in this field.

Busemann found the social climate in Britain so akin to his temperament that he shortly accepted an offer to join the staff of the Electrical Research Association and continue his studies on d.c. transmission. These resulted in a masterly series of fourteen reports covering all aspects of the subject with the exception of valves, for the study of which facilities were lacking. He played a major part in the planning of a pilot scheme which, had it matured, would have placed Great Britain in the van of development. He was without doubt the foremost authority on high-voltage direct-current transmission in Britain, and his loss will be greatly felt.

With the temporary cessation of interest in direct-current transmission, Busemann turned his versatile mind to other aspects of transmission. Among these he devised, jointly with W. Casson, a classic programme of full-scale experiments on power-system stability (Cliff Quay), described in a paper before the Institution of Electrical Engineers last year. More recently, he had been concerned with mechanical and thermal properties of soil and utilization of power cables. To all these he brought quick appreciation of decisive factors and great facility in analysis and exposition.

Behind a natural modesty Busemann had great personal charm and humour as well as perception. He was a musician of almost professional attainment and gave much service to his church and the social activities of the Electrical Research Association. He will be remembered by all who knew him for a long time to come. He leaves a widow and two daughters.

L. GOSLAND

Miss Grace M Sickles

GRACE M SICKLES, associate research scientist in the Division of Laboratories and Research of the New York State Department of Health died on June 29 at Troy, New York. An eminent bacteriologist and virologist Miss Sickles had been a member of the Health Department since 1918 with a two year period of service (1919-20) in the Communicable Disease Laboratories of the United States Army. She was a graduate of the New York State College for Teachers and a member of the principal scientific societies in her fields of research.

Miss Sickles was associated with Dr Augustus B Wadsworth in an extensive series of investigations on the production and standardization of anti pneumococcus, antimeningococcus and antistreptococcus sera, studying, as early as 1938 the action of immune serum in conjunction with chemotherapy in experimental streptococcus infections. Some of Miss Sickles' studies of diphtheria toxin and on the antibiotic activity of micro-organisms from the soil were carried out at the Marine Biological Laboratory Woods Hole, Massachusetts.

Miss Sickles was the discoverer with Dr Gilbert Dalldorf in 1947 of the coxsackie virus. The virus was identified during a study of outbreaks of polio myelitis in New York State. It was named after the

village in which the first two recognized human infections occurred. The coxsackie group now includes more than a dozen viruses which are common sources of infection in man.

Mr W E Perry

The sudden death on June 5 of Mr W E Perry, a senior principal scientific officer at the National Physical Laboratory, Teddington, removes one of the leading figures in the field of radioactive and radiation standardization. Born in 1903 Perry took his degree from Nottingham and joined the Laboratory in 1928. He was responsible for the measurement of the National Radium Standards in 1934 and for the subsequent development of radioisotope measurements. Later as head of the Radiology Section of the Laboratory, he had charge of the work on radio isotopes, X-ray dosimetry, neutron standardization and radiocarbon dating and had an international reputation for his scientific integrity and wide knowledge in these subjects. At the time of his death, he was preparing material for the ninth International Congress on Radiology at Munich in his capacity as chairman of Committee I of the International Commission on Radiological Units and Measurements.

NEWS and VIEWS

The British Association

New President

SIR GEORGE THOMSON, master of Corpus Christi College, Cambridge, has been elected president for 1960 of the British Association for the Advancement of Science in succession to Sir James Gray. Sir George has had a distinguished career as a physicist as a man who gave outstanding service to the Atomic Energy Project in its early days and as master of Corpus Christi College. The son of the late Sir J J Thomson, he was educated at Trinity College Cambridge, obtaining a first-class degree both in the Mathematical and in the Natural Sciences Tripos. After service in France with the Army, followed by research on aeronautical problems, he was appointed to the chair of physics at Aberdeen in 1923, where he carried out the epoch making work on the deflection of electron beams by thin metal foils, thereby establishing beyond doubt the wave nature of the electron. For this work he was awarded the Nobel Prize for Physics in 1937. Between 1930 and 1952 he was professor of physics in the Imperial College of Science and Technology, London, and was chairman of the first British Committee on Atomic Energy, the Mould Committee, appointed in 1949. He has played a considerable part in the development of the subject ever since, being interested not less in its social as well as in its scientific aspects. Since his appointment to the mastership of Corpus Christi College his interest in physics has continued and he has published work on gas discharges and has been chairman of Section A (Mathematics and Physics) of the British Association. Both on account of the great distinction of his scientific work and his interest in the wider implications of scientific advance he will be a most welcome president of the British Association.

Director of the Royal Aircraft Establishment

Prof M J Lighthill F.R.S.

PROF M J LIGHTHILL, Beyer professor of applied mathematics at the University of Manchester since 1950, has been appointed director of the Royal Aircraft Establishment, Farnborough in succession to Sir George Gardner who is succeeding Air Chief Marshal Sir Claude Polly as controller of aircraft at the Ministry of Supply in October.

Prof Lighthill has made outstanding contributions in many fields of fluid dynamics as well as in more general spheres of pure and applied mathematics. His applications of the fundamentals of mathematics to various aeronautical problems have been significant and widespread. He is particularly well known for his theoretical work on jet noise, this work, which has been largely substantiated by experiment, relates the noise to the turbulence in the jet. He has always displayed a continuing interest in the practical application of his theories and has been for a number of years a member of the Aeronautical Research Council. Prof Lighthill was educated at Winchester and Cambridge, and was elected to the fellowship of the Royal Society in 1953 at the early age of twenty nine.

Royal College of Science and Technology, Glasgow

Sir David Anderson

SIR DAVID ANDERSON, who is to retire from the post of director of the Royal College of Science and Technology in December 1959, was appointed principal of Derby Technical College in 1926 at the age of 31. In 1930, he became principal of the Central Technical College Birmingham and in a period of 10 years which spanned the arduous war years he laid the foundations of the College of

Advanced Technology, designated as such by the Minister of Education in 1956. In this period, too, he became increasingly concerned with the problems of technical education at national level. This was especially true of his work as a member of the Percy Committee which reported in 1946, and greatly influenced the development of post-war technical education. He was president of the Association of Principals of Technical Institutions in 1932, and chairman of Council of Association of Technical Institutions in 1951. He was a member of Council of the Institution of Mechanical Engineers during 1941-42, 1948-50. First and foremost a Glasgow man, he was educated at Whitehill School, then at the then Royal Technical College, and served his apprenticeship with the North British Locomotive Company. He returned to the College as director in 1946, and the new engineering block, the recently opened students union, the Residential School of Management Studies at Bearsden, and the new students residences are visible signs of his vigorous leadership. He has continued to serve on a large number of bodies at national level, and was knighted in 1957. After the manner of present times, we may hope that Sir David will not retire from all public work, otherwise the constructive contributions of his incisive mind will be greatly missed.

Dr S C Curran, FRS

THE Governors of the Royal College of Science and Technology, Glasgow, have announced the appointment of Dr S C Curran as principal in succession to Sir David Anderson, the retiring director. Dr Curran studied at the Universities of Glasgow and Cambridge, graduating M.A., B.Sc., Ph.D. (Glas.), and Ph.D. (Cantab.). His early researches were concerned with radiation phenomena and new methods of detection. While at St John's College, Cambridge, and the Cavendish Laboratory, he pioneered in investigations of proton capture.

During the Second World War he shared in the successful work of the Royal Aircraft Establishment on proximity fuses and of the Telecommunications Research Establishment on the research and development of centimetre radar, having charge of one of the groups responsible for H_2S and ASV , thereafter he joined the British Mission on Atomic Weapons in the United States. At Berkeley he discovered the original form of the scintillation counter and the vacuum carbon arc. Later at the University of Glasgow he introduced the modern form of proportional counter, determining with it the form of novel beta-spectra such as that of tritium. An active research group soon grew up under his leadership.

In early 1955 he joined the Atomic Weapons Research Establishment, where he later became a chief scientist and member of the Management Board responsible for the divisions of Nuclear Research and Electronics. He also served as visiting member on the Harwell Management Board. A considerable growth of nuclear research has taken place at Aldermaston during his years there.

Dr Curran was awarded the D.Sc. and Kelvin Prize of Glasgow in 1950 and elected to fellowship of the Royal Society in 1953.

Jean Senebier (1742-1809)

JEAN SENEBIER, who died of "une cruelle maladie" at Geneva 150 years ago on July 22, 1809, is an anomalous figure in the history of botany. A clergyman untrained in the scientific method, yet possessing

the true scientific spirit, endowed with curiosity, intelligence, and industry, he had many interests: theology, botany, microscopy, physics, chemistry, meteorology, library classification. His tiresome rhetoric prevented his being appreciated by his generation. The son of a protestant tradesman of French origin, he was born on May 6, 1742, at Geneva, where he became pastor in 1765 and chief librarian in 1773. In 1792 political unrest banished him from the city for seven years. Senebier is remembered chiefly for his studies on the influence of light on vegetation. Jan Ingenhousz, an engineer of Dutch extraction, in 1779, introduced the concept of balance of animal and vegetable life by showing that plants generate dephlogisticated air. This activity was demonstrated by Senebier between 1782-88 to be confined to the green parts of plants which, under the influence of sunlight, convert fixed air (carbon dioxide) into dephlogisticated air (oxygen). His "*Mémoires physico-chimiques sur l'influence de la lumière solaire pour modifier les êtres des trois règnes de la nature*" in three volumes were published in 1782. The first to formulate a theory, in strictly chemical terms, of vegetable nutrition in his 'tediously prolix' (Sachs) five-volume "*Physiologie végétale*" (1800), he stimulated his fellow Genevan, Nicholas Théodore de Saussure, to write his "*Rocherches chimiques sur la végétation*" (1804), which was to eclipse his own work. He was a corresponding member of the Institut de France and of the Royal Academy of Turin.

International Commission on Higher Education in Nigeria

SIR ERIC ASHBY (vice-chancellor of the Queen's University of Belfast and master-elect of Clare College, Cambridge) returned from Lagos on May 7, after attending the inaugural meeting of the International Commission on Higher Education in Nigeria. The Commission (*Nature*, 183, 1231, 1959), with Sir Eric Ashby as chairman, consists of two other United Kingdom members, Dr J. Lockwood (master of Birkbeck College) and Dr G. E. Watts (principal of Brighton Technical College), and three American members, Dr Frank Koppel (dean of the Graduate School at Harvard University), Dr Eric Walker (president of Pennsylvania State University) and Prof H. W. Hannali (associate dean of agriculture, University of Illinois). The Nigerian members are Shettima Kashim (formerly Federal Minister of Social Services, chairman of Nigerian College of Technology), Prof K. O. Diko (vice-principal and professor of history, University College, Ibadan) and Dr S. D. Onabamiro (senior research fellow in parasitology, University College, Ibadan).

Sir Eric Ashby, speaking at the inauguration meeting in Lagos on May 4, described the decision to set up a Joint Nigerian-United States-United Kingdom Commission as a "Landmark in educational history" as this was the first time that such an international group had been appointed to study higher education in Nigeria. He assured the meeting that the Commission would be able to recommend some of the educational needs of the first twenty years of Nigerian independence could be met, and that it would do its best to prepare for Nigeria something which could be turned into action.

'Procynyl' Dyes

Imperial Chemical Industries, Ltd., has introduced 'Procynyl' dyes, a new class of disperse dyes. It is claimed that the initial four 'Procynyl' dyes display

on nylon and other polyamide fibres the desirable attributes of the established disperse dyes—good levelling, good coverage of irregular-dyeing yarns, good compatibility in admixture, good temperature range properties and good penetration. They are applied in a similar manner. The essential difference is that the 'Procynyl' dyes are applied initially under slightly acid instead of neutral conditions, and that dyeing is completed by an alkaline fixation stage during which certain reactive groups in the Procynyl dye molecules react chemically and irreversibly with the amino or amide groups in the polyamide fibre and so produce dyeings of high wet-fastness. All forms of nylon and other polyamide fibres of both the staple fibre and continuous filament types and including woven piece goods, knitted piece goods and hosiery can be dyed satisfactorily with the new dyes, which may be applied, as necessary, on the jig (covered jigs for preference) on winches, in paddle dyeing machines and in circulating liquor machines. The initial four Procynyl dyes—a yellow an orange a scarlet and a blue—permit an extensive range of shades to be produced because of the wide inter-compatibility of the new dyes.

Only slight or negligible reaction takes place between 'Procynyl' dyes and acetate and tricotone rayons, for which the new dyes are not expected to be of much immediate interest although the wet-fastness achieved is generally better than with normal disperse dyes. With the exception of 'Procynyl Yellow G', the dyes are of minor importance on 'Terylene' and other polyester fibres. On 'Acrilan' polyacrylonitrile fibre, although 'Procynyl' dyes build up well to give heavy shades of very high wet-fastness which results from the reaction between the dye and the basic groups in the fibre, only the yellow is of particular interest, the remaining dyes giving shades of low light fastness. On acrylic fibres not modified by the incorporation of basic substances they display only limited build up.

British Ceramic Research Association

Mellor Library

THE new library of the British Ceramic Research Association—the Mellor Library—was opened at Stoke-on-Trent on June 16 by Mr Frank West, vice-president of the Association and a lifelong friend of the late Dr J W Mellor, in whose honour the library has been named. Dr Mellor, the well-known physical chemist, turned his mind to problems of the ceramic industry Wedgwood, a century and a half previously had transformed a craft into an industry, Mellor during the first three decades of the present century did outstanding service to that industry by giving it the basis of sciences that had hitherto been largely wanting. As head of the Pottery Department of the North Staffordshire Technical College Mellor taught a generation of pottery managers, as first director of research of the British Refractories Research Association (the forerunner of the British Ceramic Research Association) Mellor initiated research at a time when industrial research was a novelty. But perhaps he is best known as the author of the "Comprehensive Treatise on Inorganic and Theoretical Chemistry."

Educational Research

THE third issue of *Educational Research*, the journal of the National Foundation for Educational Research in England and Wales, contains articles on the teaching of mathematics, the ability to teach the effect

of environment on intelligence, school guidance services and a comparison of attainments in different types of primary school. There is also a selected and annotated bibliography of works on the curriculum of the secondary school (Newnes Educational Publishing Co., Tower House, Southampton St., Strand, London, W.C.2 5s 6d). In the article on the teaching of mathematics, Mr J B Biggs discusses the distaste for school mathematics so commonly reported. His conclusions evaluate the relative effect of basic personality and specific likes and dislikes particularly in the case of the maladjusted child. Many so-called lazy children are seen to have found an initial block to their number learning because of their temperament. This is heightened by accusations of laziness and consequent unimaginative driving by some teachers. The implications of this and the other stimulating conclusions are important to the teacher who might well ask himself why there is no similar anxiety concerning English.

A New Geological Documentation Service

THE wealth of information available constitutes a serious problem for the future of the research in the Earth sciences. Before 1939, published work could be covered by giving about one thousand references a month. At present, the Service d'Information Géologique of the Bureau de Recherches Géologiques, Géophysiques et Minérales indexes monthly more than 3,000 references, and it is estimated that 5,000 references should be given to ensure complete coverage of the field. The situation is complicated by the number of works now appearing in little-known languages and by the launching of new periodicals and special publications. Faced with this problem, the Service d'Information Géologique of the Bureau de Recherches Géologiques, Géophysiques et Minérales, which has taken over and expanded the work of the Centre d'Etudes et de Documentation Paléontologiques, has set itself the task of providing an extended and rapid service of basic geological information. The Service d'Information Géologique scans every week about 3,500 periodicals, more than 200 of which are published in Russian. The references are typed in the original language or if they are not in Latin characters, are translated, usually into French, then are then classified in 1,200 sections under twelve main headings (mineralogy, petrography, stratigraphy, tectonics, geophysics, geological activities, geological phenomena, applied geology, general palaeontology, biology, botany and zoology). The work is of course carried out under the supervision of scientists. Each reference is indexed by title and by content. The average number of indexes to each abstract card is five.

Central Advisory Water Committee

ON the expiry of the first period of appointment, the Minister of Housing and Local Government Mr Henry Brooke has reviewed the composition of the Central Advisory Water Committee and made various re-appointments and new appointments. The membership of the Committee is drawn from the major interests concerned with water, for example, water supply, industry, scientists, agriculture, river boards. The Minister is chairman of the Committee and the vice-chairman is the Parliamentary Secretary, Mr J R Bevin. Since its reconstitution in 1955 the Committee has published reports on the demand for water in England and Wales on information on water resources and on the law dealing with the disposal of trade effluents.

Seismological Association Meeting in Toronto

THE report of the meetings of the Section for Seismology and the Physics of the Earth's Interior, prepared by the associate secretary, Dr Markus Bath, of Sweden, has recently been published (pp 448 Strasbourg Bureau Central International de Séismologie, 1958). Most of the subdivisions into which this subject may be divided were discussed in the twenty-two sessions. Detailed reports of these meetings, the presidential address by Prof K E Bullen, of the University of Sydney, the report of the meeting of the European Seismological Commission, the Committee of the International Seismological Summary and the Committee for the International Geophysical Year are included. In addition, there are seismological reports from thirty-four countries, and the resolutions adopted at the assembly. The whole covers some 455 quarto pages. At the conference, ten sessions were devoted to seismology alone, six to joint meetings with the Association of Volcanology and two to joint meetings with the Association of Geodesy. It was at an extra session at Toronto that Prof K E Bullen announced that the U.S. Atomic Energy Commission had released information concerning the time and place of a future underground nuclear detonation in Nevada, so that seismologists could prepare to participate in the recording. The International Geophysical Year Committee discussed particularly the recording of earthquakes with epicentres in the arctic and antarctic regions, and it is noteworthy that M E Guyot is proceeding with the preparation of a seismological dictionary which it is hoped will be published without delay.

Soil Survey of Great Britain

THE soil survey of Great Britain, with headquarters at Rothamsted, will occupy many years, and reports are to be published as each county is completed. The magnitude of the task can be realized from the memoir on Anglesey (Agricultural Research Council Memoirs of the Soil Survey of Great Britain—England and Wales. The County of Anglesey. Soils and Agriculture. By E Roberts. Pp viii + 116 + 11 plates. London: H.M. Stationery Office, 1958, 10s net), which includes also a small proportion of Caernarvonshire, nearly fifty soil series, which are the mapping units, are identified and described. Anglesey is relatively flat, but there are considerable variations in the land surface due to the rugged outcrops of the Mona complex, the sharp escarpment of the Carboniferous limestones, the igneous rocks, wind-blown sands and glacial features. The varying thickness of the boulder clay has contributed to the irregular undulations of most of the fields.

Classification and mapping of the soils are based on the soil profile, since it reflects the action and balance of the many processes that have led to its formation, drainage has a profound effect, and is taken into account in the classification. Although familiar to soil scientists and to many advisory officers, the subject is new to workers in related subjects, and to farmers. The Soil Survey of Great Britain will be the foundation for a planned approach to fertilizer and cropping problems for many years, and such reports will have to be studied, and the maps referred to frequently. The one inch to the mile soil map that is provided may prove too small for reference to some individual farms on or near the margins of the soil areas, but a 6 in map is available for reference at Rothamsted.

Grassland Productivity

"The Measurement of Grassland Productivity" was the subject of the sixth Easter School in Agricultural Science which was held at the University of Nottingham School of Agriculture, Sutton Bonington, during April 13–16, and was organized by Prof J D Ivins. Twenty papers were read, primarily concerned with techniques of grassland evaluation. Assessment of productivity from the botanical point of view, in terms of animal production, the consumption of herbage by grazing livestock and grassland productivity on a farm scale were considered. New varieties of herbage plants have been produced and then requirements have been explored to a great extent. New techniques have been developed which have resulted in vast increases in the production from grassland, but a constant problem and hindrance to development has been—and still is—the lack of methods which may be used with validity to measure and compare grassland productivity. Some 140 members from Britain and overseas exchanged experiences and ideas and discussed the limitations and applications of techniques of measuring the productivity of grassland. The proceedings will be published.

Safety in Mines Research

THE thirty-sixth annual report on Safety in Mines Research (pp 81 + 4 plates. London: H.M. Stationery Office, 1958. 5s net) is a general review of progress in the year 1957 of the Safety in Mines Research Establishment of the Ministry of Power. The report describes research undertaken in the general fields of explosives and blasting devices, explosion hazards, breathing apparatus, fire hazards, engineering and metallurgy, dust control and pneumoconiosis hazards, and in certain other fields, together with a record of testing services carried out by the Establishment. A significant feature of some aspects of the work is the active co-operation and interchange of results with kindred establishments in France, Germany and Poland. More than ninety topics are discussed, it is difficult to select individual topics for special mention, but perhaps attention may be directed to the work reported on the fluid mechanics of coal dust explosions, a subject of interest to all concerned with fires and explosions due to organic dusts. There are, in fact, many topics reported which are of interest and importance to several industries in addition to the mining industry, including breathing apparatus, engineering and metallurgical problems of importance in conveying, winding and supports, and the study of dusts and of pneumoconiosis.

Morbidity Statistics from General Practitioners

IN the series of Studies on Medical and Population Subjects, the first volume of morbidity statistics collected from general practitioners has recently appeared (General Register Office. Studies on Medical and Population Subjects No 14. Morbidity Statistics from General Practice, Vol 1 (General). By Dr W P D Logan and A A Cushion. Pp iv + 174. London: H.M. Stationery Office, 1958. 15s 6d net). A number of practitioners agreed to keep records of all consultations with patients on their list, and the General Register Office went to considerable trouble to obtain the correct population at risk to which these consultations could be related. While the practices were not chosen as a representative sample of the total population, this is the

first time that a survey has been taken, and that data showing the load on general practitioners have become available on this scale. The present publication shows consultation rates and rates of patients consulting for different age and sex groups and different diseases. It is expected that a further volume which will contain figures on occupational morbidity will be issued in the future.

Mammals of the Belgian Congo

A PAPER by J. Verschuren on the ecology and biology of the larger mammals of the Garamba National Park in the north-east of the Belgian Congo forms the ninth fascicle of the results of H. de Sager's expedition for the exploration of the park (Exploration du Parc National de la Garamba Mission H. de Sager Fascicule 9 Écologie et Biologie des Grands Mammifères (Primates, Carnivores, Ongulés) Par Jacques Verschuren Pp 226+2 planches Bruxelles Institut des Parcs Nationaux du Congo Belge 1958). In the region studied the larger mammals are much more difficult to observe than in East Africa owing to the much denser vegetation in which they seek refuge, but the author has made good use of the two years that he was in the field and has collected much valuable information about their biology. After a short introduction describing the country and the methods employed the work is arranged systematically, and each species is dealt with under the headings: particulars of specimens examined, local names, geographical distribution, systematics and morphology and ecology and biology. For most species the last section is by far the largest and is full of carefully recorded observations of the greatest interest. Fifty-one species are dealt with, distributed among the Primates, Pholidota, Carnivora, Tubulidentata, Proboscidea, Hyracoidea, Perissodactyla and Artiodactyla. The author adds that his lengthy experience of mammals in the wild has convinced him of the invalidity of many of the innumerable forms, subspecies, and races that have been so profusely described by some writers—a remark that will be heartily endorsed by other field zoologists. The value of the paper is enhanced by a large number of photographic illustrations including two plates in colour.

Collision Broadening of Spectral Lines

COLLISION broadening is an important process in the formation of stellar absorption lines and collision shifts have been discussed as a possible explanation of that part of the red shift of solar lines which is unaccounted for by the Einstein gravitational shift. W. R. Hindmarsh (*Mon. Not. Roy. Astron. Soc.*, 119, 11, 1959) has recently reported the results of the first of a series of measurements of collision effects in atomic spectra. The collision shift and broadening of the neutral calcium line $\lambda 4227 \text{ \AA}$, due to an external pressure of helium, have been measured. The line was formed in absorption by passing white light through calcium vapour in the presence of helium at various pressures less than one atmosphere. The half-intensity damping width of the line was found to be $1.72 \times 10^{-10} \text{ cm}^{-1} \text{ per atm. cm}^2$ of helium, and the shift $0.05 \times 10^{-10} \text{ cm}^{-1} \text{ per atm. cm}^2$ towards the violet. The ratio of broadening to shift on the Lindholm theory is 2.76, and the shift is predicted to be towards the red. The observed ratio is much larger and the observed shift is in the opposite direction. This discrepancy must be due to the involvement of the short range repulsive forces

between calcium and helium atoms as well as the long range van der Waals forces. Hindmarsh also shows that the collision shift of the calcium line is a negligible component of the solar red shift and cannot account for the difference between observed and predicted solar red shifts. In the second paper following the above W. R. Hindmarsh and K. A. Thomas show that for two argon lines the collision shifts are in reasonable agreement with the Lindholm theory.

Hot Laboratory Equipment

'Hot Laboratory Equipment' is a revised and enlarged second edition of the 'Hot Laboratory Catalogue', which constituted the major portion of 'Chemical Processing and Equipment' (TID 5278) published by the U.S. Atomic Energy Commission as one of the several volumes for the 1955 International Conference on the Peaceful Uses of Atomic Energy. The new edition (pp. vii+429, Washington D.C. Government Printing Office 1958, 2.50 dollars) which is fully illustrated, contains descriptions of facilities, equipment and accessories for handling moderate to large amounts of radioactive materials. It lists 229 items compared with 126 in the first edition, and includes newly developed items as well as items omitted for various reasons from the first edition. Acknowledgment is made wherever possible to the organization responsible for the development of the particular equipment described. Most of the equipment listed was developed by national laboratories or contractors to the Commission but some were developed by private firms. The contents is confined to hot laboratory equipment produced in the United States but the reader is referred in the preface to two British publications (*Remote Handling Equipment* by A. Apperly, Atomic Energy Research Establishment F/R 1291, and *Radio Isotope Instrumentation and Accessories* by D. Taylor and A. G. Pearce, Scientific Instrument Manufacturers' Association, 1955) for information on similar equipment available in Great Britain.

Textiles and Dyes at the University of Leeds

THE eighty-fourth report of the Textile Industries and Dyeing Advisory Committee on the work of the Departments of Textile Industries and Colour Chemistry and Dyeing in the University of Leeds (pp. 47, Leeds: The University 1959) covers the session 1957-58, in which applications for admission greatly exceeded places and very full programmes of teaching and research were maintained. In the Textile Industries Department, full-time students numbered 351 and in that of Colour Chemistry and Dyeing 59. Lists of publications are included. In textile physics work continued in X-ray diffraction, electron microscopy, infra-red absorption and sedimentation in the ultracentrifuge. A second electron microscope was installed. In textile chemistry a method of producing a permanent lustre on all wool fabrics has been developed and the chemical mechanism of permanent set, especially that obtained with sulphite-bisulphite solutions, was re-examined. Work on the effect of variations in the nature of the keratin in the assessment of wool quality continued. The constitution of some sun pigments which may be involved in the staining of wool, the surface activity of steroids and proteolytic degradation of cholesterol are being studied and a brief examination of the dielectric properties of lanosterol indicated its suitability for use in impregnated paper capacitors.

In textile engineering good progress is reported in the analytical study of loom noise and in a study of the drying of textiles. In textile technology, work on the chemistry and practice of finishing fabrics made from both wool and man-made fibres continued and on the measurement of yarn irregularity. The chemical properties of pigmented wool, the action of concentrated sulphuric acid on wool, the removal of compounds of high molecular weight from textile materials and the degradation and yellowing of nylon were also studied.

In the Department of Colour Chemistry and Dyeing the course of the changes which occur in the reaction of aromatic carbonyl compounds with basic substances was examined, a study of stilbene-quinone and its derivatives was completed, and work on elimination of groups from vat dyes on reduction and on the reactions of sulphonic acids with azo compounds and azines continued. A group of diazonium salts soluble in benzene was prepared, and a study of the interaction of aminoanthroquinones and aminofluorenes with nitrobenzene and α -nitronaphthalene was completed, as well as work on the vapour pressure and absorption energies of some anthroquinone and azo dyes. The influence of the acetyl value of acetate rayon on the rate of dyeing and affinity for disperse dyes is being studied.

Journal of Nutrition

DR RICHARD H. BARNES, dean of the Cornell University Graduate School of Nutrition, Ithaca, New York, has been appointed editor of the *Journal of Nutrition*. He succeeds Dr George R. Cowgill of the Yale Nutrition Laboratory, who has served as editor for twenty years. Dr Cyril L. Comar, director of the Laboratory of Radiation Biology, New York State Veterinary College, has been appointed associate editor. The appointments became effective July 1, 1959. The editorial offices of the *Journal of Nutrition* are being moved from Yale University to the Cornell University campus. Manuscripts should be sent to Dr Barnes at the Graduate School of Nutrition, Savage Hall, Cornell University, Ithaca, New York.

Nature Conservancy Awards for 1959

THE Nature Conservancy announces the following awards of research studentships for postgraduate training in ecology, tenable for periods up to three years at the universities shown: *Botany* J. K. Marshall (Cambridge), D. P. Nicholas (Liverpool), W. J. Roff (Cambridge), J. T. R. Sharrock (Southampton), D. T. Streeter (London), *Zoology* M. L. Clark (Leeds), E. R. Creed (Oxford), J. M. Edington (Durham), C. J. Henty (Oxford), J. B. Nelson (Oxford), G. C. Phillips (Oxford), *Geography* I. G. Simmons (London).

University News

Edinburgh

PROF. A. D. RITCHIE, professor of logic and metaphysics in the University of Edinburgh, retires on September 30, his long and distinguished career was mentioned in reviewing his recent book, "Studies in the History and Methods of the Sciences" (*Nature*, July 4, p. 4). Prof. E. E. Harris, formerly professor of philosophy in the University of the Witwatersrand, has been appointed acting head of Prof. Ritchie's Department for one year.

Swansea

THE following appointments have been made in the University College of Swansea for the session 1959-

60, Dr J. R. Cross, superintendent of the Chemistry Laboratories, Miss Glenys Thomas, map curator and cartographer in the Department of Geography, Mr P. W. Davies, assistant lecturer in metallurgy, Dr H. E. Evans, lecturer in engineering, Mr B. W. Preece, assistant lecturer in engineering.

Announcements

MR. WALTER GARNER, formerly chairman of the Yorkshire Section and at present chairman of the London and District Section of the Textile Institute, and Dr A. R. Urquhart, honorary secretary of the Institute and an assistant director of the British Cotton Industry Research Association, have been awarded the Service Medal of the Textile Institute.

PROF. H. MARK, director of the Polymer Research Institute of the Polytechnic Institute of Brooklyn, New York, will deliver the Fourth Baekeland Memorial Lecture under the title "Recent Progress in Polymer Chemistry". The Lecture will be delivered on October 22 at the Royal Institution, Albemarle Street, London, W.1.

THE International Commission on Zoological Nomenclature has been given accommodation in the British Museum (Natural History). This will greatly facilitate the work of the Commission by reason of the unique library facilities and wide range of specialist advice available. Correspondence should in future be addressed to Mr N. D. Riley (Honorary Secretary), International Commission on Zoological Nomenclature, c/o British Museum (Natural History), London, S.W.7.

THE second session (1959-60) of the Welsh Soils Discussion Group will open with a meeting in the Department of Agricultural Chemistry, University College, Bangor, on October 28. The subject for discussion will be "Mineralogical Aspects of Soil Science", the introductory speakers will be Dr F. Smithson and Mr R. I. Davies (Bangor) and Mr. D. F. Ball (Nature Conservancy, Bangor). Further information can be obtained from Mr J. A. Taylor, Geography Department, University College, Aberystwyth.

THE Scottish Conference on "Relationships in Industry: Some Changing Concepts of Management", which is being organized jointly by the British Institute of Management and the Ministry of Labour, will be held at Gleneagles Hotel during October 23-24. It will be opened by Sir Alexander Fleck, chairman of Imperial Chemical Industries, Ltd. Further information can be obtained from the British Institute of Management, Management House, 80 Fetter Lane, London, E.C.4.

IN November 1859 Charles Darwin published "The Origin of Species" and Queen Victoria granted the Royal Title to the Royal Society of Victoria. To mark these two centenaries, the Society is organizing a symposium on the Evolution of Living Species, to be held in Melbourne during December 7-11. Dr Ernest Mayr of the United States will be the guest speaker. Further information can be obtained from the Honorary Secretary, Royal Society of Victoria, 9 Victoria Street, Melbourne, C.1, Victoria.

REFERRING to the review in *Nature* of June 27, p. 1766, Messrs Chapman and Hall state that the present American price of Cox's "Planning of Experiments" is 7.50 dollars.

MOLECULAR AND ATOMIC MOTIONS BY RADIO-FREQUENCY METHODS

MAXWELL-A.M.P.E.R.E. CONFERENCE

A JOINT meeting of the Colloque A.M.P.E.R.E (Atoms et Molécules par Etudes Radio Electriques) and the British Radio Frequency Spectroscopy Group was held during April 1-3 at Queen Mary College, University of London. The meeting was attended by more than two hundred scientists, mostly from the British Isles but with strong representation from France, Holland, Switzerland and the Eastern European countries in particular. The subject for discussion at the Conference was, 'Molecular and atomic motions in liquids and solids by radio frequency methods'. In the tradition of the A.M.P.E.R.E meetings the subjects covered were, dielectrics, nuclear magnetic resonance, quadrupole magnetic resonance and electron spin resonance. However, the range of the papers was constrained somewhat more than has been usual at the A.M.P.E.R.E conferences by the specification of a subject for discussion, albeit rather widely interpreted.

The forty four papers presented showed the power and range of the radio-frequency methods in studying molecular and atomic motion and there was an impressive consistency and similarity in the information produced by the very different experimental methods. It was regrettable that time did not allow the inclusion of mechanical and ultrasonic absorption measurements although these received mention in several of the papers.

Since many people versed in one discipline attended lectures in another, the occasion was a suitable one for having a general introductory lecture in each subject, and these were given by Prof H. Fröhlich (Liverpool) on "Dielectric Theory", Dr J. G. Powles (London) on "Motional Effects in Nuclear Magnetic Resonance" and by Dr M. Buylo Bodin (Grenoble) on "Motional Effects in Pure Quadrupole Resonance". Even so, many of the discussions became extremely technical and specialized and the difficulty in having a meeting on a subject which cuts across the traditional interests and compartments of science was apparent. This difficulty is a common one in conferences these days although highly specialized discussion is said to be evidence of 'immaturity' of a subject. It is regrettable that the cross fertilization which should be brought about by conferences such as this one is so difficult to achieve. It is therefore very valuable to have organizations 'd'Informations mutuelles' such as the Colloque A.M.P.E.R.E and the British Radio Frequency Spectroscopy Group the membership of which cuts across the traditional disciplines and contrasts with the extreme specialization of many organizations.

It was a source of great sorrow to all present, and particularly to the writer, that Prof. Freymann (Paris), the inspiration of the Groupement A.M.P.E.R.E, was unable to be present owing to illness, and that this should be the first A.M.P.E.R.E Conference he has missed.

The conference overcame in large measure the difficulties occasioned by the fact that it was held outside France for the first time (apart from a foray to Geneva in 1957) and was well attended by French scientists. Although some 50 per cent of the papers

were presented in French, the British members appeared to survive the ordeal without severe discomfort, and it may be that the teaching of French in our grammar schools is not as ineffective as is commonly supposed. The language difficulty was lessened by the provision of pre-prints of most of the papers.

It would obviously be impracticable to mention all of forty four papers and a brief summary only will be presented in an attempt to give some idea of the scope of the conference.

The conference was opened by Prof H. Fröhlich, who gave a masterly summary of the present situation in the theory of dielectrics, the main point of which was that the whole of the general theory has been worked out. The continuing appearance of papers on 'general theory' are no more than mathematical exercises, and whether these results are correct or not they are irrelevant. This point of view was undoubtedly novel to many present. He elaborated his position by discussing the whole field of dielectric loss in which he distinguished four types all but one of which are well understood. He was particularly concerned with the extent to which the theory can be dealt with macroscopically, which is of first importance because of the long range nature of dipolar forces, and with the number of independent parameters required for an understanding of the phenomena involved. He did point out nevertheless that a great deal of work remains to be done in the theory of dielectrics but that this should be concerned with the detailed interpretation, using models and so forth and in the search for information about materials and processes.

This lecture led on naturally to the more detailed discussion of a number of papers on dielectric loss in liquids and solutions, which depends in large measure on molecular properties and in which the 'model' aspect was very evident.

J. D. Hoffman (National Bureau of Standards, Washington) introduced a session on solids with an account of his work on systems having multiple relaxation times leading to bimodal, or even multimodal, loss curves which he explains in terms of multiple minima in the energy as a function of the orientation of a dipole. A paper by H. Gränicher and C. Jaccard (Zurich) summarized the present position in the interpretation of the dielectric properties of ice. B. Szegedi (Liverpool) described his recent work on a so far unobserved librational absorption process which should be found in crystalline long-chain substances.

There were a number of papers on the dielectric properties of systems in which water or a gas was adsorbed on materials such as silica gel.

The session on nuclear magnetic resonance was opened by J. G. Powles (London) who gave a summary of motional effects which can be studied by nuclear magnetic resonance including numerous examples of the various types of effect which may occur. He pointed out that examples of many of these would be found in the following papers but gave a number of extra ones in order to provide a balanced picture of the potentialities of the method.

two soils in pots. The specific activity of calcium absorbed by barley and ryegrass fell steadily during growth owing to a slow equilibration with forms of calcium other than exchangeable calcium. As roots locally depleted supplies of labile calcium, more calcium came into circulation. Exchangeable and available calcium can no longer be regarded as synonymous, and the latter is affected by the activities of plant roots.

Dr R. Scott Russell (Agricultural Research Council Radiobiological Laboratory) directed attention to different steps in nutrient absorption by roots and stressed that the effective area of absorption was restricted to a region near the apices. The availability of a nutrient to a plant may be influenced by interactions with other ions either by competition or by physiological changes. Dr Scott Russell referred to work which suggested that the individual root-absorption characteristics of different crops influenced the apparent availability of a nutrient such as phosphorus in a soil.

The probable parts played by micro-organisms were described by Mr J. S. Waid (Levington Research Station, Ipswich), who stressed that much of the evidence was circumstantial and required further substantiation. Organisms are known to be able to increase the water solubility of nutrients by oxidation or reduction, and by the decomposition of organic materials, the availability of nitrogen is intimately bound up with biological processes. Soil organisms may compete with roots for soluble nutrients especially when stimulated by supplies of organic materials, some of which may be provided by the roots themselves, production of carbon dioxide or toxins may affect the physiological activity of plant roots.

Dr G. W. Cooke's paper (Rothamsted Experimental Station) described the problems of assessing the nutrient status of a soil for advisory purposes.

here the criterion is the probable economic response of various crops to fertilizer dressings, and in this field soil analysis has not made much progress. The results generally distinguish between the broad levels of nutrient status for phosphorus and potassium, but in order to avoid crop failure in the exceptional cases the overall application of these fertilizers is about double the amount that is economically justified. The assessment of the nitrogen status of soils is even more uncertain, and there is an acute need for the development of fresh analytical techniques tested against field trials. Dr Cooke suggested that a more successful approach might lie in the use of soil analysis for 'fertility control' whereby a record was maintained of the fertility status of a soil so that warning was given of abnormalities before they became acute.

In the open discussion which followed these papers the following points were among those made.

Correlation between soil analyses and field responses is poorer in tropical and other under-developed areas than it is in Britain, yet the need for reliable soil tests is even greater. Different speakers stressed the importance of studying the anomalous soils in order to discover which factors affecting the availability of nutrients have been neglected. Analysis should not be divorced from examination of profiles since often these showed some physical property which meant that, while nutrients might be available in the chemical sense, they were inaccessible to plant roots.

The value of plant analysis in relation to fruit crops and forestry was mentioned, by this means it may be easier to recognize an interaction effect which is not revealed by soil analysis. Some progress was also reported on the development of techniques for determining the nitrogen status of soils: this seems to be greatly affected by re-wetting of air-dry samples.

D. V. CRAWFORD

AHMEDABAD MILLOWNERS' TEXTILE INDUSTRY'S RESEARCH ASSOCIATION

A TEXTILE research laboratory, created and sustained by the co-operative effort of the industry and the Government of India, was envisaged by the Ahmedabad Millowners' Association as early as 1944. In 1947, the Ahmedabad Textile Industry's Research Association was registered with a membership of seventy-one mills. Ahmedabad thus became the proud pioneer in establishing a co-operative research centre for the cotton textile industry in India.

The Association started functioning in 1949, and its impact was soon felt by the industry in and around Ahmedabad. It became clear to the original members that the benefits accruing from research could with advantage be placed at the disposal of the industry on a nation-wide basis. With this object in view, the constitution of the Association was suitably amended so that mills outside Ahmedabad could become members and enjoy the same research benefits as the original founders. The present strength of members including all categories stands at eighty-eight mills and allied concerns, comprising thirty lakhs of spindles and sixty-three thousand looms—roughly one-third of the Indian cotton textile industry.

The policies of the Association are decided by an autonomous body known as the Council of Adminis-

tration. At present, the twenty-member Council is made up of representatives of management, nominees of the Government of India, the director and secretary of the Association as well as directors of other research organizations, and co-opted scientists. The Textile Commissioner is one of the nominees of the Government of India. Shri Kasturbhai Lalbhai has been the chairman of the Council from its inception.

The composition of the Council ensures a balanced and co-ordinated research policy which takes into account similar efforts by other textile research institutions and national laboratories. Further links with Government and with national research in related spheres have been established through the Ministry of Scientific Research and Cultural Affairs.

The Association began modestly in 1949 in three rooms in the Mafatlal Gazalbhai Science Institute. The foundation stone of the present building, which is housed on a 50-acre campus to the west of Gujarat University, was laid by Sardar Vallabhbhai Patel in November 1950. The building was completed towards the end of 1953 and formally declared open by Shri Jawaharlal Nehru in April 1954.

The laboratories of the Association are equipped with instruments for research in textiles and allied fields. Some of these instruments have been designed and fabricated there. The physics laboratory has equipment for studying the structure and physical and mechanical properties of fibres, yarns and fabrics. The chemistry laboratory has, in addition to the usual facilities for analysis of textile materials, a unit processing section equipped for the treatment of samples of yarns and fabrics through processes such as bleaching, dyeing, printing and finishing. The pilot mill is a versatile unit and its machinery offers a wide range of processing sequences in spinning, weaving and chemical processing. The workshops are equipped for the dual purpose of servicing mill machinery and of designing, fabricating and servicing laboratory instruments.

The Association owes its success in large measure to the enthusiasm of its workers. Most of these workers have been recruited from universities and, initiated into specialized fields of industrial research. When necessary, training has been supplemented by periods of study in overseas institutions. Technical assistance schemes such as the Point Four Programme, the Colombo Plan and the Imperial Chemical Industries Fellowships have been of great value. From a small group of about twenty-five workers in 1949, the Association has developed into an organization with a total strength of 200, which is made up of 75 scientists and technologists, 25 administrative workers, 40 skilled operatives and 60 service personnel.

The services of a number of foreign specialists have been secured from time to time with the assistance of organizations like Unesco and the International Labour Organization, in 1950 the Association was recognized by Gujarat University as a teaching centre for postgraduate research. At present most of the research students are awarded scholarships or fellowships by the Government of India, the Council of Scientific and Industrial Research, Gujarat University and the Association.

In a technologically under-developed country, it is often the path of least resistance to apply to one's own use the findings of more advanced countries. During the early days, the Association emphasized the application of scientific and technical knowledge already available to the problems of the industry. This practice of helping the industry to implement the findings of research has paid rich dividends and constitutes one of the main activities of the Association at present. In the process, industry has become wide awake to the potentialities of original research and has cordially welcomed the Association's efforts.

While being primarily a research organization the Association tries to help industry in other ways. Training in various skills, such as management and supervision, statistical methodology and testing procedures, is given to the staffs of member mills. Such trained personnel not only become better equipped for their work, but also help in securing more effective implementation of the Association's programmes. Often, they form the nucleus of research and training groups in their own organizations.

GLASSHOUSE CROPS RESEARCH INSTITUTE

THE annual report of the Glasshouse Crops Research Institute for 1957* shows that, although full facilities are not yet available, the physical development of the Institute has made good progress and some of the major problems associated with commercial glasshouse practice have been investigated. Physiological studies of the growth of tomatoes have continued, and practical problems of plant spacing and pruning have received attention. Previous studies at Chesham and the Institute have shown that retention of lateral branches below the first truss, on widely spaced plants, of the variety 'Potentato' gave a yield nearly three times as great as on single stemmed plants. It was of importance to discover whether this constituted an increase in yield per unit area of glasshouse space, the factor of most concern to the grower. This has been investigated in preliminary experiments by comparing the yields from plants having no side shoots and plants in which side shoots below the first truss had been allowed to develop. Three different spacings between the rows were used. The greatest yield per unit area was obtained from single stemmed plants at the two closest spacings, namely, 2 ft and 3 ft, although multistemmed plants at 3 ft and 4 ft spacings had the greatest mean weight of individual fruit. No treatment had any effect on weight per unit area of early fruit.

A review of the literature on spacing of tomato plants in commercial cultivation, included in the report, shows that there is no simple answer to the

question of optimal planting density for maximum yield. It is thought that this may be because sufficient attention has been given to possible interactions between planting density and watering and manuring. The study of the composition of the tomato fruit has been continued by the Chemistry Department, especially in relation to variety and state of ripeness of the fruit, with special reference to fruit quality and ripening disorders. It was concluded that the latter, evident by their effects on the outer fruit wall, were also related to the composition of the inner portion of the fruit. Further investigations were made of the changes during ripening. The acidity in the wall increased from the green stage to the first appearance of yellow pigmentation, but there was no consistent trend as ripening proceeded. This was in contrast to the situation in the inner portion of the fruit, where acidity decreased and sugars (mainly glucose and fructose) increased. The concentration of soluble solids in the expressed sap of the tomato varies considerably in relation to fruit quality and variety. These investigations will be facilitated by the demonstration that measurement of refractive index by a simple hand refractometer gives a reliable indication of total dissolved solids.

Work on urea-formaldehyde compounds as slow acting nitrogenous fertilizers has been concluded and a report gives the relative merits of the several compounds tested. Liquid feeding of tomatoes is of considerable topical interest, especially in connexion with automatic irrigation and research on this problem has been resumed. Magnesium deficiency

* Glasshouse Crops Research Institute. Annual Report 1957. Pp. 161. (Littlehampton: Glasshouse Crops Research Institute 1958.) 10s.

in glasshouse tomatoes is common, and preliminary results indicate that foliar sprays containing magnesium are more effective than soil treatments in maintaining normal leaf colour. The plant-breeding programme is concerned mainly with improvements of tomato, cucumber and lettuce.

The investigations on *Didymella* stem rot of tomato have been continued by the Plant Pathology Department, which is also concerned with powdery mildew of cucumber and wilt disease of carnation as well as mushroom diseases. Some experiments were carried out on chemotherapeutic control of tobacco mosaic virus in the tomato, but it was concluded that this approach is not promising. Although insecticides

properly applied should give adequate control of white fly, there are sometimes risks of chemical injury to plants, and for this reason interest has been revived in the method of biological control by wasp parasites. The Entomology Department has begun a series of studies on the effects of environmental factors on the fecundity and development of white fly and on the host/parasite balance. Other investigations by this Department include mushroom pests and the red spider mite. The Crop Protection Department is concerned with the control of mildew of chrysanthemums and aphids on lettuce and with the residual toxicity of certain sprays.

E C HUMPHRIES

RADIOLOGICAL HAZARDS TO PATIENTS

AT the end of 1956, the Secretary of State for Scotland and the Minister of Health appointed a committee "to review the present practice in diagnostic radiology and the use of radiotherapy in non-malignant conditions, having regard to the report of the Committee on the Hazards to Man of Nuclear and Allied Radiations".

This committee, under the chairmanship of Lord Adrian, has now produced an interim report (Ministry of Health, Department of Health for Scotland, Radiological Hazards to Patients. Interim Report of the Committee. Pp 22. London: H.M. Stationery Office, 1959. 1s 3d net) for the one completed part of its survey, namely, the use of X-rays for mass miniature radiography. The conclusion is drawn that, when properly conducted, examinations by this method make a negligible contribution to the total radiation to which the population is daily exposed. Even on the most pessimistic assumptions, the indefinite continuation of mass miniature radiography at the present rate could add no more than 20 cases of leukaemia to the annual incidence of 2,500 cases in Great Britain; it is also possible that it would produce no additional cases at all. The gonad doses, which determine the long-range genetical damage, have been found to be even smaller than previously estimated. These very small somatic and genetical risks have to be considered in relation to the undoubtedly large benefits of mass miniature radiography to the health of the population. In 1957, these examinations led to the discovery of nearly 18,000 cases of pulmonary tuberculosis and some 63,000 other abnormalities, which included lung cancer, heart disease and pneumoconiosis. For children and pregnant women, mass miniature radiography is not recommended and should be replaced by normal radiographic procedures with strict limitation of the

field to the chest. Some general principles are also given for reducing unnecessary exposure in other forms of diagnostic radiology, in particular fluoroscopy, but the survey of this area is not yet completed.

There is one statement in the introduction (paragraph 10) which may give rise to serious misunderstandings. It is stated, correctly, that a dose of radiation which would double the present mutation-rate would cause perceptible damage to the population, and that this dose is estimated to lie between 10 and 100 r per generation. It is also correct to say that at present the dose due to medical radiology does not exceed 3 rads per generation. But it is only for the sake of convenience that genetical damage is usually estimated in terms of the 'doubling dose'. There is no lower threshold to the genetical effects of ionizing radiation, and serious genetical damage will be produced already by doses which are far below the doubling dose. In fact, the report of the Medical Research Council came to the conclusion that, from the point of view of genetical hazards, "the upper limit, which future knowledge may set to the total dose of extra radiation which may be received by the population as a whole, is not likely to be more than twice the dose which is already received from the natural background, the recommended figure may indeed be appreciably lower than this". On this evidence, the danger limit has already been reached or even exceeded in countries where X-rays are used extensively for medical purposes. Against this damage to future generations we must, however, set the benefit to the present one and, although all means must be used to cut down avoidable exposure to radiation, a high amount of exposure will remain unavoidable if the present standards of medical service are to be maintained.

FEEDING THE HUNGRY

THE practical way to wage war on want was the theme of an outstanding address at St John's College, Annapolis, Maryland, on April 9 by Mr Gerard Piel, publisher of *The Scientific American*. Following an account of the way in which science has given man unlimited power and opportunities to change the material conditions of life, Piel shows how it is now possible to bring the elimination of want within the reach not only of the present

generation but also of all future generations. Want is no longer a challenge to technology, but to economics and politics; it is a social problem. Thanks principally to the control of mortality, the underprivileged peoples are living longer and feeling well enough to do something about their plight. These aroused people are still extracting the irreplaceable resources of their lands to feed the voracious appetite for raw materials of Western peoples. At present the

United States imports from overseas iron ore, bauxite, oil and a host of commodities in greater volume than ever before. In some American sections the technology is perilously dependent upon riches supplied so cheaply. The goodwill and complacency of the natives have immediate relevance to the American price structure.

It is impossible to stop at the churlish counsel that the Colonials should reduce their numbers. Their population is rising because the medium of sanitation introduced to protect white Colonials in their midst has reduced their rate of mortality as well. Their numbers are increasing, according to United Nations studies, at a rate that exceeds 1 per cent per annum. Since the end of the Second World War their material condition has been in corresponding decline, their calorie intake has actually fallen.

To offset the claim of population growth and reverse the decline in their condition, they must increase their production not at a rate greater than their population growth. To negate the differential, the faster will their lot improve. Such an objective is not only technologically but also politically and economically feasible. American industrial growth has averaged 5 per cent over long periods: it has reached 8 per cent under intense pressure. The growth of agricultural output has correspondingly proceeded at the rate of 2 per cent in normal times. In response to the economic cycle and to controlled prices and other regulatory devices, it fluctuates over an even wider range. The present curtailment of grain production in the United States represents 200 000 tons, which approximates to the calorie deficit for the underfed portion of the world population.

About 500 billion dollars over the next fifty years would secure an average gain per annum of 2 per cent in industrial production and a corresponding increase in agricultural output in non-Western areas. Not all the 500 billion dollars would have to be supplied from outside. At about the halfway point the new industrial centres would begin to generate some additional capacity of their own.

Bed rock investments, however, are not particularly attractive to the world's capital market. These

involve such elementary public utilities as communication systems, including highways as well as railroads, and dams for flood control and irrigation. Investments in such projects call for the kind of funds now written off on armaments. A long range view should be taken in looking for return on investment.

Western technology is specially qualified to contribute to the soaring demand for electrical energy which will attend industrialization programmes. But the demand for huge volumes of energy, heavy equipment and big investment would not come at the outset. First, there is need for planning and, then, engineering. Many of the early gains in these areas would be achieved with very little expenditure on capital goods. The first requirement is for brains and knowledge.

An example of what can be accomplished is furnished by Mexico. For the past twenty years the Rockefeller Foundation has been working with the Ministry of Agriculture and Animal Husbandry of Mexico. At a cost of less than 2 million dollars a year, American agronomists have been supplied to Mexico, and young Mexicans have been trained in the agricultural sciences. In this period, the food production of the country has risen 80 per cent. The gains have been achieved by improved yields of Mexico's own staple crops, the development of new varieties of wheat and potatoes and the establishment of something like the American county agent system for farmer education. Not a single tractor or fertilizer plant is in the expense account: the money has been spent on the intangibles of information, education and expert consultation. The 4 per cent per annum gain safely exceeds the 3 per cent increase in population and has brought an improvement in the people's diet which is already showing up in vital statistics.

Somewhere in American material and intellectual resources the capacity to expand on this precedent could be found. If a beginning could be made it would soon be possible to have additional wealth and brains available for the task as a result of the attenuation of the arms race on which prosperity now rests so heavily and insecurely.

SYMPATHETIC POSTGANGLIONIC MECHANISM

By PROF J H BURN, FRS, and M J RAND

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DURING recent years it has been demonstrated that acetylcholine exerts an action in various organs similar to that of sympathetic stimulation. Since this action is seen in the presence of atropine and is also exerted by nicotine it follows that the action is not a muscarinic but is a nicotinic action. An example of this action is the contraction of the arrectores pili muscles in the skin of the cat's tail. This was first described by Brückner¹ for acetylcholine, and a few years later by Coon and Rothman² for nicotine. Most of the hair was removed from the cat's tail except for a few tufts, and acetylcholine or nicotine was injected into the skin at the base of the tufts. Pilo erection was then observed. Normally the pilomotor muscles are caused to contract by sympathetic stimulation, and they also contract

after the intravenous injection of adrenalin or nor-adrenalin. Other examples of sympathomimetic effects caused by acetylcholine or by nicotine in the presence of atropine are the relaxation of the isolated intestine of the kitten by nicotine³, the acceleration of the isolated atria of the rabbit⁴ and the constriction of the vessels of the perfused rabbit ear by acetylcholine and by nicotine⁵, the contraction of the isolated nictitating membrane of the cat by nicotine⁶, do Burgh Doly and Scott (unpublished work) have observed that acetylcholine injected into the splenic artery during perfusion of the spleen with blood caused contraction of the spleen. We are grateful to them for allowing us to quote this result.

These nicotine-like effects of acetylcholine, exerted at sites peripheral to sympathetic ganglia thus

the effects of sympathetic stimulation, are not seen in preparations from animals with reserpine. Tissues innervated by sympathetic nerves were found by Schmitterlów⁷, Euler and Purkhold⁸ to contain noradrenaline or with a much smaller amount of adrenaline. Treatment of rabbits with reserpine, the noradrenaline which can be extracted from the heart ears⁹. Similarly after treatment with reserpine, noradrenaline disappears from the aorta of the ear of the rabbit, from the skin of the rabbit's ear and from the skin of the cat's tail, from the cat's ear and from the iris of the cat's eye¹⁰.

The nicotine-like actions of acetylcholine are also seen when the sympathetic fibres degenerate, and this degeneration is also accompanied by a loss of the noradrenaline which can be extracted from the nerves^{8,10b}.

The conclusion may therefore be drawn that the nicotine-like actions of acetylcholine which have been described are due to the release of noradrenaline (possibly with adrenaline also) from the sympathetic nerves.

At present we are uncertain of the location of the noradrenaline in the organ. Euler¹¹ believes that it is contained within the postganglionic fibres, calculating that the amount may be 3-30 mgm/gm. This is one thousand times more than that in postganglionic fibres before they reach the organ. This amount is only of the order of 15 µgm/gm. The disappearance of the noradrenaline after degeneration of the nerves is readily explained if it is present in the nerves.

There is some evidence, which as yet is only suggestive, that the noradrenaline and adrenaline in the organs might be present in cells containing chromaffin granules. Such cells have been described in human skin by Adams-Ray and Nordenstam¹², and also by Burch and Phillips¹³. They have been found in the skin of the rabbit's ear, in the skin of the cat's tail and in the nictitating membrane. The chromaffin granules are greatly reduced or disappear in the tissues of animals treated with reserpine, or in tissues in which the sympathetic fibres have degenerated^{10a,c}. Thus it is possible that the nicotine-like actions of acetylcholine are due to the release of noradrenaline and adrenaline from cells containing chromaffin granules. However, Muscholl and Vogt¹⁴ have found that reserpine depletes the noradrenaline stores in the sympathetic neurones more readily than those in chromaffin cells.

Tyramine is a sympathomimetic amine which ceases to act after degeneration of the sympathetic fibres¹⁵. Its pressor action is also absent in the cat previously treated with reserpine¹⁶. The conclusion may be drawn that tyramine exerts its action by liberating noradrenaline and adrenaline from the store in the organ. Since an infusion of noradrenaline into the vein of a cat or into the blood perfusing the hind-leg of a dog increases the pressor and constrictor action of tyramine, or restores it when it is absent due to previous treatment with reserpine, it appears that the store of noradrenaline in the organ can be increased by taking up noradrenaline from the blood stream¹⁷.

The effect of sympathetic stimulation also is increased as a result of an infusion of noradrenaline. If the volume of one hind-leg of a dog is recorded in experiments in which the lumbar sympathetic chain is stimulated, then, atropine having been given, the threshold strength of stimulus for causing vaso-

constriction in the hind-leg can be determined. Following an infusion of noradrenaline, the total amount given to the dog being 0.2-1.0 mgm in the course of 20 min., the threshold has been observed to fall to a mean of 40 per cent of its previous value. In experiments in which the dog's hind-leg has been perfused it has been observed that the effect of a given sympathetic stimulus was greatly increased. These observations indicate that the efficiency of sympathetic stimulation depends on the amount of noradrenaline in the neighbourhood of the nerve endings. This may be taken up from the blood into the nerve endings themselves or into chromaffin cells, one of the functions of the noradrenaline secreted by the adrenal medulla may be to fill up this store.

We have now considered evidence that the nicotine-like actions of acetylcholine are due to the release of noradrenaline from a store near the sympathetic nerve endings, we have seen that this store can take up noradrenaline which is circulating in the blood, and we have seen that the effect of sympathetic stimulation depends on the size of this store. We now turn to the sympathetic impulses themselves.

When a cat is treated with reserpine with the result that the stores of noradrenaline and of adrenaline are depleted, the effect of tyramine on the nictitating membrane is completely absent, but stimulation of the postganglionic sympathetic fibres still causes a contraction. The threshold strength for this effect is greater than the threshold in the normal cat. We have found that the contraction produced is augmented by eserine and is abolished by atropine, and the contraction must therefore be due to the release of acetylcholine from the sympathetic fibres. The presence of cholinergic fibres in the sympathetic supply to the nictitating membrane was suggested by Bacq and Fredericq¹⁸. Recent work shows that the presence of cholinergic fibres is still more widespread. Thus Gillespie and Mackenna¹⁹ have found that when a rabbit is treated with reserpine, the isolated colon is caused to contract by sympathetic stimulation instead of to relax, and that the contraction is abolished by atropine. They concluded that cholinergic fibres are present in the sympathetic supply.

Huković²⁰, working in this Department, has made an isolated preparation of rabbit atria with the sympathetic nerves attached, when the sympathetic fibres from the stellate ganglion were stimulated the rate and amplitude of the atrial beat increased. If the rabbit was treated beforehand with reserpine some preparations responded to sympathetic stimulation by inhibition, the inhibitor effect being increased by eserine and abolished by atropine. This result suggests that cholinergic fibres are present in the sympathetic supply from the stellate ganglion to the atria.

Observations have also been made on the cat spleen, recording the changes in volume of the spleen by a plethysmograph. The nerves were separated from the splenic artery near the beginning of the artery. Stimulation caused contraction of the spleen which was unaffected by atropine. When the cat was treated beforehand with reserpine, it was found that in some preparations acetylcholine caused a dilatation of the spleen, and that stimulation of the nerves was also followed by dilatation. This dilatation was increased in the presence of eserine and abolished by atropine. Thus the splenic nerves also contain cholinergic fibres. Observations have also been made on the

virgin cat uterus, recording its contractions *in situ* under chloralose anaesthesia. When the hypogastric nerves were stimulated, inhibition followed. When the cat was treated beforehand with reserpine, stimulation of the hypogastric nerves caused a small contraction which was greater in the presence of eserine and which was abolished by atropine. The evidence suggests that the hypogastric nerves contain cholinergic fibres.

The observations that the nicotine-like effects of acetylcholine resemble those of sympathetic stimulation, and that these effects are exerted by the release of noradrenaline (or adrenaline) must now be put aside by side with the evidence of the existence of cholinergic fibres in postganglionic sympathetic fibres in various places where they were not suspected. It then appears that such cholinergic fibres may be adrenergic in their effect, because the acetylcholine which they liberate will cause the discharge of noradrenaline or of adrenaline from the peripheral store. The stimulation of such fibres can in theory have two effects, one, normally much the smaller, due to the direct action of the acetylcholine released, an action which is sensitive to atropine, and the other, normally much the greater, due to the released acetylcholine causing a discharge of noradrenaline from the store, a nicotine-like action not affected by atropine. This double effect may actually be present in the nictitating membrane where the response to postganglionic stimulation in the normal cat is slightly diminished by atropine, for example to about 80 per cent of its initial size.

Such a double effect might explain the response to stimulation of the sympathetic supply to the muscles of the dog's hind leg, where Burn¹⁴ observed that a stimulus for 3 sec caused dilatation, while the same stimulus applied for 30 sec caused in the main constriction. A double effect is possible only when acetylcholine has a direct muscarinic action of its own. Thus in the cat treated with reserpine, stimulation of the sympathetic fibres has no pilomotor effect

in the tail. The accumulated evidence thus requires consideration of a new possibility. The adrenergic sympathetic fibre has been thought of as liberating noradrenaline in the same way as cholinergic fibres liberate acetylcholine. However, cholinergic fibres, which seem widespread in the postganglionic sympathetic supply, may liberate noradrenaline from the store at the nerve endings and thus be adrenergic in effect.

In this account we have kept open the possibility that noradrenaline may not always be the main component of the peripheral store and that around some sympathetic nerve endings in the virgin cat uterus for example adrenaline may be more important. We have no evidence on this as yet. We may also recall that Pines¹⁵ has described the chromaffin cells in sympathetic ganglia and has given a detailed account of his findings that they are innervated.

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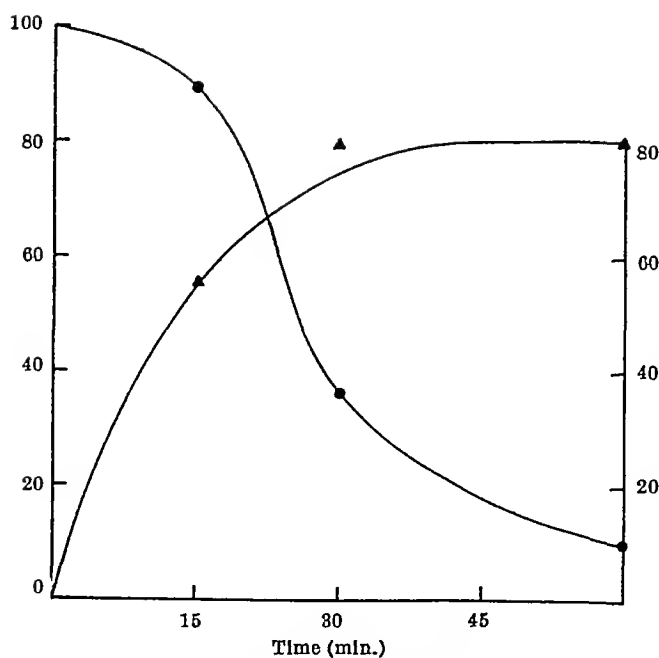
PROTEIN BIOSYNTHESIS AND OXIDATIVE PHOSPHORYLATION IN ISOLATED RAT LIVER MITOCHONDRIA

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ELECTRON microscopy combined with differential centrifugation of sucrose homogenates has shown that liver parenchymal cells have a complex cytoplasmic structure¹. After intravenous injection of amino acids labelled with carbon 14 the proteins of the subcellular cytoplasmic structures of these cells become labelled at different rates. In both rats and guinea pigs the liver microsomal fraction is labelled considerably more rapidly than the mitochondrial material. Labelling is particularly rapid in the ribonucleoprotein fraction of the microsomes². The suggestion has been made that protein synthesis takes place mainly in the microsomal ribonucleoprotein fraction and that mitochondria acquire radioactive protein from the microsomal fraction. The present results and those of Bates *et al.*³ indicate that rat liver mitochondria are capable of independent protein synthesis.

Mitochondria were isolated from rat liver by differential centrifugation of a 1:4 sucrose homogenate. Best results were obtained with a mixture containing sucrose (0.3 M), versene (0.002 M) and nicotinamide (0.03 M); this mixture will be referred to as SVN. The fraction collected between 1.000 and 0.0007 was washed by four successive cycles of re-suspension and precipitation from SVN. Washed mitochondria in a mixture of sucrose (0.16 M), phosphatidyl (0.01 M), tris buffer (0.02 M), MgSO₄ (0.008 M) and sufficient KCl to maintain tonicity showed negligible incorporation of labelled amino acids into mitochondrial protein during aerobic incubations. The mitochondrial protein was obtained by precipitation with trichloroacetic acid and treatment to remove adsorbed amino acids, ribonucleic acid and lipids. Incorporation was stimulated by the addition of either succinate or α -ketoglutarate.



Ordinates left, per cent of initial rate of oxidative phosphorylation, right, counts per min.

Fig 1 Dependence of incorporation of amino-acid into mitochondrial protein upon oxidative phosphorylation. Washed mitochondria from about 3 gm rat liver were suspended in 5.5 ml of medium of the following composition: *tris* buffer (0.05 M), potassium phosphate (0.01 M), potassium succinate (0.01 M), magnesium sulphate (0.008 M), potassium chloride (0.065 M), versene (0.0013 M), nicotinamide (0.02 M), ^{14}C -*Chlorella* protein hydrolysate (5 μC), sucrose (0.11 M), added as 2.0 ml boiled cell sap. Incubations were at 30°, in an atmosphere of oxygen. Oxidative phosphorylation was measured essentially as described by Slater (ref 10), glucose-6-phosphate was estimated by the method of Kornberg and Horecker (ref 11).

together with cell sap. At an early stage in the investigation it was found that, contrary to the report of Greengard⁴, boiled cell sap was just as effective as whole cell sap. Both the rate and the duration of amino-acid incorporation into mitochondrial protein could be increased by adding progressively larger quantities of boiled cell sap. The incorporation reaction was stimulated by incubation in oxygen instead of air and almost completely inhibited by incubation in nitrogen or by the addition of dinitrophenol or cyanide. The behaviour of the incorporation reaction towards inhibitors indicated that incorporation was probably linked to oxidative phosphorylation, amino-acid incorporation and oxidative phosphorylation were accordingly measured in the same mitochondrial preparation. The results (Fig 1) showed that as the rate of oxidative phosphorylation declined, the rate of incorporation declined in a similar manner.

The duration of oxidative phosphorylation in isolated rat liver mitochondria is notoriously sensitive to conditions of incubation⁵. Calculation of the amount of adenine nucleotide in boiled cell sap indicated that the final concentration of nucleotides in the incubation mixture was below that usually required to maintain mitochondrial structure and oxidative phosphorylation. Accordingly, the boiled cell sap was supplemented with 0.004 M adenosine monophosphate and 0.0005 M diphosphopyridine nucleotide. Mitochondria incubated under these conditions were able to maintain oxidative phosphorylation and incorporation of labelled amino-acids for 2 hr at 30°, although the rate of incorporation was falling off after 1 hr. The work of Siekevitz and Potter⁵ and of Pressman⁶ indicates that the balance of nucleotides and of inorganic phosphate

inside the mitochondrial membrane is best maintained when an acceptor for energy-rich phosphate bonds is present in the medium. Thus when the system was further supplemented with hexokinase and glucose, incorporation of amino-acids into mitochondrial protein could be maintained at, or near, a linear rate for 2 hr at 30°. Incubations have not been carried beyond 2 hr.

Mitochondria are composed of a structurally complex double membrane within which are disposed various soluble but rather firmly bound enzymes. It was found that in the presence of adenosine monophosphate and diphosphopyridine nucleotide, both with and without hexokinase, the insoluble proteins of the mitochondria were effectively labelled either by a mixture of amino-acids labelled with carbon-14 or by a single labelled amino-acid (phenylalanine). Soluble protein was not, however, significantly labelled even after 2 hr at 30° (soluble protein was released either by the butanol method of Morton⁷ or by the extraction of an acetone-dried powder of mitochondria with phosphate buffer). Increase in the amount of boiled cell sap, with maintenance of the adenosine monophosphate and diphosphopyridine nucleotide concentration at the level given above, resulted in a substantial improvement in the efficiency of labelling of the insoluble protein and produced slight activity in the soluble protein. Boiled cell sap contains substantial quantities of amino-acids (80 μgm amino-nitrogen/ml) and it was found that these could be replaced by a complete mixture of 20 amino-acids. It was found that, as the concentration of these amino-acids in the incubation medium was progressively increased, the incorporation into insoluble protein rose to a maximum at an amino-acid concentration of 30–40 $\mu\text{M}/\text{ml}$. The incorporation into soluble protein was initially low, but as amino-acid concentration was increased, the radioactivity of the soluble protein continued to rise in an approximately linear manner. Thus the incorporation into soluble protein of the mitochondria progressively becomes a greater proportion of the total incorporation, as amino-acid concentration is increased. The most likely explanation of these results is that there are relatively few sites of protein synthesis in mitochondria (templates?). When these sites become saturated with incoming radioactive amino-acid further increase in amino-acid concentration (of fixed specific radioactivity) will not result in any further increase in radioactivity of insoluble protein. Increased amino-acid concentration will result, however, in a progressively greater tendency for newly synthesized protein to be displaced from the sites of synthesis into the intracisternal spaces so that there will continue to be a progressive increase in the rate of accumulation of radioactivity in soluble protein.

There is no doubt that the amino-acid incorporation reaction measured in these experiments is truly intramitochondrial and is not due to adherent microsomes. First, incorporation is not abolished by thorough washing of the mitochondria as described previously (this washing procedure has been shown to remove at least 95 per cent of microsomes labelled with carbon-14 added to the sedimented mitochondria), secondly, the incorporation reaction does not require fresh cell sap with its supply of soluble ribonucleic acid⁸ and 'amino-acid activating' enzymes, thirdly, the incorporation is much more prolonged than that obtained with microsomes *in vitro*, and fourthly, the incorporation is quite unaffected by addition of ribonuclease to

the incubation mixture. This does not, however, prove that ribonucleic acid plays no part in amino acid incorporation since we have found that, even after 2 hr at 30° in the presence of ribonuclease, mitochondria retain about 70 per cent of their ribonucleic acid (originally 17 µgm/mgm mitochondrial protein). Indeed, the incorporation reaction in mitochondria may have closely similar characteristics to that occurring in microsomes since we have found that an extract of mitochondria will catalyse an amino acid-dependent exchange between adenosine triphosphate and radioactive pyrophosphate (Table 1).

Table 1 AMINO-ACID ACTIVATION IN RAT LIVER MITOCHONDRIA

| Extract of mitochondria prepared from | c.p.m. per µmole adenosine triphosphate | | |
|--|---|---------------------|------------------------------------|
| | No amino-acids | Plus amino-acids | Increment due to amino-acids |
| 0.6 gm. Liver | 1,810 | 2,400 | 580 |
| 1.2 gm. Liver | 3,060 | 4,280 | 1,220 |

Mitochondria were isolated and washed four times in an acetone powder was prepared and extracted with 0.1 M tria buffer pH 7.6. This soluble extract was incubated with tria buffer pH 7.6, 100 µmoles magnesium chloride, 2 µmoles adenosine triphosphate, 5 µmoles a mixture of 12 amino-acids, 2 µmoles of each ³²P pyrophosphate about 2 µmoles 160,000 c.p.m. vol 1 ml incubated for 16 min 37°.

Before one can be convinced that the amino acid incorporation observed in these experiments represents true synthesis of protein, it would be necessary to demonstrate synthesis of a specific protein. In this regard the synthesis of cytochrome c has already been demonstrated in isolated mitochondria from rat liver² and calf heart³. The presence of numerous enzymes within mitochondria suggests that this *in vitro* system should be a valuable tool in further studies on protein biosynthesis. Work has already been initiated along these lines.

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STRUCTURE OF A MELANOCYTE-STIMULATING HORMONE FROM THE HUMAN PITUITARY GLAND

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A MELANOCYTE-STIMULATING substance from human pituitary glands has recently been isolated in pure form by ion-exchange chromatography.¹ It has been shown to be a slightly basic polypeptide which migrates as a single substance when submitted to ionophoresis on paper in pyridine acetic acid buffers at pHs of 3.6 and 6.5.

The amino acid sequence of the polypeptide hormone has been investigated by methods similar to those described^{2,3} for the elucidation of the structure of a melanocyte-stimulating hormone from pig pituitary glands. The particular methods which have been used were to a great extent determined by the limited amount of the substance (4-6 mgm.) which was available for study.

Specific colour tests⁴ carried out on the intact polypeptide showed that it contained tryptophan, tyrosine, histidine and arginine; and when a total acid hydrolysate was submitted to qualitative chromatographic analysis on paper the following amino acids were shown to be present: alanine, arginine, aspartic acid, glutamic acid, glycine, histidine, lysine, methionine, phenylalanine, proline, serine and tyrosine.

A sample of the hormone (2.5 mgm.) was allowed to react with chymotrypsin (0.1 mgm.) in 0.05 M ammonium bicarbonate (2 ml.) at pH 8.0-8.5 and 37° for 10 hr. When the product was fractionated by ionophoresis on paper in pyridine acetic acid (pH 6.5) at 40 volts/cm for 2 hr it was resolved into five peptide fragments.

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Table 1 AMINO ACID COMPOSITION AND C-TERMINAL AMINO-ACIDS OF PEPTIDES PRODUCED BY CHYMOTRYPSIN HYDROLYSIS OF HUMAN β -MELANOCYTE-STIMULATING HORMONE

| Peptide | Amino-acid composition | C-terminal group |
|----------------|-----------------------------------|------------------|
| C ₁ | Ala, Asp, Glu, Gly, Lys, Pro, Tyr | Tyr |
| C ₂ | Arg, Asp, Gly, Lys, Pro, Ser, Tyr | Asp |
| C ₃ | Arg, Glu, His, Met, Ile | Phe |
| C ₄ | Asp, Gly, Lys, Ile, Ser | Asp |
| C ₅ | Arg, Tyr | Tyr |

The amino acid compositions of these five peptides (C₁, C₂, C₃, C₄, and C₅) were determined by means of specific colour tests⁴, and by paper chromatographic analysis of their total acid hydrolysates, the corresponding C-terminal amino-acids were determined by means of carboxypeptidase⁵. The results, summarized in Table 1, showed that the human melanocyte stimulating hormone was of the β melanocyte stimulating hormone type, and that it was closely related in terms of chemical structure to β melanocyte-stimulating hormone⁶ from pig pituitary glands. Thus, peptides C₁, C₂, C₃, and C₄ were found to have the same electrophoretic mobilities at pH 3.5 and pH 6.5, and the same qualitative amino acid compositions (with the exception of C₃, which contained arginine instead of lysine), as the corresponding peptide fragments⁶ derived from pig β -melanocyte stimulating hormone by digestion with chymotrypsin. Peptide C₅ on the other hand differed from the corresponding peptide fragment from pig β -melanocyte-stimulating hormone both in electrophoretic and chromatographic behaviour, and in amino-acid composition, although the C-terminal amino-acid,⁷

tyrosine, and four of the other constituent amino-acids—aspartic acid, glutamic acid, glycine and proline—were common to both peptide fragments

The presence of lysine suggested that C_1 would be susceptible to the action of trypsin. It was therefore allowed to react with trypsin for 4 hr at 37°, when the product of reaction was fractionated by ionophoresis at pH 6.5 it was resolved into two major (C_1TA_1 , C_1TB_1) and two minor (C_1TA_2 , C_1TB_2) components. Their qualitative amino-acid compositions were determined and are given in Table 2.

Table 2. AMINO-ACID COMPOSITION AND C-TERMINAL AMINO-ACIDS OF PEPTIDES PRODUCED BY TRYPTIC HYDROLYSIS OF PEPTIDE C_1 (Table 1)

| Peptide | Amino-acid composition | C-terminal group |
|-----------|------------------------------|------------------|
| C_1TA_1 | Asp, Glu, Gly, Lys, Pro, Tyr | Tyr |
| C_1TB_1 | Ala, Glu, Lys | Lys |
| C_1TA_2 | Asp, Glu, Gly, Pro, Tyr | Tyr |
| C_1TB_2 | Lys | — |

One of the minor peptide components, C_1TA_2 , appeared to be identical with the N-terminal peptide, Asp Glu Gly Pro Tyr, in pig β -melanocyte-stimulating hormone⁶, as judged by its electrophoretic mobility at pH 6.5, R_F in butanol-acetic acid-water (4:1:5), amino-acid composition, and C-terminal group. The two major peptide components, C_1TA_1 and C_1TB_1 , were both found to contain lysine, and the fact that a significant amount of free lysine (C_1TB_2) was also formed in the tryptic reaction suggested that the parent molecule, C_1 , contained a Lys-Lys bond, and that it was the N-terminal peptide (Ala, Glu) Lys Lys (Asp Glu Gly Pro) Tyr in the human β -melanocyte-stimulating hormone molecule.

After their homogeneity had been established both by electrophoretic and chromatographic analysis, peptides TA_1 , TA_2 , TB_1 and C_2 were submitted to partial acid hydrolysis (12 N hydrochloric acid, for 3–6 days at 37°), peptide C_3 was hydrolysed with subtilisin⁸ (12 hr at 37°). The respective products of reaction were fractionated by ionophoresis on paper and were characterized by the procedures which have been described previously^{3,6}. The results are summarized in Table 3.

Peptide C_2 was shown to give additional amounts of C_5 and C_6 when it was redigested with chymotrypsin, showing that C_5 and C_6 formed contiguous sequences in the molecule. By means of carboxypeptidase, C_6 was shown to be a dipeptide containing arginine and tryptophan, in a similar manner aspartic acid was shown to be the C-terminal amino-acid in both C_2 and C_3 , showing that these two peptides formed the C-terminal sequence, Arg Try (Gly, Ser, Pro, Lys). Asp, in human β -melanocyte-stimulating hormone (cf ref 6).

Although it was not possible to undertake quantitative amino-acid and end-group analyses on the parent molecule, the results which have been

Table 3. PEPTIDES IDENTIFIED IN PARTIAL ACID* (12 N HYDROCHLORIC ACID, 37°) AND SUBTILISIN† HYDROLYSATES

| Peptide | Products of partial hydrolysis |
|-------------|--|
| * C_1TB_1 | Ala Glu, Glu Lys |
| * C_1TA_1 | Lys Asp, Lys Asp Glu, Glu Gly, Gly Pro Tyr |
| * C_1 | Ser Pro, Ser Pro Pro, Ser Pro Pro Lys, Pro Pro Lys, Pro Lys, Lys Asp |
| † C_2 | Arg Met, Arg Met Glu, Glu His, Glu His Phe |

obtained with peptide fragments derived from it by hydrolysis with chymotrypsin and trypsin nevertheless appear to be sufficient to establish that human β -melanocyte-stimulating hormone contains twenty-two amino-acid residues, and that they occur in the following sequence

1 2 3 4 5 6 7 8 9 10 11
H—Ala Glu Lys Lys Asp Glu Gly Pro Tyr Arg Met
12 13 14 15 16 17 18 19 20 21 22
Glu His Phe Arg Try Gly Ser Pro Pro Lys Asp —OH

This appears to be the first of the polypeptide hormones from the human pituitary to be isolated in pure form and to be characterized in terms of its complete chemical structure. The amino-acid sequences of human, pig^{6,7} and ox⁸ β -melanocyte-stimulating hormones and pig α -melanocyte-stimulating hormone^{2,3} are compared in Fig 1.

Although human β -melanocyte-stimulating hormone manifests a structural 'species' difference of the 'classical' type, namely, the replacement of a lysine residue (position 6 in pig and ox β -melanocyte-stimulating hormone) by arginine (position 10 in human β -melanocyte-stimulating hormone) in structurally related positions, the presence of the additional N-terminal tetrapeptide, Ala Glu Lys Lys, represents a hitherto unprecedented structural species variation among naturally occurring biologically active polypeptide and protein molecules of relatively low molecular weight (for example, vasopressins^{10,11}, corticotropins¹², insulins¹³ and hypertensins^{14,15}).

Ox β -melanocyte-stimulating hormone⁸ is found to differ from pig β -melanocyte-stimulating hormone only in position 2 (Fig 1), where the glutamic acid residue in the pig hormone is replaced by a serine residue in the ox hormone. It is perhaps significant that the replacement of one amino-acid by another which is structurally unrelated to it occurs in a part of the molecule which does not appear to be specifically essential for its biological activity³ (cf corticotropins¹²). Presumably genetical alterations which produce structural modifications of this type in essential parts of the molecule would result in the formation of molecules in which biological specificity was either modified or destroyed. Consequently the fact that a lysine residue in the pig and ox hormones is replaced by the structurally related amino-acid, arginine, in the human hormone, and that the structural features common to all known β -melanocyte-stimulating hormones and corticotropins^{12,16}

| | | | | | | | | | | | | | | | | | | | | | | | | |
|----------------------|----|-----|-----|-----|--------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|---------------------|-----|-----|-----|-----|-----|-----|
| α -MSH (pig) | | | | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | | | | | | | |
| | | | | | CH ₃ CO | Ser | Tyr | Ser | Met | Glu | His | Phe | Arg | Try | Gly | Lys | Pro | Val-NH ₂ | | | | | | |
| β -MSH (ox) | H- | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | | | | | |
| | | Asp | Ser | Gly | Pro | Tyr | Lvs | Met | Glu | His | Phe | Arg | Try | Gly | Ser | Pro | Pro | Lys | Asp | -OH | | | | |
| β -MSH (pig) | H- | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | | | | | |
| | | Asp | Glu | Gly | Pro | Tyr | Lys | Met | Glu | His | Phe | Arg | Try | Gly | Ser | Pro | Pro | Lys | Asp | -OH | | | | |
| β -MSH (human) | H- | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | |
| | | Ala | Glu | Lys | Lys | Asp | Glu | Gly | Pro | Tyr | Arg | Met | Glu | His | Phe | Arg | Try | Gly | Ser | Pro | Pro | Lys | Asp | -OH |

Fig 1. Amino-acid sequences of melanocyte stimulating hormones from pig, ox and human pituitary glands. MSH, melanocyte-stimulating hormone.

remain intact, suggests that the amino acids which occupy these key positions in β melanocyte-stimulating hormone are directly associated with its biological activity in the *in vivo* environment in which it has been designed to function as a hormone.

In a melanocyte stimulating hormone, on the other hand, there is an interchange of lysine and serine residues between positions 3 and 11 (Fig 1), which correspond to positions 6 and 14 in pig and ox β melanocyte stimulating hormones and to positions 10 and 18 in human β melanocyte stimulating hormone. This would suggest that factors other than the linear arrangement of amino acid residues must be taken into consideration in relating structure to biological function in the living cell even in comparatively small peptide molecules which do not appear to possess any ordered secondary or tertiary structure in aqueous solution.

I am indebted to Dr H. B. F. Dixon for his generous gift of the sample of pure human melanocyte-stimulating hormone. Most of the experimental work was carried out in the Division of Biochemistry of the Massachusetts Institute of Technology, and I am indebted to Dr Vernon Ingram for his kindness in placing the facilities of his laboratory at my disposal. [May 6]

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GROWTH PATTERNS IN NEUROSPORA

A Biological Clock in Neurospora

MANY fungi produce alternating zones of different growth type in response to diurnal light-cycles and temperature cycles, and in some cases the zonation will continue to be produced for a time in continuous darkness and at a constant temperature. In 1953 Brandt¹ reported observation of zonation in the growth and conidia formation of *Neurospora crassa* mycelia in standard glass race tubes maintained in constant darkness, humidity and temperature. Inspection of Brandt's photographs suggested to us that the zones were formed with a frequency of approximately one a day and we have tested the implication that there does occur in *Neurospora* a typical biological daily clock—that is, a rhythmic system with an innate circadian ('about a day') period which is relatively independent of the temperature. (We are here adopting the suggestion (personal communication) of Prof F. Halberg that the word 'circadian' obviates all the long standing confusion inherent in the words diurnal, daily, 24 hr., as adjectives to describe the rhythms with which we are concerned.)

Brandt reported that he obtained zonation in only one (No 21807, prolineless) strain of several that he examined, and that the zonation occurred on only one of the supplemented media (Grav's) that would support growth of this strain. Zonation occurred at constant temperature either in a 24 hr light-dark cycle or in continuous darkness after a brief period of initial growth in white light. Zonation does not develop if the mycelium is maintained in continuous white light; but we have found that it can develop in continuous red (carbon) light.

In the experiments reported here the same strain and media as those used by Brandt were also used. Freshly inoculated race tubes were placed in a tem-

perature-controlled cabinet containing a 14 watt cool white fluorescent lamp. About 40 hr later when the mycelium was growing well, the white light was discontinued and a red lamp was turned on. At this time and at 24 hr intervals thereafter the advance of the mycelial front was observed (in the red light) and marked on the race tube. When the growth had reached the end of the agar, the tube was removed from the growth cabinet and a densimeter device was used to measure relative density of the mycelium along its entire length. The observed phenomenon consists of alternating zones of sparse and dense mycelium. Preliminary experiments failed to reveal any significant difference in the linear growth increments in the 4 hr intervals throughout any 24 hr interval. The distribution of mycelial density has accordingly been converted from its observed spatial scale to a temporal scale. Regions of dense growth show up as maxima on the densimeter graphs.

Fig 1 illustrates the results so obtained from two typical race-tubes, one maintained at 31°C and the other at 24°C. Table 1 summarizes more extensive data on the time interval between successive maxima on the densimeter graphs. This interval, which is the period of the rhythm, is about 22 hr and is the same at the two temperatures.

The zonation of *N. crassa* thus is regulated by a rhythmic phenomenon which manifests the essential features of a biological clock.² The rhythm has an innate free running period which is close to 24 hr, relatively independent of the temperature. The rhythm can be entrained by a 24 hr light cycle. In addition to possessing these functional prerequisites of a good chronometer the rhythm also possesses other features of typical circadian systems: (1) The phase of the rhythm can be established by a single transition from light to dark; (2) as with many other plant rhythms the manifestation of the rhythm is

Table 1 74 A (WILD-TYPE) \times 21803a (*pat* *nil*)

| No of asci | Genotypes of ordered spore pairs |
|-------------------|--|
| 4 | <i>pat</i> + <i>pat</i> + <i>A</i> <i>pat</i> + <i>pat</i> + <i>A</i> <i>pat</i> <i>pat</i> <i>a</i> <i>pat</i> <i>pat</i> <i>a</i> |
| 2 | <i>pat</i> + <i>pat</i> <i>a</i> <i>pat</i> + <i>pat</i> <i>a</i> <i>pat</i> <i>pat</i> + <i>A</i> <i>pat</i> <i>pat</i> + <i>A</i> |
| 2 | <i>pat</i> + <i>pat</i> + <i>A</i> <i>pat</i> <i>pat</i> + <i>A</i> <i>pat</i> <i>pat</i> + <i>A</i> <i>pat</i> <i>pat</i> <i>a</i> |
| Totals | |
| No of spore pairs | Genotype |
| 10 | <i>pat</i> + <i>pat</i> + <i>A</i> |
| 10 | <i>pat</i> <i>pat</i> <i>a</i> |
| 6 | <i>pat</i> + <i>pat</i> <i>a</i> |
| 6 | <i>pat</i> <i>pat</i> + <i>A</i> |
| | Growth on Gray's medium |
| | no lag |
| | no lag |
| | no lag |
| | 8 day lag |

Note: Different patterns of second division segregation have been grouped together for brevity.

with proline) and in complete medium* were carried out in race tubes in the same light and temperature conditions, but not all the *pat* segregants gave clear out cycle growth patterns.

Normally, growth began quickly on Gray's medium and extended 1-4 cm down the length of the race

Table 2. *pat* *a* \times *n* *nil* *A*

| No of asci | Genotypes of ordered spore pairs | Simplest cross-over events required assuming following order of loci I II III |
|------------|--|--|
| | | <i>A</i> <i>a</i> <i>pat</i> centromere <i>n</i> <i>nil</i> |
| 4 | <i>a</i> <i>pat</i> <i>n</i> <i>nil</i> + <i>a</i> <i>pat</i> <i>n</i> <i>nil</i> + <i>A</i> <i>pat</i> + <i>n</i> <i>nil</i> <i>A</i> <i>pat</i> + <i>n</i> <i>nil</i> | no crossing over |
| 4 | <i>a</i> <i>pat</i> <i>n</i> <i>nil</i> + <i>a</i> <i>pat</i> <i>n</i> <i>nil</i> <i>A</i> <i>pat</i> + <i>n</i> <i>nil</i> <i>A</i> <i>pat</i> + <i>n</i> <i>nil</i> | single cross-over in III |
| 2 | <i>a</i> <i>pat</i> <i>n</i> <i>nil</i> + <i>A</i> <i>pat</i> + <i>n</i> <i>nil</i> <i>a</i> <i>pat</i> <i>n</i> <i>nil</i> <i>A</i> <i>pat</i> + <i>n</i> <i>nil</i> | single cross-over in II |
| 1 | <i>a</i> <i>pat</i> <i>n</i> <i>nil</i> + <i>A</i> <i>pat</i> + <i>n</i> <i>nil</i> <i>a</i> <i>pat</i> + <i>n</i> <i>nil</i> <i>A</i> <i>pat</i> + <i>n</i> <i>nil</i> | single cross-over in I |
| 1 | <i>a</i> <i>pat</i> <i>n</i> <i>nil</i> + <i>A</i> <i>pat</i> + <i>n</i> <i>nil</i> <i>a</i> <i>pat</i> + <i>n</i> <i>nil</i> <i>A</i> <i>pat</i> + <i>n</i> <i>nil</i> | 2-strand double in II III |
| 1 | <i>a</i> <i>pat</i> <i>n</i> <i>nil</i> + <i>A</i> <i>pat</i> + <i>n</i> <i>nil</i> <i>a</i> <i>pat</i> + <i>n</i> <i>nil</i> <i>A</i> <i>pat</i> + <i>n</i> <i>nil</i> | 3-strand double in II III |

Note: Different patterns of second division segregation have been grouped together for brevity.

tube after 24 hr. However, six of the cultures had a lag period of about three days before any growth appeared. These were the six proline requiring *pat* + segregants of the first cross (Table 1). There is thus a physiological interaction which might be described as partial suppression of *pat* by *pat* (though it could also be suppression by mating type gene *a*). Whether this interaction is related to the function of the biological clock is unknown. (The lag period occurred only on Gray's medium; none of the cultures lagged on minimal medium plus proline or on complete medium.)

The tests for proline requirement were made on plates containing the sugar sorbose; this causes growth to remain restricted to the spot of the inoculum, rather than spreading over the plate. The use of sorbose medium allows as many as twenty five growth tests to be performed on a single plate. It was observed that some of the test colonies did not remain confined on the sorbose plates, but were expanding radially 5-10 mm per day. The 'sorbose escape' condition turned out to be characteristic of the patch segregants. This was a consistent correlation: all 42 *pat* progeny from the two crosses escaped on sorbose while all 42 *pat* + progeny remained confined on sorbose. There was no evidence of any cyclic pattern in the sorbose escape colonies. Sorbose-escape was achieved even on plates held in constant light, a condition in which the cyclic growth pattern is not observed on Gray's medium.

The sorbose-escape classification demonstrates that the presence of the patch gene can be detected in a situation in which it is not visibly related to a biological clock. It is possible that the patch gene is not directly involved in the function of the biological clock but, rather, effects a growth habit which reveals an underlying clock. However, this could only be determined conclusively by a demonstration of clock activity in a *pat* + strain.

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PROTHORACIC GLAND STIMULATION BY JUVENILE HORMONE EXTRACTS OF INSECTS

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THE juvenile hormone was first recognized as the agent which prevents maturation of young insects¹. A second role for this hormone, discovered shortly thereafter, was in egg development where,

in many insects it is necessary for oötheca deposition². The present article describes what appears to be a third role for the juvenile hormone, namely stimulation of the prothoracic glands. This trophic action has hitherto been assigned either to a hormone secreted by the insect's brain³ or occasionally to low

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Evoked responses to flash were displayed on an oscilloscope and filmed while the cat was resting facing the stroboscope. The flash, delivered once in approximately 2 sec, was of 1-m sec duration with an intensity of approximately 1 lambert. A mouse was introduced between stroboscope and cat, separated from the latter by a transparent plastic sheet. During the first few presentations of the mouse, the cat usually was intensely excited, but later it sat still, intently watching the mouse with little or no pilo-erection, or unsheathing of the claws. At this time 20 evoked responses to flash were recorded. Ten of these experimental responses were selected at random from the 20, together with 10 control evoked responses from the resting animal, recorded immediately before introduction of the mouse. The mean of each of these sets of results was calculated. These means for each animal were tabulated and the significance of any differences between experimental and control conditions obtained by applying a paired *t* test. It was found that when the cat was watching the mouse the electrocorticograph was flattened. The surface positive component of the primary wave of the evoked potential was decreased by 27 per cent ($P < 0.001$), and its duration reduced by 20 per cent ($P < 0.01$). The amplitude of the surface negative component was decreased by 21 per cent ($P < 0.02$). The excursion of the second wave of the response was reduced by 19 per cent ($P < 0.02$) and waves of the later components by 51 per cent ($P < 0.001$).

In order to orientate the cat's behaviour to a non-visual modality, the animal was conditioned to receive a slight shock to the fore-limbs after several tones, each delivered in the interval between consecutive flashes. The number of tones delivered prior to the shock was varied between 2 and 10 in any trial. After the first few trials, shocks were only occasionally applied. During the early stages of conditioning, at the onset of the tones, the cat looked intently around the box. At this time the electrocorticograph was reduced in amplitude. The surface positive component of the primary wave was reduced by 21 per cent ($P < 0.02$) and its duration by 19 per cent ($P < 0.02$). The amplitude of the second wave of the response was attenuated by 34 per cent ($P < 0.01$) and the later oscillations by 40 per cent ($P < 0.02$).

At a later stage of conditioning, the cat did not look around the box during the tones, but remained still except for some slight shifting of the fore-limbs,

twitching of the facial muscles and flicking of the ears. Occasionally at this stage the cat got up during the tones and settled in another part of the cage. Measurement of records taken when the animal showed minimal movement and when its response to the acoustic stimulus was accompanied by little or no visual searching component showed that the amplitude of the electrocorticograph was diminished. The amplitude and duration of the evoked responses were not, however, significantly different from those recorded under control conditions.

From the above results it appears that photically evoked responses in the visual cortex are not attenuated when a cat's behaviour is orientated to an acoustic stimulus, so long as there is no visual searching component in the animal's behavioural response. On the other hand, when the animal's behaviour is directed to a stimulus in the visual field, or shows some visual searching component in its response to a non-visual stimulus, evoked potentials are reduced in amplitude. It might be argued that when the cat was looking at a mouse the information contained in the flash was irrelevant and so attenuated. However, when the animal's behaviour was directed to the acoustic stimulus, in the absence of visual searching activity, the information from the flash was likewise irrelevant. The evoked potentials in these two situations should therefore have been treated similarly. They were not.

Reduction in amplitude of an evoked response to a given photic input may be brought about in one or more ways (for example, inhibition, reduction of facilitation, occlusion). Whatever the mechanism, one of the effects of such activity may be, in some circumstances, to increase sensory contrast and so improve the sharpness of input boundaries. Absence of such input attenuating activity in the visual system, as when behaviour is directed to an acoustic stimulus, could give a greater absolute sensitivity in the visual pathway. The animal would thus monitor its environment more sensitively so providing central mechanisms with a maximum of information on which to act.

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INFLUENCE OF UNBALANCED GROWTH ON SUBSEQUENT X-RAY-INDUCED INHIBITION OF DEOXYRIBONUCLEIC ACID SYNTHESIS IN *ESCHERICHIA COLI* 15_T

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IN an earlier report¹ it was demonstrated that the number of survivors among X-irradiated *Escherichia coli* strains B/r and 15_T (thymine-less) was increased when log-phase cells were incubated in the presence of chloramphenicol prior to X-ray exposure. In the case of *E. coli* 15_T deoxyribonucleic acid synthesis was necessary for the development of radioresistant cells, since when deoxyribonucleic

acid synthesis was prevented by the removal of thymine from the pre-irradiation incubation medium, radioresistance was not enhanced by chloramphenicol. One interpretation of these results was that 'surplus' deoxyribonucleic acid formed in the presence of chloramphenicol (higher ratio of deoxyribonucleic acid/protein than in non-treated cells) was biologically active and increased the number of sensitive sites

in the bacterium¹. An additional possibility considered was that pretreated cells, unbalanced in macromolecular constituents, were in special physiological states such that the probability of overcoming X ray induced lesions was increased. Using cells in the several unbalanced states with regard to protein, deoxyribonucleic acid, and ribonucleic acid levels we have studied deoxyribonucleic acid synthesis after X ray exposure of such cells. In the present work results are presented which show (1) An inhibition by chloramphenicol of phasing or 'synchronization' of the deoxyribonucleic acid synthesizing system and (2) that the radiosensitivity of the synthesizing mechanism is altered by previous chloramphenicol exposure.

The conditions for obtaining log phase as well as establishing 'unbalanced phase' growth were those previously described¹. Following the various treatments to be described for obtaining unbalanced growth the cells were cooled in an ice bath, harvested, washed and resuspended in cold minimal salts-glucose medium to give a final concentration of about 20 times the original number ($1-2 \times 10^{10}$ cells/ml) in order to obtain satisfactory levels of material for chemical analysis. The concentration of cells during exposure was higher than the level used in the earlier studies by a factor of approximately 100, as a result the number of colony formers found after a dose of 10,000 r was higher in the experiments reported here²². Following X ray exposure at ice bath temperature the cells were added to twice the original culture volume of pre-warmed minimal medium supplemented with 20 μ g./ml. thymine and re incubated with aeration at 37° C. Aliquots of this culture were removed at intervals for analysis as detailed earlier¹.

Prior to treatment with 10,000 r of X rays, log phase *E. coli* 15r- cells were incubated in minimal medium at 37° C for 1 hr under the following conditions: (A) incubation in the presence of thymine (normal log phase cells), (B) incubation in the presence of 10 μ g./ml. chloramphenicol and (1) plus thymine (increased ribonucleic acid and deoxyribonucleic acid/protein content), or (2) without thymine (increased ribonucleic acid/deoxyribonucleic acid and protein content), (C) incubation in the absence of thymine (increased ribonucleic acid and protein/deoxyribonucleic acid content).

In normal log phase *E. coli* 15r- (condition A) exposed to 10,000 r of X rays deoxyribonucleic acid synthesis proceeded rapidly for 30-60 min (Fig 1). This was followed by a period in which no net synthesis was detectable. In other experiments in which survival was higher than that found in the experiment from which the data of Fig 1 were taken, renewed synthesis was sometimes seen by 90 min. The number of colony forming cells in the irradiated suspensions (10-25 per cent of the controls) remained constant or showed a slight decline during the first 30 min. A rapid increase then occurred that probably accounted for the renewed synthesis observed in some experiments.

When chloramphenicol was added to log phase cells (condition B1) ribonucleic acid and deoxyribonucleic acids continued to accumulate while protein synthesis was largely inhibited¹. Such cells washed free of the antibiotic and re-incubated in thymine supplemented minimal medium showed a delay of approximately 30 min before net deoxyribonucleic acid synthesis resumed (Fig 1). When the washed cells treated with chloramphenicol were exposed to 10,000 r of

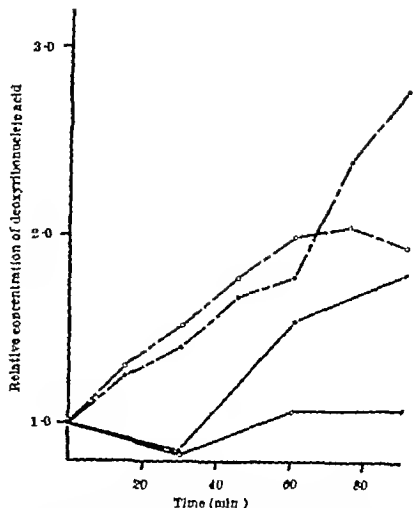


Fig 1. The influence of prior chloramphenicol treatment on subsequent deoxyribonucleic acid synthesis. Prior to treatment with 10,000 r of X rays log phase *E. coli* 15r- cells were incubated for 1 hr under the following conditions: (A) normal log phase cells (condition A of text), (B) condition B and then exposure to 10,000 r, (C) condition B1 then exposure to 10,000 r, (D) condition B2 then exposure to 10,000 r, (E) condition C then exposure to 10,000 r.

X rays and then resuspended in thymine-supplemented medium no net increase in deoxyribonucleic acid content was observed during the 2 hr the cultures were studied (only the first 90 min are shown in Fig 1). A similar result was found for cells washed free of thymine prior to incubation in thymine free minimal medium to which chloramphenicol has been added (condition B2). During such incubation only ribonucleic acid was observed to accumulate in large amounts during the 1 hr exposure to the antibiotic¹. As seen in Fig 2 deoxyribonucleic acid synthesis in such cells was completely suppressed after X ray exposure.

Log phase cells washed free of thymine and then re incubated for 1 hr at 37° C in thymine free minimal medium (condition C), showed a marked increase in ribonucleic acid and protein nitrogen while deoxyribonucleic acid synthesis was essentially nil¹. This was the 'unbalanced growth' reported for this strain of *E. coli* by Barner and Cohen⁴. Following this treatment the cells after harvesting and washing at ice bath temperature, appeared to be 'synchronized' with respect to deoxyribonucleic acid synthesis (Fig 2). The deoxyribonucleic acid nearly doubled in 30 min. This was followed by a period of reduced deoxyribonucleic acid synthesis before a new rate of deoxyribonucleic acid accumulation was seen. X irradiation did not greatly alter the synthesis during the initial doubling period (Fig 2). However, after this initial burst no further increment was found during 120 min of observation. The loss of acid insoluble deoxyribonucleic acid observed in the irradiated cell culture after 60 min was due to lysis of a portion of the cells as reflected in a decreased turbidity of the cultures as well as a reduction in the harvested cell yield (not shown). The surviving cells did not grow at

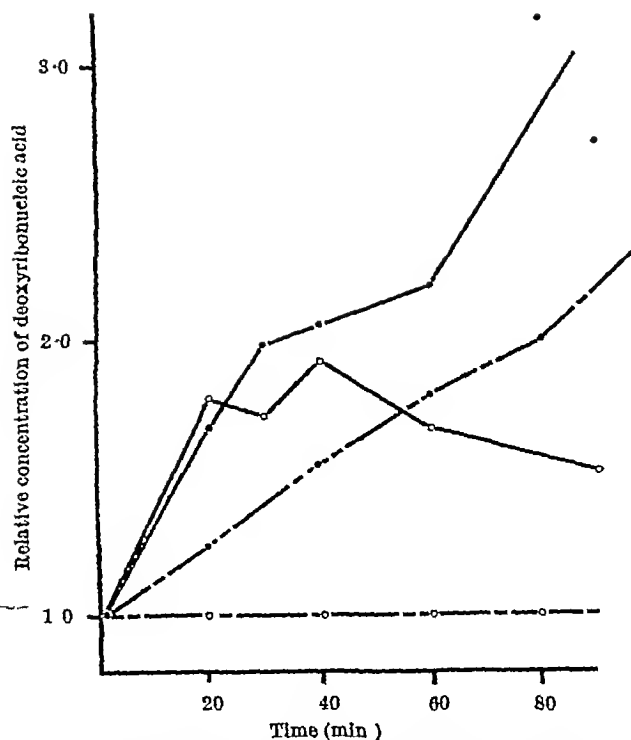


Fig. 2 The effect of thymine starvation during chloramphenicol exposure on subsequent deoxyribonucleic acid synthesis. Prior to treatment with 10,000 r of X-rays, log-phase *E. coli* 15T- cells were incubated for 1 hr under the following conditions: ●—●, incubation in the absence of thymine (condition C of text), ○—○, condition C, and then exposure to 10,000 r, ●---●, exposed to chloramphenicol in the absence of thymine (condition B2), ○---○, condition B2, and then exposure to 10,000 r

rapid rate to be reflected in the analysis during these 2 hr. It required more than 2 hr for dividing survivors to reach the initial level of unirradiated cells of the controls.

Thus, during the incubation in the absence of thymine (condition C), a radioresistant synchronization of deoxyribonucleic acid appeared to have occurred. Similar treatment did not synchronize ribonucleic acid or protein synthesis⁶. The addition of chloramphenicol to such cells prevented the development of the radioresistant system synthesizing deoxyribonucleic acid. It is also apparent that the addition of chloramphenicol to log-phase *E. coli* 15T- incubated in the presence of thymine resulted in a physiological state such that deoxyribonucleic acid synthesis did not occur immediately after removal of the antibiotic. Cells in this physiological state could not synthesize deoxyribonucleic acid until a radiosensitive process had been initiated. Although the mechanism whereby chloramphenicol brings about this effect is unknown, it is tempting to speculate that the antibiotic-induced inhibition of protein synthesis was involved. The protein (and/or ribonucleic acid) synthesized in a given time period (in the presence or absence of net deoxyribonucleic synthesis) may be a necessary prerequisite for subsequent deoxyribonucleic acid synthesis. One may envisage this protein as being involved in the formation of a template⁷⁻¹⁰ or as specific enzymes perhaps similar to the polymerases described by Kornberg and collaborators¹¹ which were found to be capable of *in vitro* deoxyribonucleic acid synthesis. Additional experiments planned may provide further insight into the true nature of the radiosensitive process inhibited by chloramphenicol.

ults with irradiated *E. coli* 15T- correlate the findings of others in plant¹² and

animal^{13,14} studies that there is a radiosensitive process involved in deoxyribonucleic acid synthesis, which is not the deoxyribonucleic acid replication system itself. The radiosensitive process occurring prior to actual deoxyribonucleic acid synthesis may involve protein synthesis as suggested from the results presented here. Log- or stationary-phase cell suspensions when exposed to X-rays contain organisms in various phases of their division cycle. One may speculate that there occurs, in normal growth of individual cells, a phase such that the products of the radiosensitive process are exhausted and must be synthesized anew before deoxyribonucleic acid replication can proceed. If most cells of an exposed population were in the active deoxyribonucleic acid synthesizing (radioresistant) phase they would continue to make deoxyribonucleic acid until a predetermined level would have been reached. Therefore at doses of X-rays in which most of the population no longer were colony-forming cells a good amount of deoxyribonucleic acid as well as ribonucleic acid and protein synthesis would occur⁵. The extent of deoxyribonucleic synthesis would be determined by the length of the deoxyribonucleic synthetic period relative to that of the sensitive pre-synthetic phase. In a log-phase population most cells would be in the deoxyribonucleic acid synthesizing phase if this period occupied most of the division cycle of the cell. Based on this model our results would suggest that most log-phase cells are not in the radiosensitive period since irradiated populations increased significantly their deoxyribonucleic acid levels upon reincubation. The radiosensitive pre-synthetic process, having been inhibited by radiation exposure, would no longer function and thus deoxyribonucleic acid synthesis would come to a close if it is assumed that the radiosensitive process is permanently inhibited by irradiation. When sufficient numbers of survivors were present these would grow at a rate reflecting their physiological state prior to exposure and eventually produce measurable amounts of deoxyribonucleic acid. If the number of survivors were high enough and exhibited little lag upon resuspension in a complete growth medium they would produce sufficient amounts of deoxyribonucleic acid to be measurable soon after exhaustion of deoxyribonucleic acid synthesis in dying cells. Thus the termination of deoxyribonucleic acid synthesis in dying or dead cells would be masked by the dividing viable cells. At higher doses of X-irradiation deoxyribonucleic acid synthesis may be completely suppressed by the destruction of the radioresistant deoxyribonucleic acid synthesizing mechanism itself⁵.

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LETTERS TO THE EDITORS

GEOPHYSICS

Great Earthquakes and the Astronomical Positions of Uranus

THANKS to the excellent collection of uniform data of earthquakes given by Gutenberg and Richter¹, it is now easily possible to study statistically the influence of different factors on earthquakes. In the course of a study of tidal effects on earthquakes², the astronomical positions of the planets have also been taken into account and a remarkable correlation between the positions of Uranus and the moment of great earthquakes has been established for a certain period. Gutenberg and Richter's data of all earthquakes equal or greater than magnitude 7½ have been used. The investigations will be published in detail later, but here attention is directed to the results concerning the position of Uranus.

A total of 134 earthquakes has been investigated in this fairly significant amount of cases has been found, where Uranus was very near its upper or lower transit of the meridian of the epicentre in the time of great earthquakes. Closer investigation showed that this occurred especially during the years 1004 where Gutenberg-Richter's data start, and also 1005 and 1006. The results for this period are given

in Table 1, which contains the data for the earthquakes and also the Right Ascension of the meridian of the epicentre at the time of the earthquake and the position and the meridional distance in Right Ascension of Uranus at that time. The latter data have been divided into two groups. Group I contains all the cases when Uranus is within a distance of $\pm 1h$ from upper or lower transit through the meridian. Group II comprises all cases with greater meridional distances, that is, within $\pm 1h$ to $\pm 6h$. The probability of Uranus being found in group I is one sixth of the total cases and that for group II is five-sixths of the total, if the distribution of the times of the earthquakes is entirely by chance. As Uranus completes each day very approximately all the possible meridional distances, there occurs within the period of 1 000 days, represented in Table 1 a total of 2,180 transits (upper and lower). Therefore if the times of occurrence of earthquakes are distributed by chance, a uniform distribution of the positions of Uranus can be expected. This is corroborated by the fact that the positions of the Sun or the Moon show no significant deviation from pure chance. For example, in Table 1 the Sun is found to be five times near transit which is very near the expected value for chance distribution of group I. But the result for Uranus is quite different and unexpected.

Table 1 GREAT EARTHQUAKES $M > 7\frac{1}{2}$

| No | Date | G.M.T. | Lat | Long | Local time | R.A. Mer | R.A. Ur | Uranus merid dist (I) | Uranus merid dist (II) | Remarks |
|----|----------------|----------|----------|----------|------------|----------|---------|-----------------------|------------------------|------------------------------------|
| | | h m s | | | h. m. | h. m. | h. m. | h. m. h | h. m. h | |
| 1 | 1903 Dec 28 | 2 58 00 | 7° N | 127° E. | 11 24 | 17 46 | 17 44 | -0 02 | | Epicentre ± 5 Sun near transit |
| 2 | 1904 Jan 20 | 14 52 06 | 7° N | 70° W | 9 35 | 17 30 | 17 50 | +0 20 | | |
| 3 | June 25 | 14 45 36 | 52° N | 180° E. | 1 22 | 10 35 | 17 50 | | -1 40 | |
| 4 | June 25 | 21 00 30 | 52° N | 180° E. | 7 59 | 1 51 | 17 50 | | +4 00+12 | |
| 5 | June 27 | 00 00 00 | 52° N | 180° E. | 10 45 | 5 04 | 17 40 | +0 45+12 | | |
| 6 | Aug 24 | 20 59 54 | 30° N | 180° E. | 6 40 | 3 51 | 17 43 | | +1 52+12 | |
| 7 | Aug 27 | 21 58 06 | 64° N | 161° W | 11 52 | 10 16 | 17 42 | | -4 32+12 | Sun in transit |
| 8 | Dec 20 | 05 44 18 | 8° 5' N | 83° W | 0 12 | 6 06 | 18 00 | -0 06+12 | | Sun in transit |
| 9 | 1905 Jan 22 | 02 43 51 | 1° N | 193° E. | 10 58 | 18 50 | 18 09 | -0 51 | | |
| 10 | Feb 14 | 08 46 36 | 53° N | 178° W | 20 55 | 6 20 | 18 13 | -0 16+12 | | |
| 11 | April 4 | 00 50 00 | 33° N | 70° E | 5 54 | 18 41 | 18 18 | -0 23 | | Kangra |
| 12 | June 2 | 05 30 42 | 31° N | 132° E. | 14 23 | 7 09 | 18 13 | -0 55+12 | | |
| 13 | July 6 | 16 21 00 | 39° 5' N | 145° E. | 1 51 | 20 47 | 18 09 | | -2 39 | |
| 14 | July 9 | 00 40 24 | 40° N | 99° E. | 16 16 | 11 23 | 18 07 | | -5 16+12 | |
| 15 | July 23 | 02 44 12 | 40° N | 09° E. | 9 18 | 5 10 | 18 05 | +0 46+12 | | |
| 16 | 1906 Jan 21 | 13 40 35 | 34° N | 133° E. | 23 02 | 7 02 | 18 25 | -0 38+12 | | |
| 17 | Jan 31 | 15 36 00 | 1° N | 81° 5' W | 10 18 | 18 58 | 18 25 | -0 22 | | Greatest earthquake |
| 18 | April 18 | 13 12 00 | 35° N | 123° W | 6 00 | 18 43 | 18 21 | -0 09 | | San Francisco |
| 19 | Aug 17 | 00 10 42 | 51° N | 170° E. | 12 07 | 9 45 | 18 21 | | -3 24+12 | Sun in transit |
| 20 | Aug 17 | 00 40 00 | 33° 8' | 72° W | 10 52 | 17 20 | 18 21 | +0 51 | | |
| 21 | Sept 14 | 18 04 18 | 7° 8' | 140° E. | 2 00 | 1 31 | 18 20 | | +4 48+12 | |
| 22 | Nov 19 | 07 18 18 | 22° S | 109° E. | 14 31 | 18 21 | 18 22 | +0 03 | | |
| 23 | Dec 22 | 18 21 00 | 43° 5' N | 85° E. | 0 01 | 6 03 | 18 35 | +0 33+12 | | Sun in transit |

+ 2h. Uranus culminates 2h later + 1h. lower transit, R.A. Mer. Right Ascension of meridian at the time of earthquake
Local time local sidereal time at the time of earthquake

Table 2

| No | Date | G.M.T. | Lat. N | Long. E. | Local time | R.A. Mer | R.A. Ur | Uranus merid dist | Place | Magnitude |
|----|----------------|----------|---------|----------|------------|----------|---------|-------------------|--------|-----------|
| | | h m s | | | h m | h. m. | h. m. | h. m. h | | |
| 1 | 1933 Sept 1 | 02 53 36 | 35° 2' | 130° 5' | 12 17 | 10 54 | 23 09 | +0 16+12 | Tokio | 8.2 |
| 2 | 1933 Mar 2 | 17 30 51 | 39° 25' | 144° 5' | 03 09 | 13 40 | 01 10 | -0 30+12 | Honshu | 8.3 |
| 3 | 1950 Aug 15 | 14 00 30 | 23° 5' | 06° 5' | 20 30 | 18 09 | 06 35 | +0 20+12 | Assam | 8.6 |

Of 23 cases, listed in Table 1, not less than 15 belong to group I and only 8 are in group II. The expected number for group I would be 3.8. Application of the chi-square test gives $\chi^2 = 41$, with Yates's correction $\chi^2 = 37$, that is, for one degree of freedom, a probability much less than 0.0001 for its being a chance distribution. The deviation is therefore highly significant. The fact should be stressed that Table 1 is complete, that is, it includes all the earthquakes of magnitude equal to or greater than $7\frac{1}{2}$ (including intermediate and deep shocks) which occurred during this period.

Two points must be cleared up. First, for how long does the period extend with this marked correlation, and secondly, how far is it characteristic of Uranus? Or does the period include some other cosmic direction which only accidentally coincides with the position of Uranus during this period of observation? Regarding the first point, it can be stated that after 1906 the correlation becomes less significant, but it remains greater than average. As an example, Table 2 shows the meridional distance of Uranus for three remarkable earthquakes of later years, when the position of Uranus had already greatly changed. No. 1 is the Tokyo earthquake in the course of which 100,000 people were killed and 500,000 houses were destroyed. No. 2 is the second largest earthquake of the first half of this century (the greatest is No. 17 in Table 1) and No. 3 is the famous Assam earthquake (*Nature*, 167, 128, 1951). In each of these cases Uranus is near the meridian—not farther away than 30 min from its lower transit. There is a certain difficulty in extending the investigation back to the years before 1904, as in many cases the epicentres are either not known or only very inaccurately. A collection of data has been given by Gutenberg³. Using his data and limiting the investigations to all cases where the epicentres are known with an accuracy of at least $\pm 5^\circ$ of their geographical position, their number is 23 for the years 1900–3. In eight cases the position of Uranus is in group I, the expected number is 3.8. Therefore, the correlation extends back to 1900, but with diminished significance.

It should be mentioned that the years 1904–6 corresponded to a conspicuous maximum of energy release by the Earth through earthquakes. According to Gutenberg³, the annual release during each of these years is 10.6, 22.2 and 34.1, against 6 in 1903 and 4.9 in 1907 (in units of 10^{24} ergs).

So far as the role of Uranus is concerned, it may be noted that the planet was nearly symmetrically opposed, during these years, by Neptune and Pluto and went into direct opposition to Neptune in 1906. The cases of 1906 are therefore also cases where Neptune was simultaneously near its transit at the times of the earthquakes. An opposition of Sun, Venus and Mars to Uranus also occurred at the time of the Tokyo earthquake (Table 2).

The correlation cannot be explained by a tidal effect, since the statistical investigation for all the great earthquakes ($M = 7\frac{1}{2}$) during 1904–50 in regard to the absolute and relative positions of the Sun and the Moon give no indication of a significant deviation from chance distribution. The tidal forces of the planets are extremely small compared with those of the Sun and the Moon. That the accumulated stresses within the Earth's crust are released at times which, at least for a period of several years, are strongly correlated with certain positions of Uranus may,

therefore, not be a relationship of cause and effect in the usual mechanical sense.

R. TOMASCHEK

Breitbrunn/Chiemsee,

Bavaria

March 27

¹ Gutenberg, B., and Richter, C. F., "Seismicity of the Earth", 2nd edit (Princeton Univ. Press, 1954)

² Tomaschek, R., "Handbuch der Physik", 48, 843 (Springer, 1957)

³ Gutenberg, B., *Trans. Amer. Geophys. Union*, 37, No. 5, 608 (1956)

Air Density in the Upper Atmosphere from Satellite Orbit Observations

From the rate of change of period of a satellite, it is possible to derive the density of the atmosphere at the altitude of the perigee of the orbit. Now that some ten successful satellite launchings have taken place, giving orbits with various perigee heights, the variation of air density with height can be derived over a considerable range of altitude. Many perigee heights have been less than 230 km, the exceptions being *Explorer IV* (1958 ζ) at 260 km, *Explorer I* (1958 α) at 365 km, *Vanguard I* (1958 β 2) at 656 km, and the recently launched *Vanguard II* (1959 α) at 558 km. The air density at greater heights is therefore less well established. From an analysis of data from six different satellites, the smoothed set of values in Table 1 has been derived. The accuracy, estimated by fitting a quadratic variation with height to the logarithm of the density, is of the order of 20 per cent at the lower heights and 50 per cent at the greater heights.

Table 1. VALUES OF AIR DENSITY DERIVED FROM OBSERVATIONS ON SATELLITES 1957 α , β AND 1958 α , β , γ AND ϵ

| Height (km) | Air density (gm/c.c.) | Height (km) | Air density (gm/c.c.) |
|-------------|-----------------------|-------------|-----------------------|
| 150 | 1.2×10^{-12} | 450 | 3.8×10^{-16} |
| 200 | 3.8×10^{-13} | 500 | 1.9×10^{-16} |
| 250 | 1.4×10^{-13} | 550 | 9.0×10^{-17} |
| 300 | 5.0×10^{-14} | 600 | 5.3×10^{-17} |
| 350 | 2.0×10^{-14} | 650 | 3.2×10^{-17} |
| 400 | 8.4×10^{-15} | 700 | 2.0×10^{-17} |

Above 300 km, the values of air density depend chiefly on the *Explorer I* and *Vanguard I* observations. After this analysis had been carried out, the rate of decrease of period for these two satellites increased comparatively rapidly to a new nearly constant value. The increase amounted to a factor of 1.51 for *Explorer I* and to a factor of 2.52 for *Vanguard I*, showing the effect to increase with height. For *Vanguard I*, the slope of the period-time curve has recently returned to its original value, and the local time at perigee, while the slope had the greater value, ranged from about 12.00 hr to 18.30 hr. For *Explorer I*, the slope has also returned to its original value and is at present about to change again, the greater value being maintained for approximately the same range of local time as *Vanguard I*. If this change is attributed to a variation in air density, then the values in Table 1 need to be increased by the above factors when local time lies in the range 12.00–18.30 hr.

The scale height of the atmosphere H is the height interval over which the density changes by an exponential factor. Values for H in the region of 200 km have been deduced in the following three ways.

(1) From the above density-height profile H is obtained¹ as $46 (\pm 5)$ at 200 km. H increases with

bought and values of 52, 61, 72 and 89 km are obtained for 300, 400, 500 and 600 km altitude, but the observations are too scanty to enable the accuracy of these values to be estimated. The gradient of the scale height at 200 km is obtained as 0.06 km/km.

(2) From the decrease in perigee distance. From *Explorer III* H is obtained³ as $39 (\pm 9)$ km at 180 km, and from *Atlas* (1958 ζ) as 36 km to within a few kilometres for the same altitude.

(3) From the change in perigee height due to the Earth's equatorial bulge⁴. This method is suitable for satellites at approximately the molination of the Russian artificial satellites, when the perigee moves slowly around the orbit and a significant part of the change in perigee height arises from the Earth's equatorial bulge. From *Sputnik II*, H is obtained⁵ as $36 (\pm 15)$ km. For *Sputnik III* rocket (1958 δ_1), methods 2 and 3 lead to inconsistent values.

A few rocket measurements of air density at the 200 km. level exist for comparison with the satellite values. A value of 2.7×10^{-12} gm./o. at 200 km has been reported⁶ from a U.S.S.R. rocket firing at 50° N. The Viking 7 flight in August 1951 at White Sands, New Mexico, gave⁷ 1.4×10^{-12} gm./o. (to within a factor of 2) for the density and 43 km. for the scale height at 200 km. The latitude of White Sands is 30° N., and most of the observations upon which Table 1 is based refer to perigee latitudes between 30° N. and 33° S. The agreement between the scale heights is very close and that between the densities is just acceptable. On the other hand, an *Aerobee H* fired in July 1957 at Fort Churchill, latitude 50° N., gave⁸ 7.0×10^{-12} gm./o. (± 30 per cent) for density and 94 km. for scale height at 200 km. altitude. A considerable latitude effect is therefore indicated at higher latitudes and there is clearly a need for satellites with orbital inclinations near 90°, so that densities may be determined at the highest latitudes. Two further Fort Churchill firings have given⁹ a winter day value of 3.0×10^{-12} gm./o. and a winter night value of $1.3 \pm 0.6 \times 10^{-12}$ gm./o. at 202 km.

At the 200 km. altitude, the scale height seems to be in the region of 40 km. for equatorial and sub-tropical latitudes. The corresponding temperature for an assumed molecular weight of air of 25 would be $1,100^\circ$ K.

The results given here agree closely with those of D. G. King Holm¹⁰.

Acknowledgment is made to the Smithsonian Institution, the Naval Research Laboratory Washington, and the Royal Aircraft Establishment Farnborough for their issues of orbital data on which these calculations have been based.

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PHYSICAL SCIENCES

A Special Case of the Superposition of Crystal Plates between Crossed Polars and its Bearing on the Microscopy of Cellulosic Fibres

When monochromatic light is passed at perpendicular incidence through two superposed and differently orientated transparent crystal plates between crossed polars the intensity of the light transmitted by the analyser relative to that of the light entering the plates is given by the following expression, as was shown by Fresnel

$$I = -\sin^2(\psi_1 - \psi_2)\sin^2\psi_1\cos^2\psi_2\sin^2(\delta_1/2) + \sin^2(\psi_1 - \psi_2)\cos^2\psi_1\sin^2\psi_2\sin^2(\delta_2/2) + \cos^2(\psi_1 - \psi_2)\sin^2\psi_1\sin^2\psi_2\sin^2(\delta_1/2 + \delta_2/2) - \sin^2(\psi_1 - \psi_2)\sin^2\psi_1\sin^2\psi_2\sin^2(\delta_1/2 - \delta_2/2) \quad (1)$$

where I is the relative intensity as just defined, ψ_1 , ψ_2 are respectively, the angles made by the corresponding vibration directions of the plates (that is, either the 'slow' or the 'fast' directions) with the vibration direction of the polarizer and δ_1 , δ_2 are the phase differences produced by the plates. (The expression ignores any reduction in the intensity due to absorption by the analyser, such as occurs in polaroid, but for a given analyser this reduction is by a constant factor and does not affect the arguments which follow.) If the plates are of equal thickness and birefringence, $\delta_1 = \delta_2 = \delta$ and the fourth term in the expression vanishes. If also we put 20 for the angle between the corresponding vibration directions say the 'slow' directions of the plates and α for the angle between the bisectrix of 20 and the vibration direction of the polariser (Fig. 1) the expression can be reduced to the form

$$I = 4\cos^2(20)\sin^2(\delta/2)\cos^2(\delta/2)\sin^2(2\alpha) - 4\sin^2(20)\cos^2(20)\sin^2(\delta/2)\cos^2(\delta/2)\cos^2(2\alpha) + 4\sin^2(20)\cos^2(20)\sin^2(\delta/2) \quad (2)$$

(This involves making use of the following equalities

$$(\psi_1 - \psi_2) = 20, \quad \psi_1 = (\alpha - 0) \quad \psi_2 = (\alpha + 0) \quad \sin^2(\alpha - 0)\cos^2(\alpha + 0) - \cos^2(\alpha - 0)\sin^2(\alpha + 0) = -\sin^2(40), \quad \sin^2\delta = \sin^2(2\delta/2) = 4\sin^2(\delta/2)\cos^2(\delta/2))$$

By differentiating I with respect to 2α , and equating to zero it can be shown that in the general case I has a minimum value when $\alpha = 0^\circ, 90^\circ, \dots$ etc., and a maximum value when $\alpha = 45^\circ, 135^\circ, \dots$ etc., that is that the pair of plates 'extinguish' when the bisectrix OB (Fig. 1) is parallel or perpendicular to the polarizer vibration direction OP , and shows maximum brightness when in the 45° positions.

Three special cases arise. Two of these are familiar in one $20 = 90^\circ$, so that the two plates exactly compensate one another and in the other $\delta = 0^\circ$, or $n \times 360^\circ$ where n is a whole number. In both these cases $I = 0$ for all values of α . The third case is that in which $\delta = 180^\circ$ or $(n \times 360^\circ) + 180^\circ$ and the purpose of this note is to draw attention to it since its consequences do not appear to be generally realized. In this case the first two terms of equation (2) vanish since they both contain $\cos^2(\delta/2)$ which is now zero. The intensity is given by the third term alone which does not contain α , and which simplifies to

$$I = 4\sin^2(20)\cos^2(20) = \sin^2(40) \quad (3)$$

since $\sin^2(\delta/2) = 1$. The intensity of the component which passes the analyser therefore remains constant as α varies, that is as the plates are rotated in unison.

in their own plane between the polars, as for example on the stage of a polarizing microscope, there are no 'extinction' (minimum intensity) positions. The reason for this is demonstrated geometrically in Fig 2. OP_1 and OP_2 are the 'slow' vibration directions of the plates, the latter being that for the upper plate, that is the one nearer to the analyser. OB is the bisectrix of the angle between these directions. OP is the vibration direction and amplitude of the light from the polarizer. Since $\delta = 180^\circ$, or $(n \times 360^\circ) + 180^\circ$, the light emerging from each plate must be linearly polarized, and have the same amplitude as that coming from the polarizer. By applying the ordinary construction we find that the vibration vectors of the light emerging from the lower and upper plates are OL and OH respectively, and $OH = OL = OP$. It can readily be proved that the direction of OH is independent of the angle $BOP(\alpha)$, and dependent only on the angle Pl, OP_1 , (2θ). The amplitude of the component which passes the analyser, OA' , therefore remains constant as the plates are rotated in unison.

If the plates be interchanged without changing the angle 2θ , so that OP_1 now refers to the upper plate, the vibration direction and amplitude of the light emerging from this plate is found to be OH' , which makes the same angle φ with the analyser vibration direction as OH , and thus gives the same amplitude OA' for the component which passes the analyser. (In conformity with this result, the expressions given above take no account of which plate is on top.)

By rotating the analyser so that its vibration direction becomes perpendicular to that of the light emerging from the upper plate extinction results, and this extinction is not relieved when the plates are rotated in unison. Thus if OH is the vibration direction of the light coming from the top plate, extinction is obtained by rotating the analyser through the angle $(90 - \varphi)$ to OE . This angle is related to 2θ as follows

$$\sin(90 - \varphi) = \cos \varphi = OA'/OH = \sin(4\theta) \quad (4)$$

(The last step in this relationship follows from equation (3), which gives the relative intensity, that is $(OA'/OP)^2$, as $\sin^2(4\theta)$. Thus $OA'/OP = OA'/OH = \sin(4\theta)$.) Equation (4) has two solutions, since 4θ can be either $(90 - \varphi)$, or $(90 + \varphi)$, the sines of which are equal.

Extinction can also be obtained by rotating the polarizer through the angle $(90 - \varphi)$, but in the opposite direction, thus bringing OH perpendicular to the analyser vibration direction.

The above case can only apply exactly for one wave-length with any given pair of plates for which it applies at all, but if this wave-length (which we will now refer to as μ_{180}) is near to the middle of the spectrum, a good approximation to the characteristic effects which have been described is obtained even when white light is used. This can be readily demonstrated by superposing cleavage strips of mica, for each of which μ_{180} is in the yellow or yellow-green, on the stage of a polarizing microscope which is illuminated with white light. On rotating the stage, no positions of minimum intensity can be distinguished (at least with the unaided eye). By turning either the analyser or the polarizer through a certain angle, extinction or near-extinction will be secured, and this will only be slightly relieved on rotating the stage. The reason for this behaviour is that the

vibration of the light emerging from the upper plate follows a very narrow ellipse for any wave-length within a considerable range on either side of λ_{180} , and the major axis of this ellipse corresponds to much the same vibration direction and amplitude as those of the linearly polarized light of wave-length λ_{180} .

The foregoing has a bearing on the polarization microscopy of cellulosic fibres, the spiral wall structure of which causes them to behave optically in a similar way to systems of superposed plates. When light is passed through a cylindrical fibre of this type, the angle between the 'slow' directions for the front and back walls (2θ in the above treatment) and the thickness presented to the light beam are of course not constant across the fibre, so that each vertical longitudinal section shows different optical effects. Flattened, ribbon-like fibres, such as those of dry cotton, however, approximate very closely to systems of two flat plates, except where they are twisted. Taking cotton, in which the spiral angle is considerable (ca 30° with respect to the fibre axis), as an example, the following observations may be made. In immature fibres the walls are very thin and δ is very much less than 180° . Between crossed polars such a fibre shows well-defined minima of intensity when its axis is parallel to the vibration directions of the polars, and it also behaves towards compensators as though its axis were a 'slow' direction of vibration. Among the thicker fibres of mature cotton, however, some will be found which show all the properties described above for the case $\delta = 180^\circ$, or approach this behaviour very nearly, at least along portions of their length. The behaviour of such fibres towards compensators is quite ambiguous, because over a large part of the spectrum the emergent light is approximately linearly polarized, with a vibration direction which is little affected by the position of rotation of the stage, as explained above.

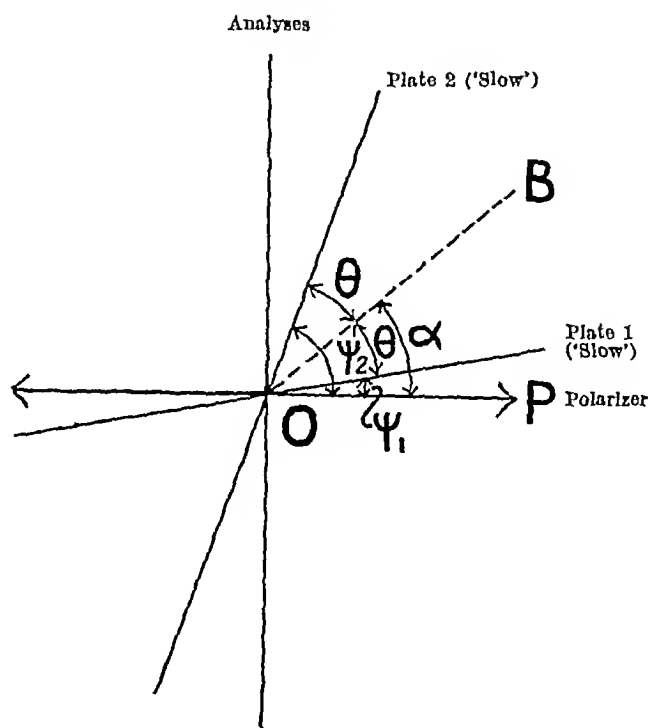


Fig 1

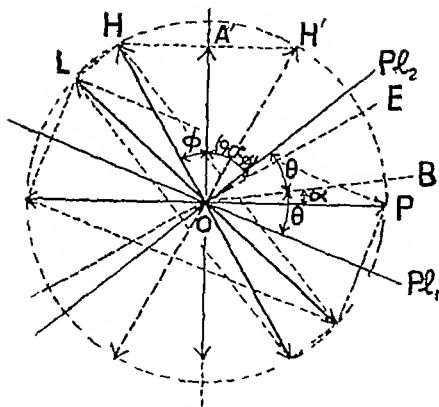


Fig. 2

By means of equation (4) it should be possible to obtain at least approximate values of the spiral angle from measurements of the angle $(90 - \phi)$ made at the wave length λ_{00} . This wave length can be estimated roughly with the aid of suitable filters, or more accurately by means of a monochromator, as being that at which the closest agreement with the theoretical behaviour for the case $\delta = 180^\circ$ is obtained.

This case and its consequences are not dealt with in any of the publications on fibre microscopy with which I am familiar.

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Birefringence of Montmorillonite Complexes

DURING a study of the optical properties of montmorillonite aggregates in salt solutions¹, some interest in preliminary observations were made on various aromatic complexes. These observations have now been followed up with the view of extending the use of optical data in characterizing clays.

The structures of various aromatic complexes of montmorillonite have been inferred from spacing measurements and one-dimensional Fourier syntheses². The monolayer complexes could be grouped into two classes, those where the plane of the ring was parallel to that of the silicate sheet (type A) and those where it was perpendicular (type B). Clearly, because the polarizability of the aromatic ring is usually much greater in the plane of the ring than perpendicular to it³, the preferred orientation of the interlayer molecules in aromatic complexes should profoundly affect the apparent birefringence of the mineral. Thus in type B complexes the effect of the interlayer molecules would be expected to reduce the strong negative birefringence of the silicate layers and even make some aggregates optically positive. In contrast, type A complexes would be

expected to be strongly negative. These expectations were strikingly confirmed when the birefringence of the nitrobenzene complex (type B) was found to be 0.003 (negative) as compared with 0.020 (negative) for the unexpanded mineral. An even larger effect was to be expected with quinoline which is more anisotropic than nitrobenzene⁴, and the orientation of the interlayer molecules is such as to increase greatly the polarizability of the complex perpendicular to the silicate sheets⁴. Measurement of its birefringence showed it to be 0.02 (positive). In contrast type A complexes were found to be strongly negative, for example, pyridinium montmorillonite (type A) was 0.024 (negative).

These large birefringence changes obtained with montmorillonite not only confirm the proposed orientation of the interlayer molecules but could be used to characterize clays in the same way as glycol and glycerol are used in X-ray diffraction analysis. For example, rapid assessment of clays for montmorillonite minerals is possible by measuring the changes in birefringence of aggregates on immersion in quinoline solutions. Where montmorillonite predominates, the optical sign is changed after treatment. Again, clays known to be homogeneous, but partially expanding and giving a complex X-ray diffraction pattern, have been rapidly and simply evaluated in terms of the percentage of expanding layers, from the change in birefringence in different solvents. When evaluation has been possible from X-ray results⁵ the agreement between the two methods has been excellent.

The preliminary part of this work was done while I held a Royal Society Exchange Fellowship 1957-59, with the Academy of Sciences U.S.S.R.

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Electron Paramagnetic Resonance at 42° K. of γ -Irradiated Polymethyl Methacrylate and Polymethacrylic Acid

THE electron paramagnetic resonance spectrum given by polymethyl methacrylate after high-energy irradiation at room temperature consists of five lines, about 23 gauss apart, with intensities in approximately the ratios 1:4:6:4:1, with a weaker intermediate pattern of four lines, both closely centred on the electron spin g factor of 2.001^{1,2}. Since this spectrum is also given by free radicals trapped during the addition polymerization of methyl methacrylate^{3,4}, it has been postulated that it arises from trapped propagating radicals of structure, $-\dot{C}H_2-C(CH_3)(CO_2CH_3)_2$, the detailed explanations involving the exact conformation of these radicals^{5,6}. Both of the explanations put forward by Symons⁷ require that the methyl group bonded to the 'radical' carbon atom rotates rapidly so that its three protons interact equally with the unpaired electron. If one of these

explanations is correct, the hyperfine structure of the spectrum should alter when the temperature is lowered sufficiently. The rotation of the methyl group might change to a torsional oscillation, thus destroying the equivalence of the three methyl protons. If however the rotation remains free, at a temperature where only the lowest rotational level is populated, symmetry conditions will govern the occupation of the nuclear spin levels.

Laboratory-prepared samples of polymethyl methacrylate and polymethacrylic acid were gamma-irradiated at room temperature with doses of about 10^7 r using a cobalt source. Their spectra were measured at 77° K and 4.2° K with a 3,000 Mc/s spectrometer using low amplitude 100 c/s magnetic field modulation with phase detection to give the first derivative of the absorption spectrum.⁷ The samples were contained in Dewar vessels inserted into the microwave cavity. At 77° K both polymers gave the well-known spectrum (Fig 1). The spectra at 4.2° K (Fig 2) also consist of nine lines with essentially the same spacings, centred on $g = 2.00$. However, a marked change in the relative intensities of the lines has occurred. Polymethacrylic acid showed no power saturation at 4.2° K, but when the temperature was further lowered, broadening of the individual hyperfine components occurred at high microwave power. At 4.2° K the polymethyl methacrylate spectrum was considerably broadened at high microwave power, and the spectrum shown was obtained at very low microwave power. Owing to overlap it is difficult to make accurate estimates of the relative intensities of the hyperfine components. The absorption-curves obtained by graphical integration were fitted by patterns with relative intensities of approximately 1 2 3 4 5 5 4 5 3 2 1, for polymethyl methacrylate and 1 1 7 2 3 2 5 2 5 2 3 1 7 1, for polymethacrylic acid. The individual line widths are similar for all three spectra, and the decreased resolution at 4.2° K arises from the change in relative intensities.

The total wave function of the radical must be antisymmetric to exchange of nuclei, and if it were behaving as a free rotator with only the lowest level occupied, only antisymmetric nuclear spin functions would be allowed.⁸ Those states in which all nuclei are aligned either with or against the electron spin would be forbidden and the outermost hyperfine components would not be present. It is clear that this effect is not operating here.

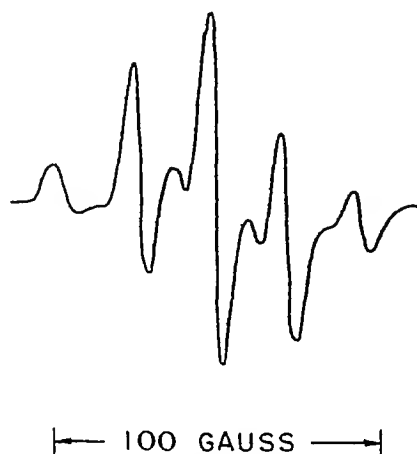


Fig 1 First derivative of electron paramagnetic resonance spectrum at 77° K of γ -irradiated polymethyl methacrylate

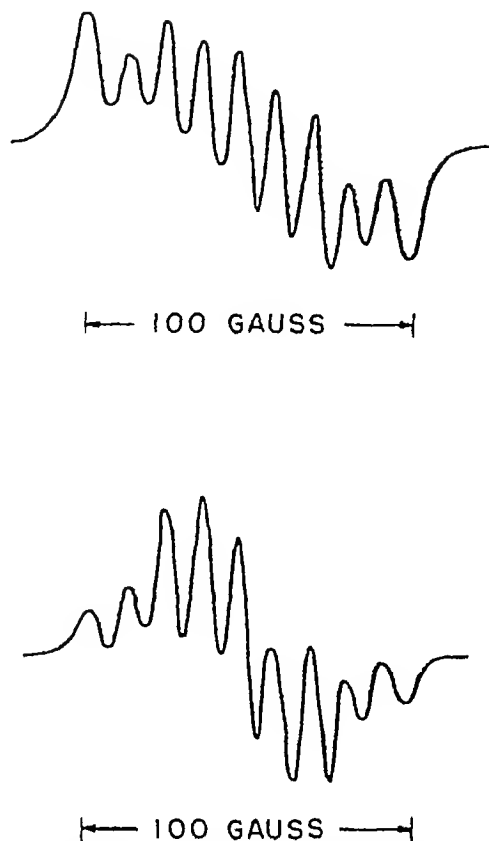


Fig 2 First derivatives of electron paramagnetic resonance spectra at 4.2° K of γ -irradiated polymethacrylic acid (upper curve) and γ -irradiated polymethyl methacrylate (lower curve)

Explanations of these spectra based on non-rotation of the methyl group have been attempted. Since the total hyperfine splitting is unchanged, the sum of the coupling coefficients of the three methyl protons must be unchanged. These coupling coefficients must be multiples of the line spacing (11.5 gauss). There are two possible cases, corresponding to two positions of the methyl group which have one proton either in line with, or orthogonal to, the 'radical' carbon atom p orbital. When these are taken with either of Symons's suggestions regarding the coupling of the methylene protons^{4,6}, nine line spectra with the observed spacings are predicted, but it is not possible to obtain even an approximate fit to the observed intensity ratios.

I am indebted to W. H. Jennings for technical assistance, and to Dr. Walter Gordy for his interest. This research was supported by the Office of Ordnance Research, Department of the Army.

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CHEMISTRY

Electron Spin Resonance and Divalency of Some Dithiocarbamates of the Coinage Metals (Cu, Ag, Au)

In a previous paper¹ one of us reported an investigation of the *N,N*-dialkylthiocarbamates of the univalent coinage metals, and in another² the reaction of the compounds in question with the corresponding thuram disulphides. Several of these compounds are not only of significant theoretical interest but they also play an important part in several branches of practical chemistry (for example, as ultra accelerators in rubber vulcanization, antioxidants in lubricants, in medicine for treatment of chronic alcoholism, etc.).

As divalent copper, silver and gold compounds all would be paramagnetic with electron configurations $3d^9$, $4d^9$, $5d^9$ respectively, it is possible to infer the existence of this oxidation state from a study of the electron spin resonance absorption spectra. This investigation gives, among other things, the first proof of the existence of the divalent oxidation state of gold.

X-ray investigations by Heese³ and Poyronol⁴ show that the copper compounds, $(R_2NCS)_2Cu$, form square planar complexes. It seems very likely that the corresponding silver and gold complexes have an analogous structure.

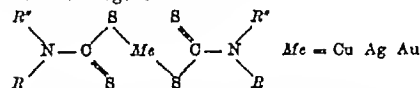


Fig. 1 shows typical spectra obtained from solutions of copper, silver and gold complexes. The spectra of the ethyl isopropyl (Fig. 1a) and methyl phenyl copper compounds are almost identical and have a g value of 2.046. The four hyperfine lines vary in width. This is typical for copper complexes and arises from insufficient averaging of the anisotropic resonance structure⁵. The high field line is so narrow (width about 4 gauss) that the hyperfine structure of the two copper isotopes copper 63 and copper 65 is resolved. The hyperfine separation of copper 63 is 7.4×10^{-3} cm⁻¹.

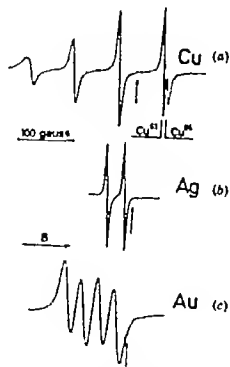
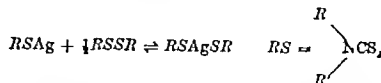


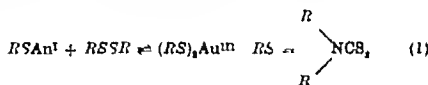
Fig. 1. Derivatives of electron spin resonance absorption curves recorded at room temperature. Microwave frequency about 9,500 Mc./s. The arrows indicate the resonance field for free electrons. Solvent benzene. (a) $(iso-C_4H_9)_2NCS_2Cu$; (b) $(iso-C_4H_9)_2NCS_2Ag$; (c) $(iso-C_4H_9)_2NCS_2Au$.

If silver(I) *N,N*-dialkylthiocarbamates are mixed with the corresponding thuram disulphides dissolved in benzene or chloroform, the solution immediately turns blue¹. The colour is most probably due to a divalent silver compound, the reaction may then be written schematically as



The electron spin resonance spectra of these solutions (Fig. 1b) definitely confirm the divalency of silver. In the same environment the general features of the electron spin resonance spectra of divalent copper and silver should be the same, and this was found to be so in an investigation by Bowers⁶. We obtained a doublet due to the hyperfine interaction of the two naturally abundant isotopes of silver both with nuclear spin of $\frac{1}{2}$. If the spectra are expanded it is just possible to see the hyperfine structure of the individual isotopes, silver 107 and silver 109 (nuclear magnetic moments -0.113 and -0.130 nuclear magnetons respectively). The line width is approximately 2.5 gauss. The widths of the two hyperfine lines differ slightly, and this can be explained in the same way as the line width variation of the copper compounds. The g value is 2.019 and the mean hyperfine separation is 2.7×10^{-3} cm⁻¹. The similarity of the g values of these and the corresponding copper compounds also indicates that the structures of the complexes are the same.

From chemical evidence the reaction between the gold(I) *N,N*-dialkylthiocarbamates and the corresponding thuram disulphides may be written schematically as follows⁷:



The reaction is rather slow. In a typical electron spin resonance experiment $RS Au^I$ and $RSSR$ dissolved in benzene separately showed no electron spin resonance absorption, but on mixing four lines of equal intensity appeared (Fig. 1c). The same spectrum was obtained by dissolving $(RS)_2Au^{II}$ ($RS = (C_2H_5)_2NCS_2$ or $(iso-C_4H_9)_2NCS_2$) in benzene. This resonance cannot be due to tervalent gold for the following reasons. No complex of the tervalent coinage metals (except CuF_2^{2+}) has been found to be paramagnetic. Also we have made preliminary static susceptibility investigations of some gold(III) *N,N*-dialkylthiocarbamates (both solid and in solution) which indicate that these compounds are diamagnetic. Furthermore, we could not detect any electron spin resonance absorption of the solid compounds. We also found by comparison with copper compounds that the intensity of the resonance absorption of the gold(III) compounds dissolved with an excess of thuram disulphide (to prevent the reversal of reaction 1), was at most 1 per cent of what one would expect if the resonance was due to tervalent gold. The electron spin resonance absorption of the dissolved gold(III) complexes decreased on adding more disulphide which should however increase the gold(III) concentration. Similarly if disulphide was added to a solution containing a large excess of the

gold(I) compound, the resonance signal stayed constant even though the gold(III) concentration was at least doubled

As it is impossible to explain the four equally intense lines in terms of hyperfine structure of free radicals we conclude that the resonance lines originate from divalent gold. The resonance data themselves give strong evidence for the existence of divalent gold compounds. The g value of the gold(II) complex is 2.040 which is close to those of the copper and silver compounds, and the hyperfine structure is consistent with the nuclear spin of gold-197 which is $3/2$. The hyperfine separation is $2.8 \times 10^{-3} \text{ cm}^{-1}$.

Further experiments including single crystal investigations are planned. We also hope to be able to clarify why the resonance line-width of the gold compounds is greater than that of the copper and silver compounds.

We wish to thank Profs. A. Fredga and K. Siegbahn for their interest in our work.

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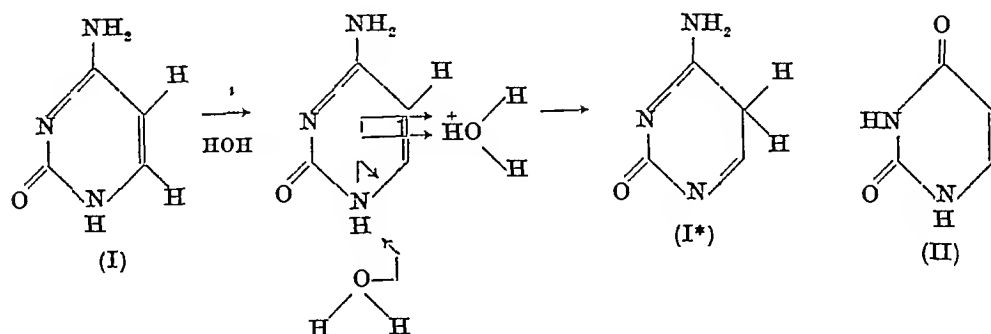
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Phototautomerization of Cytosine Derivatives on Ultra-violet Irradiation¹

UNSTABLE products were formed from certain cytosine derivatives on ultra-violet irradiation. These products had a new band at $\sim 240 \text{ m}\mu$ and lacked the characteristic $\sim 270 \text{ m}\mu$ maxima of cytosine derivatives. The products were not only reconstituted to their original compounds in the presence of acid and base but also spontaneously reconstituted themselves on standing, as indicated by the reversion of the ultra-violet spectra². Therefore, in these respects the cytosines differ from the uracils^{1,3}.

Because of the phenomenon of reversibility, investigators had classified cytosine derivatives and uracil derivatives together as one group from the point of view of photochemical behaviour². However, the electronic configurations of the two types are distinctly different. Since in aqueous solution, 4-hydroxy groups exist predominantly in the ketonic form (II) and the 4-amino group in the amino form (I), the uracils have exocyclic double bonds ($\text{C}=\text{O}$) at C^4 while the cytosines have endocyclic double bonds ($\text{N}=\text{C}$)³. Consequently, the photochemical pathway of cytosines might be altogether different from that of uracils.



Indeed, Shugar *et al.*² in their excellent study of cytosine derivatives have shown that irradiation, whether carried out in acid (pH 1-2), in alkaline (pH 9-11), or in neutral solutions produced similar photoproducts, which spontaneously reconstitute on standing. Both Shugar *et al.* and Sinsheimer² postulate the formation of photoproducts involving the addition of water. Since the photoproducts which they postulate are known to be stable only around neutrality, the existence of these molecules is most unlikely at either an extreme alkaline or acid pH during or after irradiation. If these products were actually formed, the decrease of optical densities during irradiation should have been similar to that seen upon thymine irradiation⁴. However, irradiation of cytosines at either an extreme alkaline or acid pH still gave reversible products instead of irreversible products, thus leading us to the conclusion that the unstable product probably is not a hydrated cytosine.

Irradiation of cytosine in buffered (pH 7) solution did not give a reversible product. However, irradiation in non-buffered solution gave a reversible product. Similar reversible products were produced from cytidine and cytidylic acid in either buffered or non-buffered solution. This indicated that when N^1H (N^1H) is not substituted, the salt effect from the buffer suppresses the formation of the reversible product. Therefore, it is suggested that $\text{N}^1(\text{N}^3)$ is probably involved in this photochemical change. (Synthetic $\text{N}^1(\text{N}^3)$ substituted cytosine derivatives behave similarly to that of cytosine. Using structural isomers we are now investigating the basis of this discrepancy.)

The decrease of optical densities at $270 \text{ m}\mu$ with a simultaneous increase at $240 \text{ m}\mu$ does not necessarily indicate the formation of dihydro derivatives, because these reduced compounds do not exhibit ϵ_{max} at any wave-length longer than $230 \text{ m}\mu$ ⁵.

On close examination of the absorption spectrum at neutral pH there is apparently a shoulder at $\sim 240 \text{ m}\mu$ besides the principal $\sim 270 \text{ m}\mu$ maxima. Therefore, the so-called new maximum at $\sim 240 \text{ m}\mu$ probably represents the increase of the optical density at the shoulder for that particular component structure.

From the above evidence, a tautomerization by irradiation seemed most likely to us. Indeed such an unstable tautomer (I^*) as shown involves $\text{N}^1(\text{N}^3)$ in the tautomerization. It is not a dihydro derivative resulting from a hydration product of cytosine. The shift from $270 \text{ m}\mu$ to $240 \text{ m}\mu$ is probably due to the change of a straight conjugation to a cross conjugation of the chromophore. The higher extinction at $240 \text{ m}\mu$ is probably due to the separation of charges in a molecule. Furthermore, barbitol derivatives, which have chromophores similar to that of the tautomer, have the ϵ_{max} at $240 \text{ m}\mu$ ⁶. In the dark the unstable

tautomer should revert to their most stable form, having the original spectra.

In order to demonstrate this tautomerization or isomerization, cytosine, cytidine and cytidylic acid were irradiated respectively both in buffered and non-buffered solutions. It will be evident from Figs. 1 and 2 that

isobestic points are present indicating that isomerization must have occurred? Irradiation of cytosine in buffered solution did not give an isobestic point therefore an irreversible product was formed. The spontaneous isomerization rather than the reversibility of the compounds of spectra in acid and base was the most interesting phenomenon about these observations. It indicates that an excited molecule can result from the absorption of photo energy and that this energy can be released slowly in another form, possibly available for chemical changes, without other influences, such as enzymes, heat, acidity etc. The apparent half life of the irradiated cytosine, cytidine and cytidylic acid are 50, 30 and 200 min, respectively.

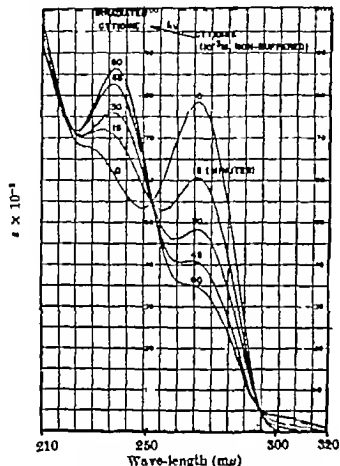


Fig 1

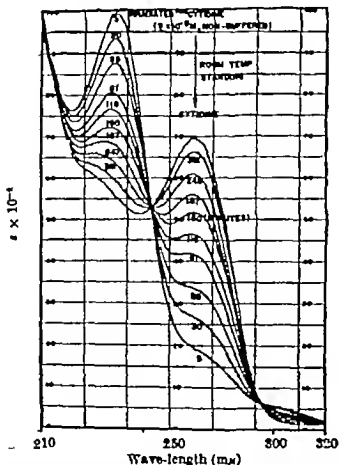


Fig 2

The above results raise the question of the possible part that this phenomenon might play in biological systems.

This work was accomplished under the Common Contract AT(30-1)911 of the generous gift of Commission with the Physiology Department Biochemistry University School of Medicine. I wish to thank M. Apicella, L. A. Johnson and M. Monyos for able assistance.

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Isotopic Composition of Boron

In a recent communication¹ it was concluded that a boron 11/boron 10 ratio of 4.00 approaches the true natural abundance ratio much more closely than the presently accepted value of 4.31. This value of 4.00 had been obtained from the mass spectra of boron hydrides and other volatile compounds.

Using a Metrovick mass spectrometer designed for the surface ionization of solids from a filament source and working with borax, we have obtained consistent results within the range 4.06-4.09 for the boron 11/boron 10 abundance ratio.

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Stoichiometry of Bismuth Telluride and Related Compounds

Bismuth telluride, bismuth selenide and antimony telluride are being actively studied as semiconductors for thermoelectric cooling.¹ After purification by zone melting these materials do not exhibit intrinsic properties.² C. B. Satterthwaite and R. W. Ure³ have shown by electrical measurements that in the case of bismuth telluride there is a slight difference between the composition corresponding to the maximum of the liquidus curve and the stoichiometric composition. Electrical properties are sensitive to physical imperfections and their interpretation in terms of chemical composition is thus open to criticism.⁴

By using a sensitive method of differential thermal analysis we have found it possible to determine the composition corresponding to the maximum in the liquidus curve. The principle of this method is the use of the fact that for this composition the solid melts congruently whereas, for slightly different compositions it yields, after a suitable heat treatment, a mixture of two solid phases having different solid transition points.

Bismuth telluride containing excess tellurium forms an eutectic⁵ melting at 413°C and excess bismuth gives rise to a peritectic reaction⁶ at 540°C. Bismuth

gold(I) compound
stant even though
least doubled
As it is
intense
radical
from

185

is characterized by a
C, associated with an
217° C, with excess
appears at 605° C The
antimony-tellurium is
with excess tellurium at
with excess antimony³

melting of eutectic phases,
peritectic reactions are
of the individual phases

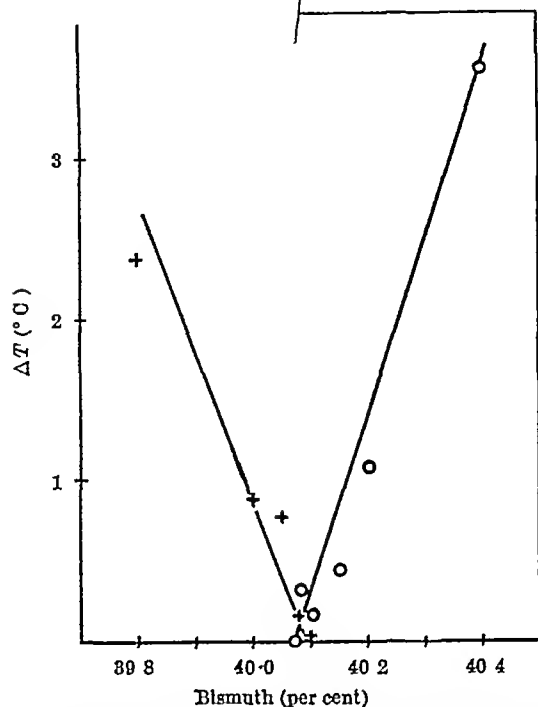


Fig 1 System Bi/Te +, Amplitudes of eutectic signals (quenched samples), O, amplitudes of peritectic signals (annealed samples)

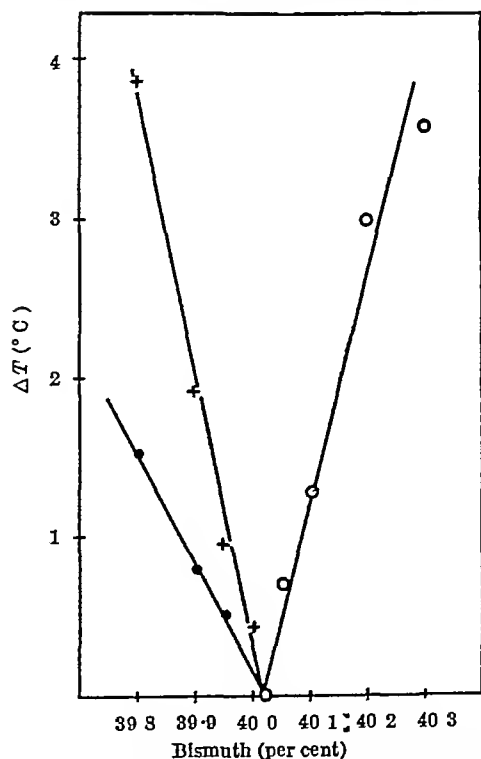


Fig 2 System Bi/Se O, Amplitudes of peritectic signals; +, amplitudes of monotectic signals, ●, amplitudes of eutectic signals (quenched samples)

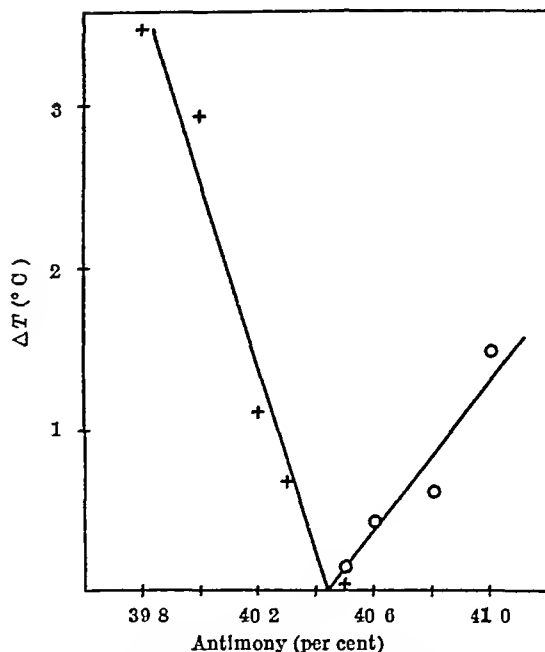


Fig 3 System Sb/Te +, Amplitudes of eutectic signals at 400° C, O, amplitudes of eutectic signals at 545° C (quenched samples)

present and may be used as a measure of their concentrations. In the case of the eutectics, the samples are quenched from the liquid state in order to avoid the formation of a solid solution, in the other case, the samples are carefully annealed at a suitable temperature in order to carry the reaction as nearly as possible to completion.

The results of the experiments are given in Figs 1, 2 and 3. It is evident that the congruent compositions for these three systems is

Bismuth telluride Bi 40.065/Te 59.935 ± 0.015

Bismuth selenide Bi 40.02/Se 59.98 ± 0.02

Antimony telluride Sb 40.40/Te 59.60 ± 0.05

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Determination of Magnesium in Blood Serum by Atomic Absorption Spectroscopy

THE present lack of detailed knowledge of the function of magnesium in the human body is due partly to the lack of rapid and reliable methods for its routine estimation in small quantities of biological materials. Recently, Hunter¹ has devised a method for determining calcium and magnesium in blood serum by titration with murexide and with 'Eriochrome T'. It uses only 0.2 ml. of serum, but has

the disadvantage of requiring prior removal of protein by coagulation or ashing, and even then the magnesium is estimated indirectly by the difference of the two titrations. Methods for determining magnesium directly normally require removal of calcium also.⁴⁻⁶ The flame photometer method of Davis⁴ requires removal of protein followed by precipitation of the magnesium by 8-hydroxyquinoline.

It has been pointed out⁴ that atomic absorption spectroscopy⁷ can be used for the determination of magnesium in the ash from blood serum, since interference by sodium, potassium, calcium and phosphate is negligible.

I have recently⁸ described the determination of magnesium by the atomic absorption method, measurements can be made in solutions containing water, in salt of ethylene diamine, results reported here are made by diluting since only 2.5 ml of solution is used for determinations and with little sacrifice of accuracy in estimating magnesium. Most of the existing methods

The solution, 10 cm air-acet and absorption 2852 Å. was measured with solutions of magnesium.

Table 1 shows prepared (a) by direct nutritive acid⁹ followed distilled hydrochloric acidization and dilution with 0.05 N acetic acid

the determination of magnesium by the atomic absorption method, measurements can be made in solutions containing water, in salt of ethylene diamine, results reported here are made by diluting since only 2.5 ml of solution is used for determinations and with little sacrifice of accuracy in estimating magnesium. Most of the existing methods

by injection into a Lundegårdh type, in resonance line at 15 mgm./100 ml

contents for samples (b) by ashing with a few drops of subsequent neutral removal of protein

Table 1 MgM CONT

(mgm./100 ml)

| Serum No | Type | Dilution | (b) Ashed | (c) Deproteinized filtrate |
|----------|---------|----------|-----------|----------------------------|
| 1 | Bovine* | 3.55 | 3.53 | 3.53 |
| 2 | Equine | 1.75 | 1.80 | — |
| 3 | Human | 2.87 | — | 2.60 |
| 4 | — | 2.22 | 2.28 | — |
| 5 | — | 3.45 | — | 2.68 |
| 6 | — | 2.60 | — | 2.66 |
| 7 | — | 1.70 | — | 1.63 |
| 8 | — | 2.22 | 2.24 | 2.00 |
| 9 | — | 1.14 | 1.04 | 1.15 |
| 10 | — | 2.10 | 1.91 | 2.10 |

* Freeze-dried bovine serum (Chemical supplied by Clinton Laboratories, Los Angeles). The magnesium values are higher than those for most bovine sera.

In view of the chemical and manipulative errors likely to be incurred in the preparation of such dilute solutions (~1 p.p.m.) by methods (b) and (c) the agreement is considered satisfactory, and the magnesium values obtained by direct dilution are probably more reliable than those obtained by the other methods. Duplicate readings on the same solution seldom differed by more than 2 per cent. Recovery of added magnesium was 100–102 per cent.

Although the present work was carried out with the air-acetylene flame, an air-coal gas flame is also satisfactory, and we are at present developing a very simple instrument which will determine magnesium in blood serum.

A fuller account of the present work will be submitted to *Analytical Chemistry*.

I am indebted to Mr E. Mason of the Commonwealth Serum Laboratories for a generous gift of horse serum and to Miss B. Splatt of the Biochemistry Department, Royal Melbourne Hospital, for the specimens of human serum.

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BIOCHEMISTRY

Action of Trypsin on α -Carbomethoxy-L-lysyl-L-serylglycine and its O-Phosphorylated Analogue

The occurrence and isolation of phosphorylated peptides from enzymic hydrolysates of casein have already been reported.¹ These peptides exhibit unusual resistance to further proteolytic action, a fact which has been correlated with the existence of O-phosphorylated serine residues in their molecules. In order to investigate further the resistance of such peptides to the action of trypsin, certain synthetic peptide substrates suitable for this enzyme have been tested. Thus α -carbomethoxy-L-lysyl-L-serylglycine and α -carbomethoxy-L-lysyl (O-phosphoryl)-L-serylglycine were synthesized as follows:

α -Carbomethoxy (α -carbomethoxy)-L-lysine (I) was prepared from α -carbomethoxy-L-lysine in a similar manner described for the carbomethoxy isomulin derivative.² The oily product thus obtained was coupled by the mixed carbonyloxy-carbonic anhydride procedure with L-serylglycine³ (II) to give α -carbomethoxy (α -carbomethoxy)-L-lysyl-L-serylglycine (III) in 50 per cent yield, melting point 204° C. Analysis calculated for $C_{18}H_{28}N_4O_8$, N 11.2, found, N 11.1. When α -tosyl (α -carbomethoxy)-L-lysine, melting point 115–117° C., or the corresponding α -benzoyl derivative, melting point 110° C., were used, the coupling did not proceed satisfactorily, probably due to steric hindrance.⁴ Hydrogenolysis⁵ of III produces α -carbomethoxy-L-lysyl-L-serylglycine (IV), $[\alpha]_D^{25} = -28.0^\circ$ (c 0.78 in water). Analysis calculated for $C_{11}H_{18}N_4O_8$, $2H_2O$, N 14.1, found, N 13.0. Compound II was treated with benzyl alcohol in the presence of *p*-toluenesulphonic acid to give L-serylglycine benzyl ester *p*-toluenesulphonate (V) in 90 per cent yield, melting point 180° C. Analysis calculated for $C_{17}H_{24}N_4O_8$, N 6.5, found, N 6.2. The ester V was condensed with I by the anhydride procedure to afford α -carbomethoxy (α -carbomethoxy)-L-lysyl-L-serylglycine benzyl ester (VI) in 50 per cent yield, melting point 186–188° C., $[\alpha]_D^{25} = -17.0^\circ$ (c 1.5 in acetic acid). Analysis calculated for $C_{24}H_{36}N_8O_{10}$, C 59.30, H 6.52, N 9.7, found, C 59.4, H 6.7, N 9.5. To eliminate the side reaction with the hydroxyl group of serine, the ester V was dissolved in tetrahydrofuran/water (6/1) in the presence of two equivalents of triethylamine and then added to the anhydride solution.

Hydrogenolysis of VI produces IV with the same optical rotation. Coupling of I with V by the carbodimide method gave VI with melting point 185–186° C. Phosphorylation of VI with diphenylphosphoryl chloride⁷ in anhydrous pyridine resulted in the production of an amorphous product, which analysis suggested was a mixture of O-phosphorylated and unphosphorylated peptide derivative, although 50 per cent excess of the chloride was used. Compound VI dissolved in anhydrous pyridine and recovered after 2 hr, showed almost no change of its optical rotation.

Removal of protecting groups from the amorphous product by hydrogenolysis in the presence of palladium on charcoal, gave a mixture in which the monophenyl derivative predominated. Final removal of this was then attempted by further hydrogenolysis in the presence of platinum as the catalyst. Following paper electrophoresis in pyridine-acetate buffer, pH 5.5, revealed three ninhydrin-positive spots. The most intense and anodically fast moving one corresponded to the phosphorylated peptide. The desired product α -carbethoxy-L-lysyl-(O-phosphoryl)-L-seryl-glycine (VII), $[\alpha]_D^{25} -23.6^\circ$ (c 1 in water), was isolated by anion-exchange chromatography (Strid, L., unpublished work). Paper electrophoresis revealed one spot. Analysis calculated for $C_{14}H_{27}N_4O_{10}P$, N 12.6, P 7.0, found, N 12.05, P 7.3.

Compounds IV and VII were respectively incubated with trypsin in 0.2 M *tris*(hydroxymethyl) amino-methane hydrochloride buffer, pH 8.25, at 25° C. Qualitative analysis of hydrolysis products, on the other hand, was carried out by paper chromatography in butanol/acetic acid/water (4:1:5) system. The course of reaction was also followed by colorimetric analysis with ninhydrin reagent⁸. To this end, aliquots were withdrawn at different time intervals, mixed with 0.2 M citrate buffer, pH 5, at 5–6° C and then analysed.

As is indicated in Fig. 1, a phosphoryl residue attached to the hydroxyl group of serine renders the lysylserine peptide bond resistant to tryptic action. Paper chromatography of the incubation mixture of VII with trypsin also supported this conclusion. On the other hand, the incubation mixture of IV revealed two spots corresponding to α -carbethoxy-L-lysine

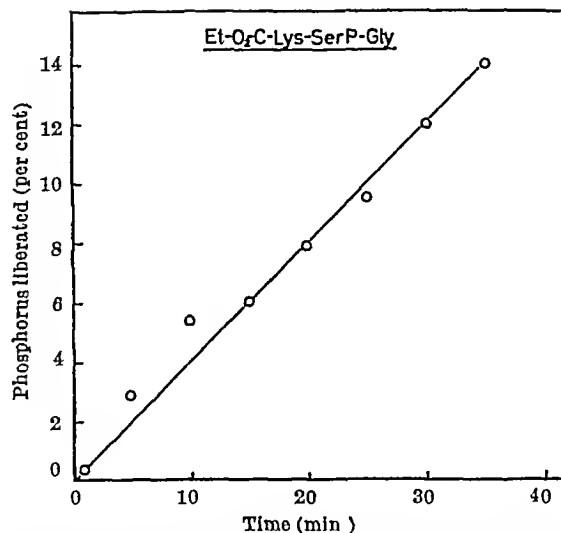


Fig. 2. Hydrolysis of O-phosphorylated L-carbethoxy-L-lysyl-L-seryl-glycine (0.01 M) with intestinal alkaline phosphatase (0.1 mgm./ml, crude preparation Lot 1105 Mann).

and L-seryl-glycine respectively.

The effect of alkaline phosphatase on α -carbethoxy-L-lysyl-(O-phosphoryl)-L-seryl-glycine at pH 9.5 (0.1 M triethylamine-carbon dioxide buffer) at 25° C is shown in Fig. 2. The amount of phosphorus liberated was determined by the modified method of Beerenblum and Chain⁹.

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A Micromethod for the Polarographic Determination of Serine

THE serological behaviour of red blood cells is known to be altered by treatment with dilute solutions of potassium periodate. There is also some evidence that during the interaction of potassium periodate solutions with red blood cells, measurable quantities of periodate ion are consumed¹. While investigating the consumption of periodate ions by red blood cells, a method for the determination of relatively small amounts of serine was developed.

Malaprade² has described how compounds containing adjacent hydroxyl groups as well as hydroxy-amino-acids are oxidized by periodate ion. Based on this observation, several methods have been devised for the determination of serine by means of the periodate ion^{3–5}. These methods, however, including that of Boyd⁴ and Bambach⁵ based on the polarographic determination of formaldehyde formed by the action of the periodate ion and separated by

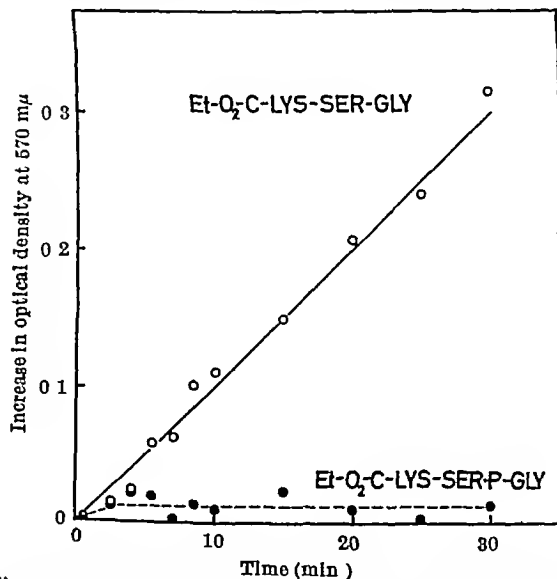


Fig. 1. Hydrolysis of O-phosphorylated and unphosphorylated α -carbethoxy-L-lysyl-L-seryl-glycine (0.01 M) respectively with trypsin (0.003 mgm N/ml, crystallized twice, 50 per cent $MgSO_4$, Lot 3388 Mann) in 0.2 M *tris* buffer, pH 8.25 at 25° C.

* Chl, Chloramphenicol, 20 μ gm/ml, 6AU, 6-aza uracil, 5 mgm./100 ml. Following exposure to ultra-violet the suspensions were incubated in minimal medium with the supplement indicated. The cells were removed from chloramphenicol by rapid centrifugation and resuspension in chloramphenicol free medium. The 6-aza uracil inhibition was reversed by addition of uridine to the medium. The auxotrophic strains were held following exposure to ultra-violet either with or without the appropriate growth supplement. In the case of cells without the required supplement, the supplement was added after lapse of the time indicated.

† Deoxyribonucleic acid synthesis resumed after 150 min incubation

Ultra-violet light induces a lag in the synthesis of deoxyribonucleic acid in *E. coli*. An investigation of the metabolic basis of this lag has been carried out, utilizing specific inhibitors of protein and ribonucleic acid synthesis and also auxotrophic strains requiring uracil, thymine or certain amino-acids (Table 1). These findings suggest that ribonucleic acid and protein synthesis (but not deoxyribonucleic acid synthesis) are required for reparation of the deoxyribonucleic acid synthetic system after damage by irradiation with ultra-violet, they are thus in agreement with recent reports^{9,10}

Table 2 EFFECT OF BLOCKAGE OF RIBONUCLEIC ACID AND PROTEIN SYNTHESIS ON SURVIVAL OF *Escherichia coli* STRAIN B FOLLOWING EXPOSURE TO ULTRA-VIOLET LIGHT

Ultra-violet dose was 2,395 ergs/mm². The suspension contained 1.4×10^8 colony forming bacteria per ml before exposure to ultra-violet. Survivors upon immediate plating following exposure were 6.0×10^4 per ml

| Post-irradiation treatment* | | Survivors ($\times 10^4$) per ml with incubation time (min) before plating | | |
|-----------------------------|-----------------|--|-----|-----|
| Incubation Medium | Added at 40 min | 40 | 120 | 160 |
| A M—N | — | 8 | 43 | 302 |
| B M—N + Chl | — | 4 | 3 | 8 |
| C M—N + 6AU | — | 8 | 14 | 31 |
| D M—N | Chl | 7 | 63 | 358 |
| E M—N | 6AU | 8 | 40 | 310 |
| F M—N+AA | — | 7 | 10 | 14 |
| G M—N+AA | Chl | 9 | 68 | 398 |
| H M—N+AA+Chl | — | 4 | 4 | 3 |
| I M—N+AA | 6AU | 8 | 116 | 480 |
| J M—N+AA+6AU | — | 7 | 11 | 17 |
| K M—N+AA+Chl | 6AU | 4 | 6 | 7 |
| L M—N+AA+6AU | Chl | 8 | 10 | 10 |

* M—N, minimal with ammonium sulphate deleted, Chl, chloramphenicol, 20 μ gm/ml, 6AU, 6-aza uracil, 5 mgm/100 ml, AA, casein hydrolysate, vitamin free, 2 mgm per ml

Table 2 shows a marked increase in survival of *E. coli* strain B with incubation in minimal medium from which the nitrogen source is deleted. The addition of amino-acids to this medium prevents the recovery observed (F). Further, the addition of chloramphenicol or 6-aza uracil to the nitrogen free cultures interferes with recovery (B, C). If, however, chloramphenicol or 6-aza uracil is added after 40 min incubation (D, E) recovery occurs. These results suggest that the recovery promoted by the M—N medium is dependent on both ribonucleic acid and protein synthesis within the first 40 min of incubation following exposure. It is obvious that this synthesis must be minor in quantity since no nitrogen source is present in the M—N medium. It seemed plausible that the recovery promoted by the M—N medium results from the prevention, due to the nitrogen deficiency, of 'unbalanced growth'¹¹ during the period required for reparation of the deoxyribonucleic acid synthetic system. This hypothesis is supported by the finding that either chloramphenicol or 6-aza uridine, if added to the medium containing amino-acids (F) after 40 min incubation following exposure to ultra-violet, promotes the same degree of recovery (G, I) that the M—N medium promotes (A). If these compounds are added immediately following ex-

posure to ultra-violet no recovery is observed (H, J). Chloramphenicol, added immediately, prevents the recovery promoted by 6-aza uridine (K) and conversely the addition of 6-aza uridine immediately prevents the recovery promoted by chloramphenicol (L). The evidence suggests that ribonucleic acid and protein synthesis during the initial period of incubation following exposure to ultra-violet is requisite to recovery, but is detrimental to recovery afterwards. Recovery apparently requires (1) synthesis of ribonucleic acid and protein in preparation of the deoxyribonucleic acid synthetic system and (2) the prevention of inactivation through unbalanced cytoplasmic growth during the subsequent period required for resumption of synthesis of deoxyribonucleic acid.

Further details of the investigation will be published later. This project was supported in part by a contract with the U S Atomic Energy Commission, AT (40-1)-2139

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High Molecular Weight Ribonucleic Acids from the Nuclei of Calf Thymus

A RIBONUCLEIC acid fraction, which gives the characteristic sedimentation pattern shown in Fig 1, has been isolated very recently from tobacco leaves¹, mouse brain² and microsomes of rat liver¹. The molecular weights of components A and B are 1.7×10^6 and 0.6×10^6 , respectively. Although the study has yet to be extended to other systems, I suggested two years ago that ribonucleic acids with molecular weights of about 1.7×10^6 exist in the cytoplasm of many types of cells³. The question that naturally arises is whether ribonucleic acids of such a molecular weight also exist in a nucleus. So far no investigation along this line has been reported. The results presented below appear to provide an answer to the question.

A preparation of nuclei was obtained from calf thymus according to Alfrey and Mirsky's modification of the procedure described by Schneider and Petermann⁴. The nuclei in such a preparation have been shown to be capable of incorporating amino-acids into their proteins⁴. With the aid of Feulgen staining, the present preparation was found to contain three intact cells and sixteen cytoplasmic strands per 360 nuclei. A purified fraction of ribonucleic acids of high molecular weights was prepared from this nuclei preparation according to a procedure that will be published elsewhere⁵. The yield was 0.18 per cent

of the dry nuclei, or 13 per cent of total nucleus ribonucleic acid. (The dry nuclei contained 1.4 per cent ribonucleic acid.) As the nuclei preparation was contaminated with only 5 per cent of cytoplasm and the same procedure produces purified ribonucleic acids of high molecular weights from mouse brain at a yield of only about 20 per cent that of total brain ribonucleic acids, it is concluded that the contamination of the nucleic acid preparation from nuclei with the cytoplasmic ribonucleic acid is slight. This preparation contained less than 0.03 gm. of deoxyribonucleic acid per 100 gm. of ribonucleic acid, as estimated by diphenylamine reaction⁴ and orcinol reaction⁵, respectively. It had the same ultra violet absorption spectrum as the ribonucleic acid preparation from mouse brain.⁶

As indicated by the representative sedimentation diagram in Fig. 2, this preparation of nucleic acids from nuclei contained two major components (a and b) in the same ratio as that found for components A and B in whole tissue or cytoplasm (of Fig. 1). Moreover, the molecular weights of components a and b were found to be the same as those of components A and B, respectively.

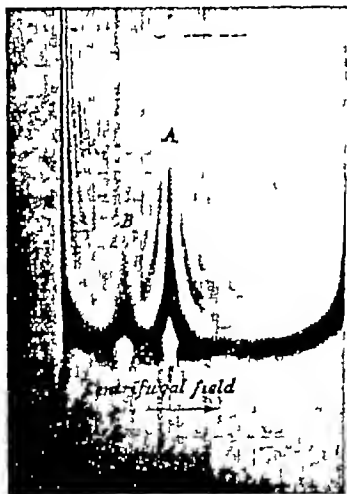


Fig. 1. Sedimentation diagram of a purified ribonucleic acid preparation from mouse brain. A solution of 0.17 per cent nucleic acid in 0.02 M phosphate, pH 7.3, was centrifuged in a single-sector cell at 8° C.

One point of difference has been observed between the ribonucleic acid preparation from whole brain and that from thymus nuclei. When a fresh preparation from the brain at a concentration of 2.5 mgm./ml was maintained in 0.02 M sodium phosphate, pH 7.3, for 3 hr. at 3° C, it showed no detectable change in its sedimentation behaviour. If the preparation was made from brain infected with Semliki Forest virus, even its infectivity was preserved. On the other hand, when the preparation from nuclei was

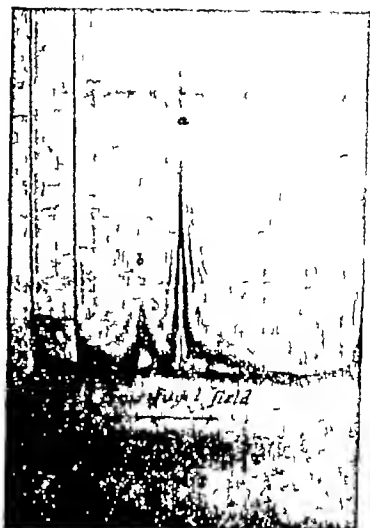


Fig. 2. Sedimentation diagram of a purified ribonucleic acid preparation from thymus nuclei. A solution of 0.25 per cent nucleic acid in 0.02 M phosphate, pH 7.3, was centrifuged in a double-sector cell at 8° C.

subjected to the same treatment, degradation occurred, single and polydisperse sedimentation boundary having a molecular weight of about 0.2×10^6 at the peak of the schlieren pattern was observed. No significant further change resulted from subsequent incubation of the preparation at a concentration of 1 mgm./ml. in 0.01 M phosphate for 15 min. at 83° C. This difference is tentatively attributed to the possibility that the preparation from nuclei was contaminated to a greater extent with some material possessing degrading activity than was the preparation from brain.

The presence of ribonucleic acids of high molecular weights in nuclei as well as in cytoplasm has several important implications. For example, these ribonucleic acids may be the templates for protein synthesis in both nuclei and cytoplasm.

I am indebted to Miss H. J. Scherer for her technical assistance.

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March 25

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Post-Exposure Analysis of Organic Compounds in the Blood by a Rapid Infra-Red Technique

THERE has long been a need for a rapid standard method for the determination of levels of circulating organic compounds foreign to the blood stream. The inability to measure efficiently the blood and urine levels of compounds handled in industrial processes has hindered toxicological research and made adequate control of the working environment more difficult. The physician when establishing a diagnosis of an acute or chronic poisoning from an industrial chemical has had no ready procedure by which to identify the specific compound or to determine its concentration in the blood stream. The infra-red method to be presented satisfies the above implied criteria for an efficient analytical procedure—simplicity, rapidity, sensitivity, and availability.

10 ml of oxalated blood are pipetted into a bacteriological culture tube with an aluminium-lined screw cap. 15 ml of carbon bisulphide, methylene chloride, or other suitable extracting solvent is added, and the tube gently agitated by end-over-end inversion for 5 min. The tube is then centrifuged for 10 min at 500*g*. In centrifuging carbon bisulphide mixtures a refrigerated chamber is used to minimize the explosion hazard. The solvent layer is transferred to a standard infra-red sample cell and its spectrum scanned from 2–16 μ . Cells of 1 mm, 3 mm, or 16 mm thickness are used depending on the sensitivity desired. Occasionally it is advantageous to compensate solvent absorptions by placing a matching cell with pure solvent in the reference beam of the spectrometer. While an improved optical null infra-red spectrometer¹ was used in this experiment, any standard infra-red spectrometer would have served as well.

Table 1 SOLVENT EXTRACTIONS OF BLOOD STANDARDS

| Material | Concentration in blood p p m (wt/vol) | Solvent | Amount extracted p p m (radioactive count) | Amount extracted p p m (infra red) |
|--|---------------------------------------|---------------------------------|--|------------------------------------|
| Benzene- ¹⁴ C | 74* | CS ₂ | 68 | 69 |
| | | | 62 | 69 |
| | 110* | CS ₂ | 96 | 88 |
| | | | 100 | 88 |
| Trichloroethylene 1,2- ¹⁴ C | 25* | CS ₂ | 28 | 28 |
| | | | 26 | 27 |
| | | | | 135 |
| Ethanol | 510† | CH ₂ Cl ₂ | | 150 |
| | | | | 233 |
| | 980† | CH ₂ Cl ₂ | | 240 |
| | | | | 43 |
| Isopropanol | 540† | CS ₂ | | 40 |
| | | | | 90 |
| | 1,010† | CS ₂ | | 83 |
| | 1,010† | CH ₂ Cl ₂ | | 360 |
| | | | | 348 |

* By radioactive count
† Added.

The efficiency of this method for the extraction of a given compound from blood is determined by adding a measured amount of the chemical to the blood and extracting it as outlined above. Organic compounds which are not readily soluble in the blood, such as trichloroethylene and benzene, must be checked carefully when standards are prepared, to ensure that

the exact amount of chemical in solution in the blood is known before extraction. Compounds labelled with carbon-14 are employed for preparation of standards when the solubility in blood is known to be low.

This method has proved satisfactory for the measurement of many commonly employed compounds, including carbon tetrachloride, tetrachloroethylene, and 1,1,1-trichloroethane. Four organic compounds, two of which are not readily soluble in blood, are presented as examples.

Table 1 shows the results obtained upon standardization of the method while Table 2 presents the values obtained after exposure of rabbits to these chemicals.

Table 2

| Rabbit | Exposure | Time after exposure (min) | Solvent | Amount extracted p p m | Calculated blood level p p m (wt/vol)* |
|--------|--|---------------------------|---------------------------------|------------------------|--|
| 1 | Benzene oral 2 ml/kgm | 35 | CS ₂ | 55 | 59 |
| | | 75 | CS ₂ | 87 | 109 |
| 2 | Benzene, oral 2 ml/kgm | 34 | CS ₂ | 66 | 71 |
| | | 80 | CS ₂ | 44 | 47 |
| 3 | Trichloroethylene-vapour 800 p p m for 7 hr | 0 | CS ₂ | 9 | 9 |
| | | 30 | CS ₂ | 2.2 | 2.2 |
| 4 | Trichloroethylene-vapour 800 p p m for 7 hr | 0 | CS ₂ | 16 | 16 |
| | | 30 | CS ₂ | 2.5 | 2.5 |
| 5 | Ethanol, oral 2.85 ml/kgm | 30 | CH ₂ Cl ₂ | 620 | 2,450 |
| | | 60 | CH ₂ Cl ₂ | 728 | 2,900 |
| 6 | Ethanol oral 2.85 ml/kgm | 30 | CH ₂ Cl ₂ | 598 | 2,350 |
| | | 60 | CH ₂ Cl ₂ | 675 | 2,700 |
| 7 | Isopropanol, oral 2 ml/kgm. | 35 | CS ₂ | 158 | 1,900 |
| | | (Acetone present) | | 66 | |
| | | 82 | CS ₂ | 135 | 1,600 |
| | | (Acetone present) | | 131 | |
| 8 | Isopropanol, oral 2 ml/kgm | 36 | CS ₂ | 159 | 1,900 |
| | | (Acetone present) | | 65 | |
| | | 89 | CS ₂ | 115 | 1,400 |
| | | (Acetone present) | | 80 | |

* The blood levels were calculated by multiplying the amount of chemical extracted, by the efficiency of extraction determined from the values presented in Table 1.

This infra-red method for measuring post-exposure blood levels of organic compounds has many advantageous features. It is a simple, rapid procedure which can be performed in any laboratory with infra-red facilities. Although the efficiency with which different organic compounds may be extracted varies considerably, depending on both the solvent and the compound, the results indicate that the efficiency is approximately constant for any particular system. Sensitivities approaching a part per million can usually be attained by the proper choice of solvent. In addition, unknown organic compounds may be identified, more than one compound may be measured with one extraction, and metabolites, such as acetone following isopropanol ingestion, may be found.

The method has also been applied successfully to the analysis of urine, and should be applicable to other biological fluids as well. Work is in progress to deter-

mine more exactly the efficiency of this extraction method for the above and other organic compounds.

We wish to thank Dr Norman Wright for suggesting this approach, and B. H. Blake for obtaining the infra red spectra.

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Localization of Haemocyanin on Starch Gel Electrophoretic Patterns

Using the Smithies technique¹ of zone electrophoresis in starch gel Woods *et al.*² have recently demonstrated the occurrence of several haemocyanin proteins in the blood sera of certain crustacean species. The identification is tentatively based on the occurrence of two or more protein bands of a similar order of mobility and which are extremely concentrated in comparison to the other blood protein components.

The finding by Woods *et al.*² of what are assumed to be several haemocyanins in certain species can be interpreted in the following ways: (1) as separate molecular forms of haemocyanin, or (2) dissociation association products or other derivatives of a single molecular form, or (3) one or more non haemocyanin proteins with physical properties similar to haemocyanin but which separate from it during gel electrophoresis. Woods *et al.*² favour, at least in part, the second interpretation of the several constituent haemocyanins. They further suggest that a non copper-containing moiety may have been isolated from other components of a possible haemocyanin polymer of higher molecular weight. In order to test the possibilities that either an intact non haemocyanin molecule which would not contain copper or a haemocyanin fragment devoid of copper may have been isolated electrophoretically, the following experiment was devised.

Crayfish serum was resolved electrophoretically in starch gel using the method of Smithies¹. The crayfish used in this study were of two species, *Orconectes viridis* (Hagen) and *Orconectes propinquus propinquus* (Girard) (kindly identified by Prof. Horton H. Hobbs, jun. of the University of Virginia). Gels were prepared with 12.5 gm of reagent soluble starch (Merk and Co. Ltd, Montreal, Canada)/100 ml of borate buffer (0.02 M boric acid and 0.008 M sodium hydroxide/litre). This gave gels of pH 8.03. The bridge buffer used consisted of 0.20 M boric acid and 0.04 M sodium hydroxide/litre. Electrophoresis was carried out at room temperature for 12 hr at a potential gradient of 0 v./cm. On completion of electrophoresis the gels were sectioned horizontally; one half was stained for protein with amido black 10B dye and the other half was placed for 24 hr in a solution consisting of 50 ml of 10 per cent aqueous sodium acetate and 3 ml of alcohol 0.1 per cent rubranic acid (dithioximide). Gomori³ cites the development of a greenish black colour in this reagent as a histochemical test for copper.

The two *Orconectes* species used gave patterns similar to *Cambarus limosus* (= *Orconectes limosus* (Raf.)) which had been found previously³ to have two haemocyanin bands. Both haemocyanin bands of *Orconectes* stained a light greenish black in the copper reagent. As a control the larval haemolymph protein pattern of the eastern tent caterpillar *Malacosoma americanum* (Fab.) was subjected to the same test. *Malacosoma* has a very concentrated protein component of about the same electrophoretic mobility as the crustacean haemocyanins. However, *Malacosoma* pattern components did not react with the reagent up to 48 hr. Serum of the horseshoe crab *Limulus polyphemus* (L.) (obtained through the courtesy of Dr R. J. DeFalso of the Serological Museum of Rutgers University), which has an extremely concentrated fast migrating haemocyanin component, was also tested in this way. The concentrated component reacted positively with the copper reagent. These observations are summarized in Fig. 1.

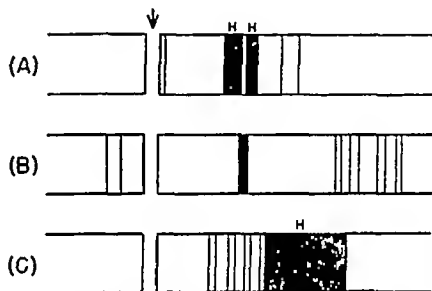


Fig. 1. Starch gel electrophoresis diagrams of the blood protein patterns of (A) *Orconectes* spp., (B) *Malacosoma americanum* larvae and (C) *Limulus polyphemus*. The anodic area is to the right of the point of sample insertion (indicated by arrow) and the cathodic area is to the left. The letter H indicates copper containing components.

This experiment does not support the possibility in *Orconectes* of the electrophoretic isolation of a non haemocyanin protein from copper-containing haemocyanin. If there is a dissociation phenomenon involved as suggested by Woods *et al.*² then copper is being distributed between more than one dissociation product.

In connexion with this test yet another possibility arises. The enzyme tyrosinase also contains copper as a co-factor. This enzyme could be present as a separate electrophoretic component or absorbed to another protein. However, *M. americanum* did contain a large amount of tyrosinase in its blood as evidenced by a rapid melanization in the absence of phenylthiourea as an inhibitor. Since copper was not found to be associated with any of the *Malacosoma* protein fractions we can probably rule out tyrosinase as a factor in these *Orconectes* experiments, where there was no appreciable darkening reaction in *Orconectes* blood.

The copper test used here provides an aid to identifying and localizing haemocyanin on invertebrate blood protein patterns. It offers another demonstration^{4,5} of the unique opportunities available

close as possible to the muscle. The photocell is protected from the 366 m μ radiation by a Wratten W-2 filter or by a combination of this filter with a Bausch and Lomb interference filter transmitting a 15 m μ band peaking at 450 m μ . Both filter combinations gave satisfactory results. The photocurrent was amplified by high gain chopper amplifiers and recorded by a galvanometer oscillograph. A 'bucking-out' circuit was used and the increment of fluorescence caused by electrical stimulation is recorded. The scale of the ordinate is given by independent spectrophotometric measurements (Fig. 1).

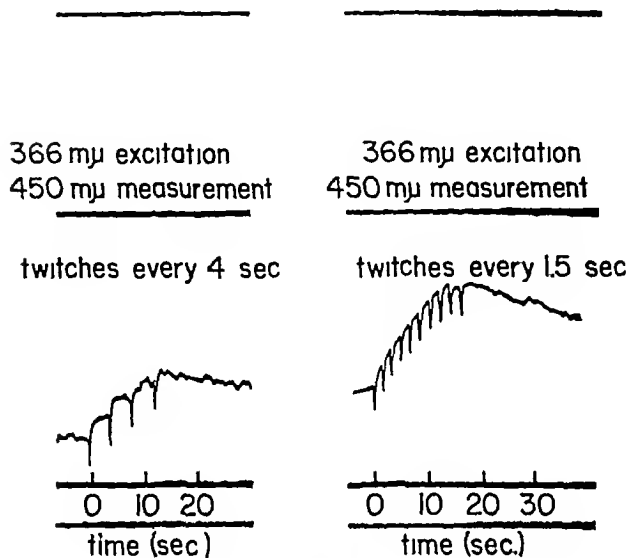


Fig. 1. Fluorescence response of frog sartorius muscle to electrical contraction at 4 (left) and 1.5 (right) second intervals. The right-hand record indicates a 'saturating' effect. Independent spectrophotometric studies give the concentration scale for the ordinate: this saturating effect corresponds to the oxidation of 0.035 μ moles/gm reduced pyridine nucleotide (ref. 8).

The excised frog's sartorius muscle was contained in a holder where oxygenated Ringer flowed freely past the exposed portion of the muscle^{3,7}. The muscle and the bathing fluid were cooled to 8°.

Fig. 1 illustrates two responses of the fluorescence of the sartorius muscle to a series of twitches. Electrical stimulation is applied every 4 sec in one case and every 1.5 sec in the other case. The twitch of the muscle is indicated as the small and abrupt deflexion on the trace which marks the moment of contraction. There is a decrease of fluorescence in a staircase fashion for the lower stimulation rate. At the higher stimulation rate the fluorescence change reaches a plateau, beyond which further stimulation causes little change. A comparison of these results with those obtained spectrophotometrically⁸ suggests that the same phenomenon is being recorded in both cases: the oxidation of reduced pyridine nucleotide caused by increased adenosine diphosphate concentration at the mitochondria. If we then accept the similarities of the kinetics as sufficient basis to identify the fluorescence decreases changes with the oxidation of intramitochondrial reduced pyridine nucleotide, we can make the following statement: (1) The concentration of adenosine diphosphate arriving at the mitochondria following a single twitch is a small fraction of that required for half-maximal activation of spectroscopic effects in isolated mitochondria (0.056 μ moles/

gm^{2,3}). (2) The staircase response for the 4 sec twitches emphasizes that the low concentration of adenosine diphosphate per twitch applies not only to the first twitch but also the second and possibly later twitches of the frog sartorius muscle.

This method has much to recommend it in terms of simplicity and sensitivity. In addition it may have the further advantages of (a) being applicable to a thick layer of muscle and (b) being relatively insensitive to haemoglobin. It may therefore be much more readily applicable to intact tissues than the spectrophotometric method.

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Frequencies of the Haptoglobin Groups in 406 French Blood Donors

The method of zone electrophoresis in starch gel enabled Smithies¹ to describe three haptoglobin groups in human sera. Using a standard technique previously reported^{2,3} we have examined the sera of 406 blood donors living in Paris. In each 'Plexiglas' tray (internal dimensions 234 mm \times 80 mm \times 6 mm) three serum samples mixed with a haemoglobin solution (0.05 ml of a solution containing 50 mgm of haemoglobin being added to 1 ml of serum) were allowed to migrate simultaneously, side by side, for 18 hr, under a potential of 100 V. After electrophoresis the starch gels were divided into two slices and stained, one with amido black, and the other with benzidine reagent for peroxidase activity. The technique was the same as that previously described and used to detect haemoglobins in agar gels⁴ but without using zinc acetate as a solution.

The haptoglobin groups were quite easily identified (Figs. 1 and 2). Particularly the difference between Hp 1-2 and Hp 2-2 was clear-cut: their electrophoretic patterns are very different and it will be seen that the haptoglobin-haemoglobin complex moves more slowly in group 2-2 than in group 1-2.

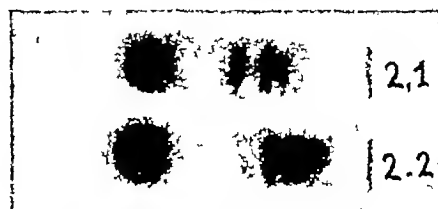


Fig. 1

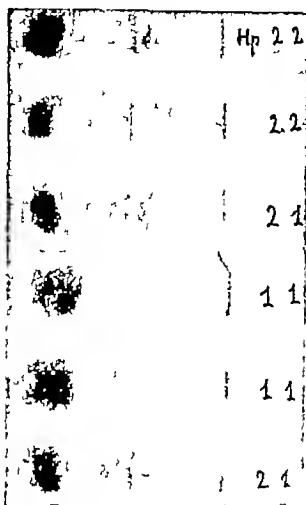


Fig 2

The frequencies of the three groups are in agreement ($\chi^2=0.505$ for 1 degree of freedom) with the genetical theory proposed by Smithies and Ford Walker* (Table 1). The gene frequencies are $Hp^1=0.4015$, and $Hp^2=0.5985$. These figures are not significantly different from those already reported, in populations of European origin by some workers, particularly from the important series of Galatius Jensen in Denmark. No mention is made in Table 1 of the results collected in a British and in a Basque sample by Allison *et al.*⁴, who found a fourth haploglobin group (0-0) and whose British series differs significantly from the expected frequencies calculated from the simple two alleles theory. We shall not discuss the interesting finding of the 0-0 group not the cause of the discrepancy: presumably it is attributable to differences in technique.

Table 1

| Authors | Total (N) | Haploglobin groups | | | | | |
|--|-----------|--------------------|--------------|-----|--------------|-----|--------------|
| | | 1-1 | | 1-2 | | 2-2 | |
| | | No | Per cent age | No | Per cent age | No | Per cent age |
| Sutton <i>et al.</i> (ref 7) (U.S.A., Canada)* | 103 | 10 | 16.53 | 54 | 52.43 | 33 | 33.04 |
| Galatius-Jensen (ref 8) (Denmark) | 2 040 | 328 | 16.03 | 967 | 47.26 | 761 | 36.71 |
| Laurell and Grubb (ref 9) (Sweden) | 46 | | 16† | | 50† | | 35† |
| Fleischer and Lundvall (ref 10) (Norway) | 500 | | 16† | | 45† | | 33† |
| Present survey (France) | 408 | 62 | 15.27 | 202 | 49.75 | 142 | 34.98 |

* Quoted from Sutton *et al.* who pooled the figures given by Smithies with their own.

† The percentage only was given in the original paper.

If we use only comparable figures, it seems reasonable to consider, from the results of Sutton *et al.*, Smithies, Galatius-Jensen, Laurell and Grubb, Fleischer and Lundvall, and from our own results, that in most of the populations living in the

occidental and septentrional part of Europe and in the white population of America, the frequencies of the genes Hp^1 and Hp^2 do not differ appreciably from 40 to 60 per cent respectively. We agree, however, that the complete system may be much more complicated.

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RADIO BIOLOGY

Increased Oxygen Consumption in Rats during Irradiation

METABOLIC changes arising during irradiation are of great importance for understanding the mechanism of the effects of radiation. In work on such changes in rats we have used the estimation of oxygen consumption as a general indicator of the metabolic state.

We used 40 rats (Wistar strain) females, average weight 190 gm. oxygen consumption was measured during irradiation at a dose rate of 50 r/min in every animal separately. The measurements were carried out in boxes 8 cm \times 8 cm \times 10 cm. The amount of air passing the box was regulated in accordance with the body weight of the experimental animal and was determined by the following formula. Amount of air (cm³/in⁻¹) = weight of animal (g) \times 2.5. The procedure was as follows. The animals were kept in the box for 50 min. During the first 20 min they became adapted to the experimental conditions. In the period 20-50 min oxygen consumption was measured. The oxygen consumption between the 20th and 30th minute was taken as the basic value (100 per cent). During the period 30-50 min the rats were subjected to total body irradiation (180 kV, 15 m.amp, 1 aluminium, 0.5 copper, focal distance 40 cm, dose rate 50 r/min.)

The oxygen consumption of control animals was measured under the same conditions but without irradiation, and they were exposed to the noise caused by opening the lead diaphragm of the X-ray tube. This noise had no influence on the oxygen consumption of control animals.

The comparison of oxygen consumption of experimental and control animals is given in Fig 1.

At the time of decreasing oxygen consumption in control rats, that of irradiated rats rises. Increased consumption of oxygen takes place during the first

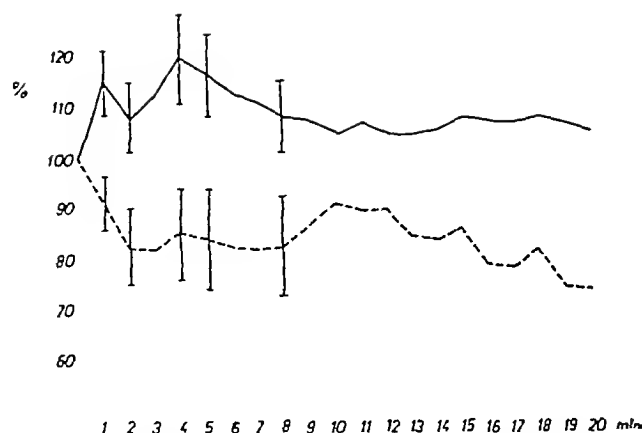


Fig 1 Comparison of the changes in oxygen consumption of control (---) and irradiated (—) rats. Standard error level is given by vertical lines

minute (50 r), at the fourth minute it reaches the maximum (200 r) and in the tenth minute it approaches the values before irradiation, but is still higher than in control animals

The difference in oxygen consumption in twenty irradiated and twenty control animals during the period from the first to the eighth minute of irradiation is statistically significant ($P > 0.01$)

We have found in the literature two reports on changes in respiratory metabolism during irradiation. In both cases the oxygen consumption was increased at higher doses of radiation than those we have used. In the first case, the rate of oxygen consumption was raised after a dose of 1,000 r in monkeys. In the second case, oxygen consumption of rats and mice was increased during irradiation with a dose-rate of 100 r/min. Our results are in accord with these, significant changes were found after the relatively low dose of 50 r

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Prophylactic Effects of Amine Oxides in Radiation Injury in Mice

In 1957, Haley *et al.*¹ found that quinoxaline-1,4-di-N-oxide reduced X-radiation mortality in mice by 50 per cent. Two mechanisms were involved, reduction of bacteremia¹ and interaction with X-ray-produced oxidizing radicals². Comparisons have been made of other N-oxides (Table 1) using groups of 20 CF-1 mice and the same radiation conditions as before¹. The 250 mgm/kg oral dose of drugs was given 24 hr prior to irradiation with 550 r. The two quinoxaline derivatives significantly increased the ST_{50} day but had less effect on total survival than quinoxaline-1,4-di-N-oxide. Erythromycin N-oxide significantly reduced the ST_{50} day and total survival while its anhydro derivative was equivalent to quinoxaline-1,4-di-N-oxide as a radiation prophylactic. All the above compounds are readily absorbed,

Table 1 ORALLY ADMINISTERED AMINE OXIDES AND SURVIVAL AFTER X-IRRADIATION

| Treatment | ST_{50} * and range Days | Slope and range | Total mortality | |
|--|----------------------------|------------------|-----------------|-----|
| | | | Per cent | Day |
| Saline control | 9.4 (8.4-10.5) | 1.29 (1.19-1.40) | 100 | 14 |
| 2,3-Dimethyl-quinoxaline-1,4-di-N-oxide | 12.4 (10.1-15.2) | 1.56 (1.32-1.84) | 85 | 30 |
| 6-Chloro-2,3-dimethyl quinoxaline-1,4-di-N-oxide | 13.4 (10.9-16.6) | 1.00 (1.35-1.90) | 80 | 30 |
| Saline control | 12.3 (10.0-14.3) | 1.41 (1.26-1.56) | 90 | 30 |
| Erythromycin N-oxide | 10.0 (9.0-11.2) | 1.20 (1.10-1.40) | 100 | 18 |
| Anhydroerythromycin N-oxide | — | — | 45 | 30 |

* ST_{50} , day upon which 50 per cent of animals are expected to be still alive. Confidence limits are calculated at $P = 0.05$ (ref. 3). All drugs 250 mgm/kg orally 24 hr pre irradiation

excreted slowly in the urine and exert antibiotic effects so the radiation bacteremia could be reduced. On the other hand not all of them can interact with equal facility with the radiation-produced oxidizing radicals. Examination of the chemical structures involved indicated that an amine oxide either in an unsaturated ring, for example, quinoxaline or within one carbon atom of a double bond, for example, anhydroerythromycin is necessary if oxidizing radicals are to be prevented from exerting their deleterious effects. In the dimethyl substituted quinoxalino compounds difficulties in oxidizing the methyl groups are probably the reason for the decrease in protectant activity even though Francis *et al.*⁴ showed that hydroxylation in the 2 position occurs *in vivo*. With erythromycin N-oxide, the double bond is lacking and the compound can be oxidized only with difficulty even *in vitro*⁵. Thus, it would appear that amine oxides with the above chemical structures can reduce mortality from ionizing radiation when administered orally 24 hr prior to exposure.

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PATHOLOGY

Formation of the Toxoid of Histamine Sensitizing Factor in *Bordetella pertussis*

It has been reported that mice injected with *Bordetella pertussis* vaccine become exceedingly sensitive to histamine.¹ Maitland *et al.*² found that antibacterial rabbit sera against *Bordetella pertussis* contain antibodies to histamine sensitizing factor. However, it seems that no biological definition of histamine sensitizing factor has been established. We believe that it is a toxin different from the accepted *pertussis* toxin. The present communication deals with formation of the toxoid of histamine sensitizing factor in *Bordetella pertussis* with the use of formalin.

The supernatant of a culture of *Bordetella pertussis*, strain 18-323, was prepared by a method already described.³ Formalin was added to the supernatant to give a concentration of 0.5 per cent. After various intervals of incubation at 37°C, the degrees of detoxification of the histamine sensitizing factor were examined. Tests of the antigenicity of the toxoid thus formed were also carried out.

0.5 ml of culture supernatant to which formalin had been added was injected intraperitoneally into dd mice, weighing about 20 gm each. Five days later the sensitivity to histamine of an inoculated group of mice was tested to determine the degree of detoxification. The mice surviving the histamine sensitivity test were inoculated 14 days later with either *pertussis* vaccine or culture supernatant in order to determine whether they were immune. Five days later their sensitivity to histamine was retested (Table 1).

Table 1 DETOXIFICATION OF HISTAMINE SENSITIZING FACTOR IN CULTURE SUPERNATANT AND ACTIVE IMMUNIZATION OF MICE WITH TOXOID OF HISTAMINE SENSITIZING FACTOR

| Incubation period of formalized culture supernatant at 37°C | Detoxification (loss of histamine sensitizing ability) | Immunization with toxoid against histamine sensitizing factor |
|---|--|---|
| 4 days | incomplete | no immunity |
| 7 days | complete | complete immunity |
| 10 days | complete | no immunity |
| 16 days | complete | no immunity |
| Control: Culture supernatant heated at 56°C for 30 min | no detoxification | no immunity |

As shown in Table 1, the culture supernatant heated at 56°C and containing histamine sensitizing factor without *pertussis* exotoxin activity, afforded the mice no immunity against histamine sensitizing factor. The antigen, when detoxified incompletely or incubated for a prolonged period (perhaps due to partial denaturation) gave the mice no immunity against histamine sensitizing factor, whereas a single injection of complete toxoid established complete immunity against it. Repeated administrations of an incompletely detoxified antigen gave no immunity. However, repeated injections of antigen after prolonged incubation afforded partial immunological protection. These findings suggest that even the presence of a small fraction of histamine sensitizing factor in *pertussis* antigens interferes with the establishment of immunity against it. The incubation period required for the formation of the complete

toxoid is subject to variation according to the preparation used.

The incubation period necessary for formation of toxoid of vaccine, in general, seems shorter than that of culture supernatant. It was estimated to be about 24 hr at 37°C. Formation of the toxoid did not occur following the addition of phenol or merthiolate to the antigen. The heating of the antigen at 80°C for 30 min. resulted in complete inactivation of histamine sensitizing factor and destruction of the antigenicity.

24 hr after intraperitoneal injection of 0.5 ml of freshly isolated sera of rabbit immunized with the toxoid, the mice received intraperitoneal injections of 0.5 ml (15×10^{10} organisms) of *pertussis* vaccine (killed by heating at 56°C) to test for the possible production of antibodies against histamine sensitizing factor. Five days later histamine sensitization was examined. One LD50 for a control group without immune serum was 29.8 mgm/kgm of histamine, while the LD50 for one group of passively immunized mice was more than 480 mgm/kgm, affording good evidence for the presence of antibodies against histamine sensitizing factor.

Rabbit immune sera were able to prevent a reduction in histamine inactivation of a homogenate of the organs of *pertussis* sensitized mice⁴ when the sera were inoculated 24 hr before administration of *pertussis* vaccine.

Thus, it seems reasonable to regard histamine sensitizing factor as a toxin, which apparently has nothing to do with preventive antigen(s).⁵

Immunologically it was demonstrated on rabbit sera immune against the toxoid of histamine sensitizing factor that the histamine sensitization due to *pertussis* vaccine has nothing to do with anaphylactic shock against horse serum.

Maitland *et al.*² and Stronk and Pittman⁶ reported that guinea pigs show no increase in susceptibility after the administration of *pertussis* vaccine. Nevertheless we found a marked reduction in histaminase activity of a homogenate of organs from *pertussis* sensitized guinea pigs using Kapeller Ador's method.⁷ No reduction was observed in the histamine inactivation of a homogenate where guinea pig ileum was employed following an extraction of histamine by a modified version of McIntire's method.⁸ However, at an early stage (first 2-3 hr) of the reaction between the homogenate and histamine, a marked reduction in histamine inactivation was observed when guinea pig ileum was used. The explanation of histamine sensitization in mice and rats, must await further studies, although a reduced activity in histaminase or histamine inactivation may account for a large part of the sensitization to histamine.

For the production of *pertussis* vaccine the existence of histamine sensitizing factor in *pertussis* antigens should not be neglected, because evidence for the existence of antibodies against histamine sensitizing factor in a human hyper immune serum was recently reported by Maitland and Guernli.⁹

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Effect of Chlorpromazine on Crocker Sarcoma and Ehrlich Ascites Carcinoma

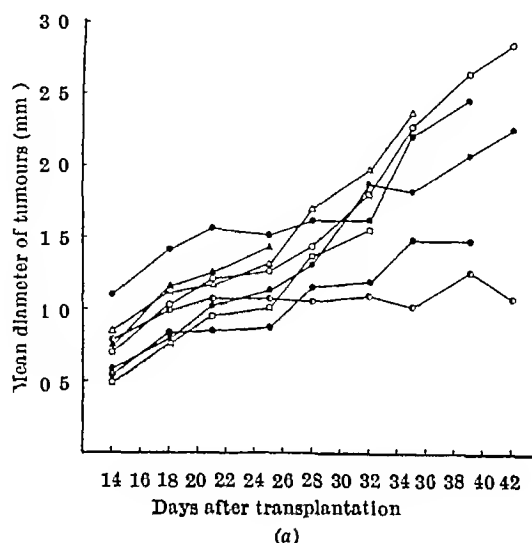
Goldin *et al.*¹ and Humpreys *et al.*² have stated that reserpine treatment in mice bearing transplanted leukaemia L 1210 caused regression of neoplasm and prolonged the survival time of these animals. These observations have directed attention to other tranquillizers as possible anticarcinogenic drugs. The growth of sarcoma 37 was inhibited by chlorpromazine treatment.³ However, according to Cranston⁴ some tranquillizers belonging to the phenothiazine group did not show any inhibitory effects on mammary adenocarcinomas in mice.

In our Department we have carried out some experiments dealing with the effects of chlorpromazine on Crocker sarcoma and Ehrlich ascites carcinoma in mice.

R III, *B_N* (an inbred strain from our own animal colony) and Swiss mice of both sexes were used. The initial weight of mice was 25–30 gm. Chlorpromazine ('Largactil'—Société Parisienne d'Expansion Chimique S.A., Specia) was given daily intraperitoneally at a dose of 2.5 mgm/kgm body-weight in about 0.25 ml physiological saline. A control group was given saline alone.

The rate of growth of Crocker sarcomas was measured by the mean diameter of the tumours, and that of Ehrlich ascites carcinomas by daily weighings of the mice and by noting their survival times.

The growth of Crocker sarcomas in chlorpromazine-treated and control mice is shown in Fig. 1. Chlorpromazine seems to have no inhibitory effect on this neoplasm—the tumours grew at the same rate as in the control group, despite the depressive effect of chlorpromazine on mice.



Chlorpromazine did not prolong the survival time in R III mice bearing Ehrlich ascites carcinoma (Table 1). However, the gain in weight of these mice was much smaller than that in control mice. The diminished gain in weight was due to the smaller gain in carcass weight, as well as to smaller production of ascites fluid. Analogous results were obtained with Swiss mice (Table 1).

Thus chlorpromazine had no inhibitory effect on the growth of either tumour despite the depressive

Table 1 SURVIVAL TIME AND WEIGHT CHANGES OF R III AND SWISS MICE BEARING EHRlich ASCITES CARCINOMA

| Strain and sex | Group | Days after transplantation | | | | | | | | | | | | | | | | |
|----------------|----------------------------------|----------------------------|------|------|------|------|-----|-----|-----|-----|-----|-----|-----|-----|------|------|-----|-----|
| | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 |
| R III ♂ | Control | 14 | 14 | 14 | 14 | 13 | 13 | 13 | 13 | 13 | 13 | 13 | 12 | 11 | 11 | 8 | 5 | 2 |
| | Average weight gain/mouse (gm.) | 0.0 | -0.5 | -0.2 | -0.1 | 2.0 | 1.3 | 2.4 | 4.1 | 4.6 | 4.8 | 5.5 | 5.2 | 3.8 | 4.1 | 3.8 | 5.1 | 7.8 |
| R III ♂ | Chlorpromazine† | 14 | 14 | 14 | 14 | 14 | 14 | 14 | 14 | 14 | 14 | 14 | 14 | 14 | 4 | 3 | — | — |
| | Average weight gain/mouse (gm.)* | 0.0 | -0.7 | -0.4 | 3.3 | 0.9 | 1.8 | 2.2 | 2.2 | 3.2 | 2.0 | 1.1 | 0.8 | 3.0 | -2.2 | -1.0 | — | — |
| R III ♂ | Chlorpromazine‡ | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 3 | 3 | 2 | — | — | — | — |
| | Average weight gain/mouse (gm.)* | 0.0 | -0.1 | -0.3 | 0.4 | 0.7 | 0.9 | 0.9 | 0.7 | 0.5 | 0.3 | 1.4 | 0.6 | 0.2 | — | — | — | — |
| Swiss ♂ | Control | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 14 | 12 | 6 | 1 | — | — |
| | Average weight gain/mouse (gm.)* | 0.0 | 1.2 | -0.4 | -1.0 | -0.4 | 1.4 | 2.1 | 3.6 | 5.0 | 5.5 | 5.1 | 5.0 | 4.0 | 5.0 | 5.6 | — | — |
| Swiss ♂ | Chlorpromazine† | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 11 | 11 | 9 | 4 | 1 | — | — |
| | Average weight gain/mouse (gm.)* | 0.0 | 1.0 | 0.2 | -0.7 | -0.5 | 1.2 | 0.8 | 1.1 | 1.1 | 1.1 | 3.3 | 2.2 | 3.6 | 8.0 | 2.2 | — | — |

* Weight changes as compared to the weight on the first day after tumour implantation

† 2.5 mgm/kgm body-weight every day until twelfth day after implantation of tumours

‡ 2.5 mgm/kgm body-weight every two days

The treatment was started on the first day after tumour transplantation

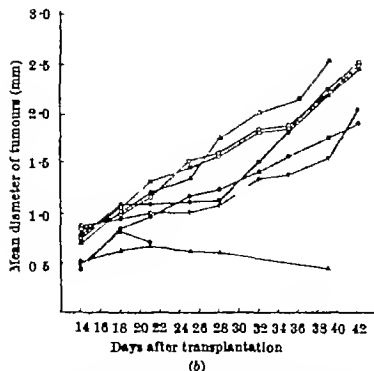


Fig. 1 The growth of Crocker sarcoma in B₆ mice. The rate of tumour growth is expressed as a mean diameter of the tumour (arithmetic mean of three diameters at right angles). Each curve represents the growth of single tumour: (a) Control mice (b) chlorpromazine-treated mice

action of the drug. The daily dose administered by us was much smaller than that given by Belkin and Hardy³. We found that a single dose of 10 mgm/kgm. that is, five times smaller than that used by Belkin and Hardy, caused a high mortality among the animals.

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Inhibition of Tumour Growth with 2,5-Dicarboxy-3,4-Dihydroxy-Thiophene

The possibility of preferential inhibition of tumour growth by antimetabolites of hexose monophosphate pathway intermediates was suggested by Sahasrabudhe¹. In pursuance of this suggestion it was shown that thiophene-2,5-dicarboxylic acid, administered as its sodium salt, significantly inhibited the growth of transplantable fibrosarcoma in mice and also increased the survival of Yoshida (ascites) sarcoma bearing rats². It was further shown that since this sodium salt is soluble in water, it was probably excreted rapidly. When the total daily dose of thiophene-2,5-dicarboxylic acid was increased and the injection schedule evenly spaced during the day to maintain adequate drug concentration, it was found that the inhibitory effects were significantly enhanced. It was therefore felt that if the free carboxy groups of the acid were esterified to reduce its solubility in water, the drug concentration might remain steady in the system for longer periods. In addition to this if two hydroxy groups are introduced at the third and fourth positions of the thiophene-2,5-dicarboxylic acid molecule, it was thought that the resemblance between the sugar intermediates of the

hexose monophosphate pathway and the antimetabolite would be increased and the effectivity against cancer might also increase. With these objectives in view 2,5-dicarboxy-3,4-dihydroxy thiophene (hereafter referred as 'Dicetol') was synthesized³. Dicetol is insoluble in water and therefore it was converted into a water soluble disodio-dicetol by treatment with ethanolic sodium ethoxide to facilitate its administration in aqueous medium. Disodio-dicetol readily hydrolyses in the presence of carbon dioxide. It was therefore felt that the water soluble compound used for practical reasons, would be transformed in the body into an insoluble dicetol which would probably be retained in the system for longer periods. The present communication reports the results of preliminary screening trials with disodio-dicetol.

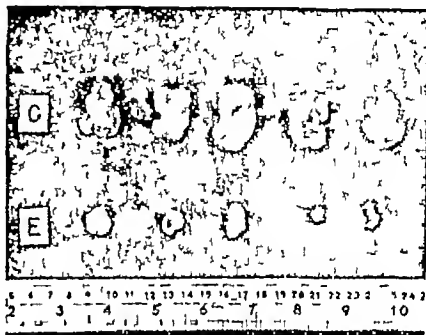


Fig. 1 Inhibition of growth of transplantable fibrosarcoma with disodio-dicetol. Top row (C) tumours from control group. Weight of tumours in this group are from left to right: 4.14, 3.61, 5.47, 4.56 and 4.33 gm. respectively. Bottom row (E) shows tumours from treated group. Weights of tumours in treated group from left to right are 1.12, 0.40, 0.92, 0.10 and 0.11 gm. respectively. Treatment was started on the eighth day after transplantation and continued for 15 days. Dose: 150 mgm/kgm body weight/day of disodio-dicetol.

Six to eight weeks-old Swiss mice weighing 20-25 gm were used. The transplantable fibrosarcoma used in the present investigation was originally obtained by Waravdekar and Ranadive⁴ from animals treated with 0.12 dimethylbenzo (1,2,5,4) dithionaphthalene. This has since been maintained in Swiss mice through several serial transplantations. Freshly dissected tumours were chopped to fine pieces and a homogeneous suspension made in normal saline. 0.5 ml of the tumour suspension was injected subcutaneously in each of the animals and the tumours allowed to grow for 8 days. Animals having uniform tumour sizes (visual observation) were divided into two groups. In the experimental group each of the animals received subcutaneous injections of disodio-dicetol in normal saline (1 mgm/0.5 ml) at 0900, 1600 and 2100 hr every day (total daily dose 3 mgm/animal). The corresponding control group received 0.5 ml normal saline only at the times mentioned. Injections were continued for 15 days. The animals were then killed and the weights and dimensions of the tumours determined. Fig. 1 shows the tumours from the control and treated groups placed side by side. The weights of individual tumours are indicated in the legend. The weights of tumours from the control group varied from 3.6 to

5.4 gm, whereas those from the treated group ranged from 0.12 to 1.12 gm. Thus there was significant inhibition of tumour growth in treated animals. Apart from the general reduction in the weights of the tumours in the treated group, there was evidence of regression in tumour size in some animals as can be seen from E4 and E5 in Fig. 1. Further, it is of interest to note that with the doses employed in the present investigation (3 mgm/day/animal, that is, 150 mgm/kgm body-weight/day for 15 days) there were no apparent signs of toxicity in the treated animals. Further work is in progress, details of which will be reported elsewhere.

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Appearance of Granules in the Cytoplasm of Tumour-Cell Cultures in Contact with Lysozyme

We have tried to establish whether or not lysozyme added in appropriate concentrations to human tumour cell cultures can produce some morphological changes in such cells. The following human tumour cells were utilized: strain Af (H Ep 2) of epithelial nature and strain A (H S 1) of mesenchymal origin. These strains were kindly supplied by Dr. A. Fjelde, State Serum Institute, Copenhagen.

Gey's liquid medium, without addition of antibiotics, was used in roller tubes. The colonies were treated two or four days after culturing and after growth had been found to be normal. At this point the liquid medium in the tube was replaced by another containing lysozyme chloride in the following dilutions: 0.1, 1, 2.5, and 5 mgm/ml medium. The control tubes contained normal Gey's medium, without lysozyme.

The tumour colonies were tested after 20-min, 1-hr, 5-hr, 10-hr, 24-hr, 48-hr and 6-days contact with the medium containing lysozyme. Slides for microscopic examination were prepared from these cells. Smears were made by using a thin rectangular strip of blotting paper, the cell colony being made to adhere to one end, the blotting paper was then gently passed over the slide, so producing a smear. After drying, the smears were fixed and stained with May-Grünwald's and Giemsa's stains.

Many azurophil granules of various sizes (approximately 1 μ diam.) were observed in the protoplasm of numerous cells from the Af (carcinoma) and A (sarcoma) colonies treated with 2.5 and 5 mgm/ml of lysozyme chloride. These granules became evident, even if small and not very clearly distin-



Fig. 1 Photomicrograph of human cancer cell (Af) treated with lysozyme: the cytoplasmic granules are visible ($\times 300$)



Fig. 2 Photomicrograph of human sarcoma cells (A) treated with lysozyme: the cytoplasmic granules are visible ($\times 300$)

guishable, after 20-min contact with lysozyme, becoming more obvious and reaching the largest size after 48 hr. or more.

The HeLa strain cultivated in Hanks medium, in stationary cultures, gave the same results. The above-mentioned type of granular formations were not observed in the controls.

Other tests were performed on fibroblasts from chick embryos, human kidney cells and monkey kidney cells cultivated both in Gey's and Hanks medium and in roller or stationary tubes. Granules did not appear in the fibroblasts, but were, in contrast, seen in human and monkey kidney cells. However, they appeared much later (after 24 hr.) than in tumour cells, and their number was much lower.

Another test was performed on cells taken from the ascitic fluid of a patient with cancer of the peritoneum. The cells were seeded in Gey's medium, following the roller tube method, and the lysozyme added immediately. The granules were very numerous in the tumour cells but absent from the cytoplasm of the lymphocytic type cells present in the liquid.

The following tests were performed in order to determine the chemical nature of the granules.

(1) *Lipids* Negative results of tests with sudan III, sudan black and Nile blue sulphate. Observation of the granules in polarized light did not reveal birefractive images.

(2) *Nucleic acid* Feulgen's nucleic reaction and the ribonuclease digestion test gave negative results. The granules displayed a certain degree of acidophilia after ribonuclease treatment.

(3) *Polysaccharide* Periodic acid and fuchsin sulphurous acid treatment (Hotchkiss's test) indicates absence of detectable polysaccharides in the granules.

(4) On phase contrast microscopy the granules appear dark, with regular outline and various diameters. They occupy the cytoplasmic portion of the cell, leaving the zone occupied by the nucleus quite free. They also display poor Brownian movement.

(5) On vital staining with brilliant cresyl blue the granules all stain blue, and none become yellow. The granules are partially and weakly stained with Nile blue, there is no tendency to metachromatic staining.

(6) Toluidine blue tests reveal that the granules have a strongly metachromatic character (acidophilia).

Various hypotheses can be formulated with regard to the nature of granules.

(a) They might indicate cellular suffering caused by possible toxic action on the part of lysozyme. (b) Lysozyme treatment may reveal pre-existing formations in the cytoplasm. For example, it might be considered that the basic lysozyme cytoplasm links up with certain protein acids in the cytoplasm. (c) Particular differentiated structures in the cytoplasm such as mitochondrial or ergoplasmic formation may be revealed.

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BIOLOGY

Transport of Driftwood from South America to Tasmania and Macquarie Island

IN February 1955 a log about 10 ft long and 5 ft in girth was found washed up on a sandy beach just inside Port Davey harbour on Tasmania's south-west coast. It was lying between two logs of Huon Pine (*Dacrydium franklinii* Hook f.) an endemic conifer of Tasmania. Unlike those logs which were well covered with marine growth it was free from such growth although the surface was 'woolly' with many pebbles embedded in it. The ends of the log were sawn and one end grooved for towing by a wire rope. The wood was identified from its anatomy as a species of *Nothofagus*, which genus is represented in Tasmania, the south-eastern portion of the Australian mainland, New Zealand, New Guinea, New Caledonia and South America. Anatomically the genus can be divided into two easily distinguishable groups, the one covering the species of New Guinea and New Caledonia and the other the remaining species. The log in question was derived from the second of these two groups and, because of the presence of spiral thickenings in the vessel elements, its specific identity could be narrowed down to one of three possibilities, namely, *N. moorei* (F. Muell.) Krasser of northern New South Wales and south-eastern Queensland, *N. pumilio* (Poepp. and Endl.) Krasser and *N. obliqua* (Mirb.) Oerst. from South America. The spiral thickenings in *N. moorei* differ from those of the two South American

species: those of the unknown resembled the thick enings observed in the South American species. Both *N. pumilio* and *N. obliqua* are restricted to South America: the former occurring from Tierra del Fuego north to latitude 30° S on the western side of the Andes; *N. pumilio* *N. antarctica* (Forst.) Oerst. and *N. betuloides* (Mirb.) Oerst. are logged commercially in the southernmost tip of the continent. All the anatomical evidence thus pointed to a South American origin of the log in question although this conclusion met with some initial opposition.

We have found no reports in the literature of driftwood travelling over such long distances (10 000 miles). Cockayne mentions in passing that logs are carried from New Zealand to the Chatham Islands, a distance of 500 miles. Matthews states that the fjords of the west coast of South Georgia contain large quantities of driftwood much of it from wrecks but some consisting of 'the trunks and limbs of several trees one with root stumps at the butt'. Matthews concludes they must have drifted from where they grew 'for no one would have brought such crooked, useless timber across the ocean'. The nearest source would be Tierra del Fuego, about 1 000 miles away. The Australian National Antarctic Research Expeditions to Macquarie and Heard Islands have also reported gnarled driftwood on the beaches of these islands which, like South Georgia, are devoid of native trees.

A request for samples of driftwood from Macquarie Island brought twenty specimens collected by the 1957 party on the west coast and one from a large log on the south coast collected by the 1958 party. All have been identified anatomically. The original twenty consisted of twelve hardwoods, seven softwoods, and one piece of bamboo. All the hardwoods were identified as belonging to the genus *Nothofagus* and seven of these had the well marked spiral thickenings in the vessels characteristic of the South American species *N. pumilio* and *N. obliqua*, other anatomical evidence pointed to *N. pumilio*. The specimen from the large log, collected by the 1958 party, was also identified as probably *N. pumilio*. Only one log was sawn at both ends; the others had no saw or mill marks. The notes accompanying the specimens and the photographs supplied indicated that the logs varied in length from 1 ft to 15 ft and from 4 in. to 30 in. in diameter. One (Fig. 1) was a split boomerang shaped piece and another had root bases protruding at one end. Of the five specimens without spiral thickenings the notes record



Fig. 1. Boomerang-shaped piece of driftwood from the west coast of Macquarie Island identified as *Nothofagus pumilio*. This appears to have been derived from a large limb. The piece was 4 ft long 6 in. tapering to 4 in. in diameter. (Aided by H. MacKay.)

that two of the logs were sawn and that the other logs ranging from 5 to 10 ft in length and from 2½ to 7 in in diameter were not sawn.

There seems little doubt that this collection of specimens has been transported by ocean currents. It would seem most unlikely that some of the pieces had been taken on board ship, even as firewood, although the sawn logs could conceivably have been transported by ship. Eight of the logs were derived from species growing naturally only in South America, 10,000 miles from Macquarie Island, and there is little, if any, commercial traffic in these species outside Chile and Tierra del Fuego. The other five could also have originated from South America. The set of currents in the 'roaring forties' makes their origin from Tasmania or New Zealand most unlikely.

Of the seven softwoods five were identified as spruce (*Picea* spp.) a genus restricted to the northern hemisphere north of latitude 36° and, as far as we are aware, not planted on a large scale in the southern hemisphere. The logs were straight and varied in length from 5 to 15 ft and in diameter from 2 to 10 in. Three had sawn ends, the largest and smallest were not sawn. It is possible that these logs were transported by a ship which was wrecked in southern latitudes but the variation in diameter makes this less likely. Large quantities of spruce are harvested and transported by water down the rivers on both the Pacific and Atlantic coasts of Canada and the Northern United States. Many must escape. Whether some combination of ocean currents would transport them to Macquarie Island must be left for future investigation. However, it is of interest to note that Heyerdahl⁷ has reported the preference of the Hawaiians in the past for drift logs of Douglas fir (*Pseudotsuga menziesii* (Murb.) Franco) for the construction of their ancient canoes.

The remaining two conifers were of the genus *Pinus*, both were derived from logs 9 in in diameter. One was identified as belonging to the southern pine group (for example, *Pinus taeda* L., *P. palustris* Mill., etc.) the other to the white pine group (for example, *P. monticola* Dougl., *P. strobus* L., etc.). The natural distribution of this genus is restricted to the northern hemisphere but many species are widely planted in Australia, New Zealand and Chile. However, representatives of the above two groups are not the ones most commonly used. Thus the chances of these two conifer specimens having their origin in the southern hemisphere are remote.

This small collection of driftwood thus has a most varied geographical origin. There seems little reason to doubt that the *Nothofagus* specimens have drifted from Tierra del Fuego (longitude 70° W) to Macquarie Island (longitude 160° E) and the west coast of Tasmania (longitude 146° E) in the track of westerly winds. Sverdrup *et al.*⁸ give the speed of the surface current in the Antarctic circumpolar drift as 15 cm/sec. Using this figure, the time taken for a log to drift from South America to Macquarie Island would be over 3 years. This represents a maximum estimate of the time for the voyage, since, if any part of the log projects from the water, it will be 'sailed' through the water by the westerly winds. However, it is interesting to mention that a message bottle dropped about 1,250 miles to the west of Macquarie Island was recovered from the beach of that island 10 weeks later, giving a surface speed of, at least, 33 cm/sec.

It is strange that all the hardwoods found and

examined have proved to be *Nothofagus*. This may be an accident of sampling but is due, more probably, to the fact that in the extreme southern latitudes of South America *Nothofagus* forms almost pure stands. It is hoped to obtain further samples of driftwood from Atlantic and Pacific Islands in southern latitudes. In this connexion it is of interest to record that two such specimens have already been received from Tristan da Cunha (12° W) in the south Atlantic and both have been identified as *N. ? pumilio*.

Determinations of air-dry density on various samples of *Nothofagus pumilio* have given values around 32–35 lb/cu ft. In this respect, therefore, they are little heavier than most of the conifers including species of *Pinus* and *Picea*.

The bearing of these results on the problem of the floristic botany of the southern continents will be discussed elsewhere. However, it does not seem impossible for seeds to be overgrown in the wood or, as Darwin observed⁹, trapped and sealed into the interstices of the roots and then transported from one continent to another. This remote chance which has presumably been available for the 100 million years since the origin of the Angiosperms may be part of the explanation of the puzzling floral similarities of the southern tips of the continents.

We wish to acknowledge the help provided in collecting specimens by the officers of the Australian National Antarctic Research Expeditions, in particular Mr. Harry Black, Officer-in-Charge of the 1957 party at Macquarie Island, and by Mr. D. H. Simpson, Agricultural and Forestry Superintendent, Tristan da Cunha. We also wish to thank Mr. W. L. Davies of the Geography Department, University of Tasmania, for his help in discussing these problems of geography.

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Sterility in *Lathyrus odoratus* L.

MALE sterility in *Lathyrus odoratus* L. was first recorded by Bateson, Saunders and Punnett¹. Male sterility was absolute and was inherited as a single recessive gene linked to light axil and cretin². Fabergé³ and Upcott⁴ reported that the sterility resulted from disturbances in the meiotic division following normal metaphase pairing. Such plants were normal and fully fertile on the female side.

Table 1

| | No of crosses or selfs | Pods with seed | Total seed | Mean seed per pod | Mean seed per pollination |
|--|------------------------|----------------|------------|-------------------|---------------------------|
| Controlled self pollinations | | | | | |
| (a) Fertile plants | 54 | 29 | 127 | 4.4 | 2.3 |
| (b) Sterile plants | 50 | 0 | 0 | 0 | 0 |
| Crosses between fertile and sterile plants | | | | | |
| (a) Fertile \times σ | 52 | 10 | 22 | 2.2 | 0.42 |
| (b) Sterile \times σ | 50 | 0 | 0 | 0 | 0 |

during prophase (Fig 1), metaphase was characterized by complete asynapsis (Fig 2). The chromosomes

Sterility affecting both male and female gametes has recently been observed in an unnamed blue flecked variety of the sweet pea. (Seed of this variety was supplied by Mr D G Taylor of the Cheshire School of Agriculture.) The anthers contained a small amount of stainable pollen (5 per cent) which rendered them partially fertile as male parents. Table I shows the results of self and cross pollinating fertile and 'sterile' plants. From many hundreds of flowers on the 'sterile' plants, one pod set (from an uncontrolled pollination) containing two seeds. Hence sterility was almost complete on the female side and high on the male side. Cytological observations of the meiotic division in the pollen mother cells showed that although normal pairing occurred

during the first division remained undivided and were randomly distributed into two or more groups. Each group of chromosomes behaved normally for the completion of the meiotic division, though seldom was a viable gamete produced, as few of the first division segregations were genomically reductional. The cytological behaviour of this asynaptic form of *L. odoratus* closely resembled the observations reported by Blakeslee *et al*³ for the asynaptic variant of *Datura*.

Segregation ratios from heterozygous material suggest that this asynaptic sterility is controlled by a single recessive gene.

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Tolerance to Skin Homografts of Adult Mice after Parabiosis

Skin grafts between mice of different inbred strains are invariably rejected within a few weeks. Hybrid (F_1) tissues transplanted to mice of either parental strain are also consistently rejected at the same rate if the parents differ at the $H 2$ histocompatibility locus¹. This uniform incompatibility was not apparent when such hybrids were united in parabiosis with parental strain inbred mice. The most frequent result of such unions was the death of only the hybrid partner, usually within a month. Hybrid death in this period was characteristically preceded by a severe wasting disease sometimes described as parabiotic intoxication².

The variability of survival time of the parabiotic unions between different strain combinations is shown in Table 1. The F_1 hybrids were all crosses between inbred mice of different $H 2$ genotypes. All animals were of the same sex and 2-3 months old when united. The parabioses that persisted beyond 60 days were eventually terminated by the 'natural' death of both partners without manifestations of the wasting disease.

Of the combinations tried here, the parabiosis of the ($CSH \times DBA/2$) F_1 hybrids with $DBA/2$ inbred mice

Table 1. SURVIVAL TIME OF PARABIOTIC UNIONS BETWEEN INBRED STRAINS OF MICE AND THEIR F_1 HYBRIDS OF THE SAME SEX AND AGE (2-3 MONTHS)

| Combination in parabiosis | No of pairs done | Pairs survived beyond 60 days | Death of hybrids Time in days | |
|--|------------------|-------------------------------|-------------------------------|-------|
| | | | Average | Range |
| ($CSH \times DBA/2$) F_1 — $DBA/2$ | 71 | 29 | 19.7 | 13-31 |
| ($B6/129 \times DBA/2$) F_1 — $B6/129$ | 6 | 0 | 14.8 | 12-16 |
| ($B6/129 \times C57BL$) F_1 — $B6/129$ | 8 | 1 | 16.1 | 14-21 |
| ($C57BL \times C57BL$) F_1 — $C57BL$ | 15 | 0 | 26.1 | 8-57 |
| ($C57BL \times C57BL$) F_1 — $C57BL$ | 17 | 0 | 20.2 | 9-31 |
| ($DBA/2 \times DBA/2$) F_1 — $DBA/2$ | 4 | 1 | 23.0 | 14-33 |

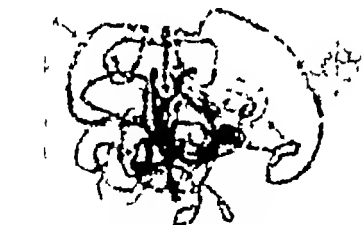


Fig. 1. Metaphase showing chromosome pairing as evidenced by (1) small impaired region, A and (2) probable inversion loop B. ($\times 1,500$)



Fig. 2. Metaphase I showing 14 unpaired chromosomes. ($\times 1,500$)

provided the most frequent stable unions. Fourteen such pairs that were not treated further survived in stable parabiosis for periods lasting 80–510 days. The two successful parabioses among other strain combinations in Table 1 survived 310 and 85 days.

Parabiotic pairs that had been together for about five months were used for the first skin grafting experiment (Table 2, Group 1). The full thickness skin of young ($C3H \times DBA/2$) F_1 hybrids were grafted to each of the five $DBA/2$ mice still in parabiosis. The grafts were all successful. Three months later the skin of inbred $C3H$ mice was placed adjacent to the earlier grafts. These were also uniformly successful, in spite of the major histo-incompatibility between the two inbred strains. Approximately two months later (10 months after parabiosis) all of the unions were surgically terminated. The host $DBA/2$ mice survived up to six months after the termination of parabiosis with all the grafts still in place. In the next experiment (Table 2, Group 2), 3 $DBA/2$ mice in parabiosis for 5 months were grafted only with $C3H$ skin. As soon as the skin was well established, the parabionts were cut apart. After another 2–3 months the grafts began to contract slowly, disappearing 3–4 months after the termination of parabiosis.

Table 2. RESULTS OF GRAFTING $C3H$ AND ($C3H \times DBA/2$) F_1 SKIN ON $DBA/2$ MICE AFTER PARABIOSIS WITH ($C3H \times DBA/2$) F_1 HYBRIDS OF THE SAME SEX AND AGE (2–3 MONTHS)

| Group | No of mice | Days after parabiosis at which indicated events occurred | | | | |
|-------|------------|--|----------------------|--|---------|-----------|
| | | Experimental | | | Results | |
| | | Skin graft while in parabiosis | Parabionts separated | Skin grafts ($C3H$) after separation | Slough | Dead |
| 1 | 5 | $\left\{ \begin{array}{l} 162-165 \\ (F_1) \\ 224-228 \\ (C3H) \end{array} \right\}$ | 307 | none | no | 418–488 |
| 2 | 3 | $\left\{ \begin{array}{l} 120-130 \\ (C3H) \end{array} \right\}$ | 176 | none | 298–317 | no (>400) |
| 3 | 1 | none | 306 | 401 | no | 446 |
| 4 | 2 | none | 154 | 209 | no | no (>270) |
| 5 | 2 | none | 82 | 98 | 144–171 | no (>270) |

In the following three groups (Table 2, Group 3–5), the $C3H$ skin was successfully grafted on $DBA/2$ mice after the parabiosis with the hybrid had already been terminated. In one instance an initial $C3H$ skin graft was accepted three months after separation of the parabionts. However, when the total period of parabiosis was just 82 days, compatibility lasted for only 2–3 months after the surgical parting. In other cases, where parabiosis had been allowed to persist for 5 months, the subsequent period of compatibility is continuing after 4 months.

It should be pointed out that in no case has a graft of $C3H$ or ($C3H \times DBA/2$) F_1 skin on untreated $DBA/2$ control mice shown comparable compatibility. More than 100 such control animals always rejected these homologous skin grafts within 3 weeks and never showed the full regrowth of hair that was characteristic of the good acceptance of $C3H$ skin in the parabiosed $DBA/2$ mice.

When ($C3H \times DBA/2$) F_1 hybrids died by the wasting disease during the early weeks after the parabiosis,

the surviving $DBA/2$ partners were tested for their reaction to grafts of $C3H$ skin. In these cases, the outcome was a typical 'second set' reaction, the rapid and violent rejection of the foreign skin. Evidently antibodies were already present when the skin homograft was presented. Other recent evidence^{3–4} indicates that the 'wasting disease' syndrome, as seen in the hybrid, is the consequence of an immunological reaction of parental strain lymphoid elements against hybrid tissues. The reverse cannot occur, the hybrid does not produce antibodies to parental strain tissue. Therefore, as expected, the wasting disease was never seen in the parental strain in parabiosis with its hybrid.

The present observations may perhaps be interpreted in the context of other studies^{5,6}, where the injection of blood and minced tissues create 'enhancement' of transplantation, rather than immune rejection. The deciding factor in these experiments seems to be the quantity of antigen and the mode of injection. While small inocula given subcutaneously provide immunity and rejection, large amounts given intravenously may do the opposite—promote tolerance. In this light, the rejection of homografted skin may be considered the result of a small antigenic stimulus by the graft itself, while the occurrence of successful parabiosis is always preceded by the continuous intravenous exchange of large amounts of antigen. Only after such successful parabiosis was tolerance to homotransplantation demonstrable.

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Common Attractant for the Tobacco Hornworm, *Protoparce sexta* (Johan) and the Colorado Potato Beetle, *Leptinotarsa decemlineata* (Say)

THE specificities of oligophagous insects to groups of related plants have been postulated and demonstrated in several instances to be mediated by secondary plant substances of limited distribution (reviewed by Dethier¹ and Fraenkel^{2,3}). These substances are variously called attractants, taken stimuli, or phagostimulants when they serve in such capacity and are generally tested on the feeding stages of the insects concerned by applying the substances on various artifices such as filter paper, pith disks, non-host leaves or agar gel diets. The insects are then allowed to discriminate the presence of the attractants by biting or feeding.

The function of specific substances in the feeding

behaviour of the Colorado potato beetle *Leptinotarsa decemlineata* (Say) has recently been a centre of interest in many laboratories, especially in France Germany, and the U.S.S.R. (see, for example the report of the symposium on "Insect and Foodplant" held at Wageningen¹). While most of the relevant work deals with the identity and function of glyco alkaloids in Solanaceae as factors of repellency or toxicity, the nature of the specific attractant has commanded little attention. Hesse and Moier² claimed acetaldehyde as the specific attractant, but this claim was not substantiated by later workers. Earlier, Chauvin³ reported the isolation from potato leaves of an attractive substance which was tentatively identified as a flavono glycoside. The technique was improved later⁴ and the attractiveness of the substance was confirmed by Thorsteinson⁵. During an investigation of the oligophagous habits of the tobacco hornworm, *Protoparce sexta* (Johan), which also feeds on members of the same family of plants Solanaceae, a glycosidic substance attractive to this insect was isolated from several plants including tomato and potato⁶. We had an opportunity to assay this material on filter paper against the Colorado potato beetle and found that the material was also highly attractive as a feeding stimulant for the beetle (Fig. 1).

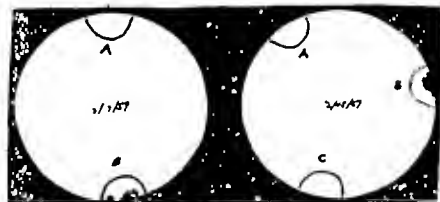


Fig. 1. Biting responses to the attractant purified from tomato leaves by the Colorado potato beetle (left) and the tobacco hornworm (right). A and C on the filter paper are control spots on which 0.01 M of sucrose was applied. B represents test spots on which a solution of the attractant was applied.

The chemical identity of this substance has not been elucidated as yet, but preliminary characterizations indicate that it is not a flavonoid derivative. In our experiments flavonoids were removed before subsequent purification and hence the flavono glycoside claimed by Chauvin as the active substance for the Colorado potato beetle might have been present in his preparation as an impurity. The results of our bioassay strongly suggest that the specific attractant for the potato beetle and tobacco hornworm is identical.

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GENETICS

Simultaneous Change in Both Differential and Interference Distances of Chiasmata

On the basis of a serial formation of chiasmata in time beginning from the centromere the effect of experimental factors on chiasma formation has been interpreted in terms of the two parameters differential and interference distances¹⁻³. By differential distance is meant the distance of the first chiasma from the centromere, and by interference distance the length of the chromosome arm between the successive chiasmata. With a change in the differential distance alone the graph showing the relation between chromosome length (x) and chiasma frequency (y) has a series of parallel lines for different temperatures, intersecting the line $y = 1$ at their respective differential distances (Fig. 1a). Mather² interprets Whitt's results⁴ from temperature experiments as showing this type of effect. On the other hand, if only the interference distance changed, the different lines would radiate from the same point (Fig. 1b). Mather² again explains the data of Moffatt⁵ on different individuals of *Culex* as representing this type of change. Apart from these examples by Mather which have become classical in studies on chiasma frequency there does not seem to have been any other interpretation of results along such lines. Data was therefore extracted from experiments of mine^{6,7} which had shown that temperature reduced chiasma frequency per pollen mother-cell in the bluebell, *Endymion nesciutus* (L.) Garek.

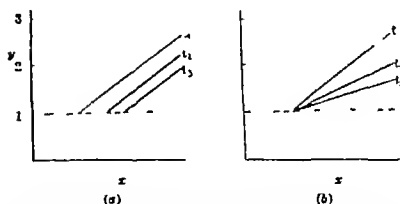


Fig. 1. (a) Graphical representation of chiasma frequency-chromosome length relationship when there is a change in differential distance only. (b) Graphical representation of chiasma frequency-chromosome length relationship when there is a change in interference distance only.

The data for the present study came from three clones (C_1 , C_2 , A_{11}) two of which consisted of two individuals each and the third one of three individuals.

The two plants of each of clones C_1 and C_2 were placed at temperatures of 10° and 25°C., and the three plants of clone A_{11} at 0°, 10° and 25°C. It is not possible to give the full results here; they will

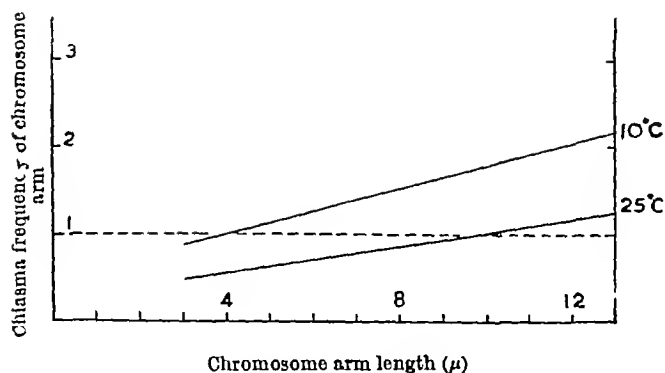


Fig. 2 Regression lines for relation between chromosome length (long arms of the complement) and chiasma frequency at 10° and 25° C (in clone C_6) in the bluebell, *Endymion nonscriptus*

be published elsewhere. They consisted of the mean chiasma frequency of each bivalent as well as its component arms in each of the plants under study (see also ref. 6). The present studies were confined to the long arms of the chromosome complement since they could each form more than one chiasma.

The graphs showing the relation between chromosome length in microns (x) and chiasma frequency (y) for each plant at a particular temperature were constructed from corresponding calculated regression lines between (x) and (y) as described below.

Clone C_6 . At 10° C the regression coefficient b was 0.1264 which was highly significant, $F = 20.5869$ ($P < 0.001$), at 25° C, b was 0.07276, also significant, $F = 18.3367$ ($P < 0.001$). The calculated regression lines are shown in Fig. 2. The two lines are clearly separated from each other and they have different slopes. They would be expected to be parallel if there was only a change in differential distance.

Clone C_8 . At 10° C the regression coefficient b was 0.13601 which was highly significant, $F = 17.37465$ ($P < 0.001$), at 25° C, b was 0.11058, also highly significant, $F = 22.6005$ ($P < 0.001$). The calculated regression lines are similar to those for clone C_6 in showing not only a change of position but also of slope. In fact, they seem to combine parallel and 'radiating' lines at the same time as one would expect with a change in both differential and interference distances.

Clone A_{18} . This clone with three plants was examined for this relationship at 0°, 10° and 25° C. The regression coefficient was significant ($P < 0.001$) at each temperature (at 0° C, $b = 0.11297$, $F = 25.4306$, at 10° C, $b = 0.11489$, $F = 36.5462$, at 25° C, $b = 0.11175$, $F = 76.1858$). The calculated regression lines show a much smaller change in slope than those for clones C_6 and C_8 , but the change is still clear. This could be inferred from the similarity in the regression coefficients at the three temperatures in clone A_{18} , and is probably also due to the relatively smaller decrease in chiasma frequency in this clone between the temperatures 10° and 25° C as compared with those in clones C_6 and C_8 . Thus it seems that in clones C_6 and C_8 , and A_{18} , both the differential and the interference distances have been altered by temperature.

Further examination was made of the long arms of the long chromosomes. Since there seems to be a better correlation between chromosome length and

chiasma frequency of the long chromosomes in a varied chromosome complement than of the shorter ones², the long arms of chromosomes A , B , C and D , which could each form up to three chiasmata, were used directly in plotting a relationship between their lengths in microns and chiasma frequency at 10° and 25° C. From these it is clear that the same sort of relationship of the two lines is obtained by this direct plotting, that is, the lines show clearly not only a change of position but also of slope.

The present results suggest a simultaneous change in both the differential and interference distances with changing temperature. A case of this joint change does not seem to have been predicted or reported. The examples given by Mather³ deal only with an independent change in either parameter.

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Anomalous Genetic Interactions observed in *Bacillus subtilis*

GENETIC transformation in *B. subtilis* has recently been reported by Spizizen¹, but as yet no paper has appeared discussing genetic interaction between the cells of spore-bearing bacteria. In this communication, a new fact will be described which was discovered while attempting to cross auxotrophic mutants of *B. subtilis* K. It involves the *de novo* appearance of characters not present in the parent strains. The complete details of this work will be published elsewhere.

Two mutants were employed: $T16$ —try, ade, str-r (requiring tryptophan and adenine, and streptomycin-resistant), and $M12$ —met, his, str-s (requiring methionine and histidine, and streptomycin-sensitive). These biochemical mutants were obtained after exposure to X-rays, and the streptomycin-resistant strain was obtained by Szybalski's agar-gradient method.

The mutants were cultivated in nutrient broth at 30° C until the cell density reached about 10^8 /ml. Centrifuged cells were washed once with phosphate buffer and the cell suspensions were plated in mixture on synthetic media supplemented with various nutrients (see Table 1). After four days at 37° C a considerable number of tiny colonies appeared on the supplemented media, but nothing appeared on the minimal medium. In general, the tiny colonies were analysed by spreading cell suspensions prepared by homogenizing the colonies in a small blender on various media.

Table 1 FREQUENCIES OF TINY COLONIES

| No. of cells plated | No. of tiny colonies appearing on | | | |
|--|-----------------------------------|----------------------|----------------------|----|
| | THS | TMS | MHS | MM |
| 716×10^7 + 312 1.0×10^7 | 14 | 8 | 44 | 0 |
| Frequencies | 1.6×10^{-7} | 9.1×10^{-8} | 5.0×10^{-7} | — |

Total cell number was determined on nutrient agar. It was impossible to count tiny colonies on MHS and MM on account of the rapid growth of back mutants.

MM: Gray and Tatum's agar medium. THS: MHS plus tryptophan 60 μ M, histidine 60 μ M and streptomycin 100 μ M. MHS: MHS plus methionine 60 μ M, histidine and streptomycin. TMS: MHS plus tryptophan, methionine and streptomycin.

(1) The occurrence of a *met*, *his*, *ura* *str* *r* strain in two tiny colonies which appeared on THS medium were subcultured on the same medium. After 2 days the cells resulting from each tiny colony were analysed. In all cases, both *try* *ade* *str* *r* and *met* *his* *ura*, *str* *r* progeny were obtained (for example one tiny colony consisted of 13×10^7 *try* *ade* *str* *r*, and 0.5×10^8 of *met*, *his*, *ura*, *str* *r*). In another experiment which was repeated from the beginning, the *met* *his* *ura* *str* *r* progeny were again obtained from the cell suspension which was prepared directly from a tiny colony but this time *try*, *str* *r* progeny were recovered instead of *try*, *ade*, *str* *r*. The appearance of the *met*, *his* *ura* *str* *r* type is of particular interest, because the requirement of uracil for growth is a new character which did not exist in the parental strains.

grow on MHS, TA and nutrient agar but not on MH medium. (b) cells grown on TA or nutrient agar yielded no colonies on MHS medium, (c) the morphology of the colonies on nutrient agar with streptomycin was different from that of T16 (Fig 1), and they could grow on MHS but not on TA or TAS media but when one of them was cultivated in nutrient broth supplemented with streptomycin they segregated out *try* *ade* *str* *r* progeny with a frequency of 10^{-2} . (d) no streptomycin sensitive progeny were obtained at all.

These facts (see Fig 2 for summary) indicate that the streptomycin dependent cells when subcultured on MHS medium maintain the potentiality to segregate *try* *ade* *str* *r* progeny. This phenomenon may be explained by the assumption that the streptomycin dependent progeny consisted of single cells which had a whole chromosome of T16 and a fragment of M12 at the same time. But the two genetic units might not fully complement one another.

A similar genetic interaction between two types of genome was reported by Bradley in *Str. colicolor*².

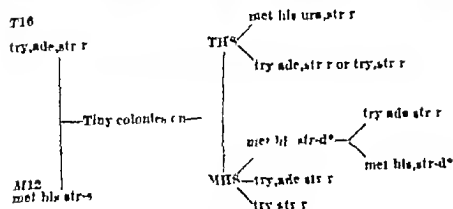
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April 1

¹ Spatzen J. Proc. L. N. Var. Acad. Sci. 44 1072 (1958)
² Bradley S. G. J. Bacteriol. 78 464 (1958)



Fig 1 Colonies on nutrient agar with streptomycin



* Phenotypic expression
Fig 2 Progeny of tiny colonies

(2) The occurrence of streptomycin dependent strains One of the tiny colonies on MHS was analysed by spreading a cell suspension on various media. It was found that the colony consisted of a large number of *try* *ade* *str* *r* (335×10^3), and a small number of *try*, *str* *r* cells (133×10^3) nothing was observed on MH medium. Despite the fact that no colonies appeared on MH medium, a considerable number of colonies (153×10^4) did appear on MHS medium. These colonies behaved as follows: (a) the cells

GEOGRAPHY

Evidence of a South Equatorial Countercurrent in the Pacific Ocean

An eastward flowing current of speeds from 10 to 25 cm/sec is indicated along a density surface ($\sigma_t = 26.81$) in the Pacific Ocean south of the equator in a position roughly symmetrical to that of the (North) Equatorial Countercurrent. Along this surface the current is found between lat 2° S and 8° S at long 105° E and progressively farther south toward the east, to between lat 10° S and 14° S at long 95° W. The depth of this surface rises to the south along the flow, from 400 to 300 m in the west and from 400 to 350 m in the east.

The evidence lies in the calculations of geostrophic flow along this surface with respect to 1,000 decibars¹. The eastward geostrophic flow is indicated on ten cross sections made by the *Equapac* expeditions (joint surveys carried out by agencies from France, Japan and the United States) in late summer of 1956, on three sections made by the *Carnegie* cruise of 1929-30 ref 2 and by combinations of stations from the *Carnegie*, *Eastrop*³ and *Downwind* (Univ. of Calif. Scripps Inst. of Oceanogr., unpublished reports) expeditions.

On this surface the path of the eastward flow coincides with a tongue of high salinity extending eastward from a maximum value in the Coral Sea.

North of the equator the (North) Equatorial Countercurrent is indicated on the same density surface by calculations of geostrophic flow. The depth of the surface rises to the north from more than 400 m at the equator to a ridge of depth less than 300 m at lat 6° N long 175° E. The ridge extends eastward to lat 10° N long 145° W at less than 300 m. It continues from there to lat 6° N.

long 115° W, where its depth is about 350 m. The eastward flowing current is evident on this surface between lat 2° N and 5° N in the west, from lat 4° N to 8° N in the central ocean, and from lat 5° to 10° N at long 120° W, and is indicated on all of the *Equapac* sections and the pertinent *Carnegie* and *Eastropic* sections all the way to the coast of America. Direct measurements⁴ made recently in the eastern Pacific have revealed that the eastward flow extends to at least 1,000 m at long 107° W.

There is evidence of an eastward flow at the sea surface south of the equator in the measurements of geostrophic flow made on the *Equapac* expeditions by the research vessels *Orsom III* (Institut Français d'Océanie, New Caledonia, unpublished report) at lat 9° S between long 170° and 180° E, where speeds as high as 15 cm/sec are indicated, and by the *Hugh M. Smith*⁵ at the same latitude between long 169° W and 135° W, with speeds as high as 8 cm/sec indicated. Of the other *Equapac* lines, none reached so far as lat 10° S except one at long 164° by the *Horizon* (Univ of Calif Scripps Inst of Oceanogr, unpublished reports) and this was so near the Solomon Islands that the geostrophic calculations, which did indicate an eastward flow, might have other interpretations.

In a combination of stations from the *Carnegie* expedition and the *Eastropic* expeditions of 1955 and the *Downwind* expedition, a weak easterly flow may be interpreted so far east as long 95° W, but the observations are sparse and the feature is very poorly defined.

In the western Pacific, other evidence for the eastward flow at the sea surface may be found in various atlases prepared from observations of set and drift of vessels. The British average⁶ of set and drift for the seasons November-January and February-April indicate a weak eastward flow at lat 10° S from long 165° E to 140° W and from long 165° E to 165° W, respectively. No evidence is found in other months, and it is to be noted that the *Equapac* observations were made in August. The more recent Netherlands⁷ monthly current charts show easterly flow along lat 10° S from long 165° to 180° E in February, March and April. The American⁸ monthly charts show almost no evidence in any month.

The east-flowing current was encountered while studying the distribution of temperature, salinity, and oxygen along the density surface $\sigma_t 26.81$, which lies in the intermediate water in the North Pacific and above the intermediate water of the South Pacific. This study is not yet completed, and further information about the flow at other depths and along other surfaces will be obtained as the work progresses.

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¹ Montgomery, B. B., *Bull. Amer. Meteor. Soc.*, 18, 210 (1937).

² Fleming, J. A., Ennis, C. C., Sverdrup, H. U., Eaton, S. L., and Hendrix, W. C., *Carnegie Inst. Wash., Pub. No. 545, Oceanogr. I-B* (1945).

³ King, J. E., Austin, T. S., and Doty, M. S., *U.S. Fish Wildlife Serv. Spec. Sci. Rep., Fish. No. 201* (1957).

⁴ Knauss, J. A., and Peplin, R., *Nature*, 183, 380 (1959).

⁵ Austin, T. S., *U.S. Fish Wildlife Serv. Spec. Sci. Rep., Fish. No. 217* (1957).

⁶ M.O. 435 Marine Div Meteor. Off., Air Ministry, London (1939).

⁷ Koninklijk Nederlands Meteorologisch Instituut, No. 124 (1949).

⁸ U.S. Navy Hydrographic Off., Misc. No. 10,053 (1944).

River Flow in Great Britain

PROF D. L. LINTON, in his article on "River Flow in Great Britain, 1955-56"¹, has a map showing 'run-off deficit', defined as "Precipitation minus run-off".

While believing that maps of this parameter are much needed, it is doubtful whether the data from which they can at present be constructed for Great Britain are sufficient for drawing isopleth maps with any degree of accuracy. The network of gauging stations is too thin for it to be possible to assume that known errors in measurement of run-off, and in assessing rainfall over a whole catchment area, can cancel each other out. The estimation of precipitation is likely to be the most unreliable in large catchment areas of high relief, and these areas happen in general to be where the river-gauging network is particularly thin. These errors can alone well account for the apparently anomalous high run-off deficits in the Scottish Highlands without necessarily invoking any other explanation.

Prof Linton comments that the geographical variations of the fractions of precipitation disposed of by run-off and by evapo-transpiration are radically different, and adds "it is doubted whether there has previously been any general appreciation of this difference by water engineers and others". There may not have been a "general appreciation" of this fact, but it has certainly been appreciated by some, who further appreciate that there is an important difference which is not revealed on his map, and which Prof Linton does not mention, between different parts of the country. In fact of course the map, allowing for the errors mentioned above, does indicate the general geographical distribution of actual loss by evapo-transpiration, this however is in some parts of the country equal (in 1955-56, as in other years) to potential evapo-transpiration and in other parts not. In the rainfall year in question, the difference between actual and potential evapo-transpiration can safely be said to have been between 0 and 2 in in many parts of western and highland Britain, while it almost certainly reached 12 in in many parts of the south of England. Thus an 'actual loss' of 20 in in Ross-shire (as shown on the run-off deficit map) would be a 'run-off deficit', with little or no 'water deficit' while a similar run-off deficit in the south of England would be accompanied by a water deficit of 12 in. It needs to be emphasized that 'water deficit' is not the same as 'run-off deficit', but values of both are needed, and there is need for a network of observations sufficient for both to be mapped. Consideration of both would reveal why there can be a high run-off deficit in the west Highlands, without any need to refer, as Prof Linton does, to the large bodies of open water there, there are, after all, large bodies of open water in the English Lake District, which had a much lower run-off deficit on the 1955-56 map.

Although, as Prof Linton points out, there is a lack of gauging stations on the western seaboard, it is possible to extrapolate the map of 'discharge ratio' to the west coast, through observation or estimation of potential evaporation.

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¹ *Nature*, 183, 714 (1959).

RESEARCH ASSOCIATIONS AND THEIR FUNCTIONS

IN its report for the year 1958 the Council for Scientific and Industrial Research discussed briefly its general policy towards the research associations expenditure on which in revenue and capital grants it envisaged as rising by about a third during the next five years, because their scope and activities are growing steadily in response to the expressed needs of industry. The Council's policy, however, is that industry should bear an increasing share of the total operating cost of the associations, and it is envisaged that over the next five years grant-earning income from industry will be 46 per cent greater than during the past five years, while the grants themselves will be only 34 per cent greater. For the year ended March 31, 1958, annual grants to the associations totalled £1,700,330, compared with £1,424,830 in the previous year, with special grants of £32,571, compared with £120,954. The total income of the associations is given as just under £7 million. It was stated that during the fifteen months ended December 31, 1958, new or revised terms of grant had been awarded to ten of these associations.

The new terms are set out in 'Research for Industry, 1958' * (see also p. 238 of this issue). This report on the work of the industrial research associations includes a summary of the report of the Industrial Grants Committee, which at the request of the Council has surveyed the work done by research associations, and the methods used to assess the applications for grants received from industry. The main conclusions and recommendations of this Committee have been accepted by the Council and, besides considering research association grant policy in the period 1957-64 the Committee's report reviews particularly the achievements of the ten associations which have received new or modified terms of grant. "Research for Industry, 1958" also includes an assessment by Dr D. T. A. Townsend of the place of the research associations in the evolution of scientific endeavour in Great Britain, and a report prepared for the Committee of Directors of the Textile Research Associations on how co-operative research serves the textile industries. These two surveys throw rather more light than the new terms of grant on how in practice the Council's new policy is being interpreted.

The Industrial Grants Committee was greatly impressed with the rapid progress of research associations towards maturity and with the rising quality of the research they carry out and the services they give to industry. The Council is satisfied that co-operative research, as fostered by the Department, is of great value to industry and the nation, and that the Department of Scientific and Industrial Research should continue to give it whole-hearted support.

Department of Scientific and Industrial Research. Research for Industry 1958. A Report on Work done by the Industrial Research Associations in the Government Scheme. Pp iv+135. (London H.M.S. Stationery Office 1959.) 7s. 6d. net.

All told, the grant aided organizations in the scheme serve about 55 per cent of British manufacturing industry and besides basic and applied research their activities include the study of factory operations and working conditions, library and information services and technical and advisory work for individual firms. The largest single function is applied research on problems common to the whole of the industry served.

The Council also endorses the Committee's view that co-operative research brings important specific benefits to industry, economizing on money and scientific manpower, and offering a scientific service to firms that cannot afford research departments of their own. It helps to guide industry towards an appreciation of the value of research in general and facilitates an exchange of technical information and other forms of mutual assistance. Finally, it builds up a store of knowledge on which the nation through Government departments can draw.

These are large claims, some of which have been challenged at least to the extent of asking whether certain functions could be more efficiently served in other ways or by changing the technical character of the associations themselves. Nevertheless their acceptance by the Council seems to dispose of any suggestion that the Council is intending to wind up some of the research associations. Indeed it is specifically stated that the expansion contemplated over the next quinquennium allows for an increase in their number, since recent estimates of the Department suggest that nearly a fifth of the net output of British manufacturing industry comes from trades which in the Committee's view are not fully covered by existing research facilities. Some of these trades might in future be appropriately served by grant aided research associations.

Until the Second World War, Government aid to research associations in Britain was based on the assumption that they would eventually support themselves entirely. In 1945, however it was decided that this policy was no longer in the national interest, and that industrial grants should become one of the continuing activities of the Department. The procedure now generally followed is to award a basic 'block grant' and supplement it with an 'incentive' payment which varies (up to a maximum) according to what income an association can raise from its members. Aid is generous to a young research association serving an industry which does not yet recognize the full value of research, but as the association establishes itself and increases both the scale of its work and the contribution science can make to the productivity of its member firms the incentive is gradually reduced, and it ceases altogether when the association reaches its appropriate size.

Even so Dr D. T. A. Townsend points out that eleven associations have an annual income of less

than £50,000 and only two receive more than £500,000. Eighteen have incomes between £50,000 and £100,000, eight between £100,000 and £250,000, and seven between £250,000 and £500,000. These are not high figures for research to day, and it could be asked whether they are always high enough for efficiency. The Industrial Grants Committee is clearly asking the right questions when a grant comes up for review at the end of five years, and the Council accepts its view that it is important to continue paying a block grant after the association has reached an appropriate size.

This size obviously must take account of the adequacy of the facilities of an association for effective research, but the Council concurs in the Committee's view that continuance of the block grant will enable the Department to exercise an important and beneficial influence on industrial research and ensure that each association has the necessary proportion of basic research in its programme. It is also argued that a channel is thus kept open for the steady flow of research results to Government departments, this helps to prevent undesirable overlapping of projects and to secure desirable co-operation on programmes of wide interest.

Before these propositions are accepted, their implications for the Council of Scientific and Industrial Research require examination. They presuppose the existence of an administrative structure for which even the Lord President of the Council has disclaimed responsibility. Some overlapping should certainly be prevented by the Council for Scientific and Industrial Research, but it should be clear from the discussion aroused by recent proposals for a programme of space research to be undertaken by Britain that there is by no means general agreement that administrative arrangements are yet such as to ensure the minimum of overlapping, much less the most desirable balance and distribution of research effort.

Since the policy of reducing incentive grants was adopted in 1951, the overall ratio of grant to industrial income has fallen from 1.165 to 1.25, and the lowest individual ratio is now 1.46. There is nothing mechanical about the trend, and although the ratio is not given for the ten associations for which the terms of grant were revised during the past year, the ratio of incentive grant to additional income varies from 1.1 to 1.2, and the maximum incentive grant from £3,000 to £18,000. These figures show, however, that the reduction of incentive grants is being exercised with the flexibility which the Council adumbrates.

It is recognized that a long time may be required for an association to convince industry of the value of its work and that if the incentive grant is reduced too quickly, industrial research may be discouraged and the purpose of the grant defeated. Likewise, changes in the purchasing power of money have to be considered, particularly when research associations receive only a block grant. An allowance to restore the real value of the grants was made in 1955, and the Industrial Grants Committee recommends a similar provision if necessary for the next quinquennium.

More important than this question of finance, however, is that of function. The Council endorses the Industrial Grants Committee's view that it is very important to keep a proper balance in the activities of the associations between basic research, applied research (including development work) and information, liaison and consultant services. In some industries pioneering studies of factory operations and working conditions are best made on a co-operative basis, and the Council believes that research associations should extend this work where conditions are suitable, and that, wherever appropriate, the Department of Scientific and Industrial Research should carry out its research in this field and disseminate the results, in close collaboration with the associations.

No indication is given as to what is regarded as a proper balance between the various activities. That will naturally vary from industry to industry, as well as with the maturity of the association. It is left for Dr Townend to supply a rough estimate as to the proportion of the £7 million of the total income which is spent on fundamental research, though this estimate does not necessarily also indicate the proportion of man-power which is devoted to fundamental research. Of a total staff of some 5,000, 1,450 are graduates or possess equivalent qualifications, 1,750 are research assistants, 850 artisans and 950 administrative staff.

Both the Council and its Industrial Grants Committee hold that, so long as co-operative research programmes do not suffer, research associations should be encouraged to undertake a reasonable amount of sponsored research. Some associations are already prepared to do so, and generally have a small proportion of their staff engaged in this way. The practice offers definite advantages in giving research workers useful experience and in strengthening the contact between research associations and industry.

The Council insists, nevertheless, that the chief task of the research associations is co-operative research and that there are other facilities for sponsored research, offered by private bodies without Government assistance. It would welcome increased participation by research associations in sponsored research, but such activities must be kept within reasonable limits. In future a grant-aided association is free to undertake sponsored projects without consulting the Industrial Grants Committee provided the income arising is unlikely to exceed 15 per cent of total income in any year, and that the estimated cost of any one project is not more than £5,000.

Dr D. T. A. Townend's review examines this question of function a little further. He points out that the present total income of the research associations in Britain, namely, £7 million, must be compared with the expenditure of private industry on research and development of £58,000,000, or 0.8 per cent of industrial output, and this £7 million is less than half the £14.4 million expended on research undertaken within the universities in science, technology, medicine and agriculture, towards which the Government provided about £12 million. The universities are mainly concerned with extending the frontiers of

scientific knowledge in an atmosphere of intellectual freedom and usually without regard to the immediate and specific applications of their work. Industrial laboratories, he suggests, are mostly devoted to study of the processes and products of a particular firm with the object of developing something which that firm can do and will do, probably to the exclusion of others.

That the last proposition should not be accepted without qualification does not, however, affect the validity of Dr Townend's claim that the research associations are in a unique position to pinpoint the research problems of importance to the whole of their respective industries. The validity of that claim depends rather on the effectiveness of their contact with the industries they serve, their ability to recruit and retain staff of appropriate experience and ability, and on the quality of their directorate. Some of these factors can be influenced by the Council for Scientific and Industrial Research, but only to a limited extent and they should be borne in mind in considering Dr Townend's argument. There is a separate domain between the universities and industry, he argues, in which knowledge of the basic principles of industrial processes has to be sought with a particular and definite objective. This region accordingly is mostly unsuitable for the universities and is also somewhat too long in range or too expensive at least for the smaller industrial firms in their own laboratories. This he claims, is particularly the domain of the research associations, with their resources and teams of scientists capable of covering a variety of disciplines with a character and individuality of their own. There is no fuss about claiming freedom of action—the Industrial Grants Committee is emphatic as to the need for preserving the autonomy of the associations—nor are unattractive features of the field of investigation neglected.

Dr Townend believes that industry in Britain has been well served by the research associations for many years in a well-defined field uniquely appropriate to the associations with no fear of overlap, and he also suggests that the practice in most associations of pursuing both long range and short-range objectives side by side contributes to the long term future of the industries they serve as well as to the vitality of the overall activity of the associations. As to the balance of research, Dr Townend refers to a recent survey of the activities of some thirty two associations, which showed that the proportion of effort devoted to basic research varied from 10 per cent to 67 per cent the average being about 28 per cent, whereas that devoted to applied research averaged 63 per cent. Close contact has almost invariably been established between the associations and the universities wherever research work of relevance to that of the association is already undertaken at universities. Sometimes the associations assist university departments by contracts or by financing fellowships or bursaries, and this assistance may be given to an existing programme in a university department, or an association may seek to arouse the interest of a university department in a new subject.

Dr Townend appears to be satisfied that these arrangements are adequate. They increase the 'thinking potential' of an association and help to relate the work of university scientists to the needs of industry. Often they are particularly effective in ensuring that university workers are provided with a correct translation of an industrial problem into scientific terms and they supplement the necessarily limited results obtained by postgraduate students with ancillary measurements and background information, thus enabling the results of the work to be applied more readily. What is not specifically stressed is the atmosphere for research which the associations could provide and which was rightly stressed by Mr J. Wilson in his Hinchley Memorial Lecture last year, and this atmosphere is one which the Council for Scientific and Industrial Research could certainly foster.

Clearly the interchange of staff between the research associations and the universities can be beneficial here but Dr Townend notes that such transfer has decreased in recent years, possibly in consequence of the general shortage of scientists and of the rapid growth of departments of science and technology within the universities. This interchange could well be as important as the interchange of staff between the associations and industry itself and valuable as may be the contributions of the associations in research, they will only render their full service to industry when such interchange of staff proceeds freely and to the maximum extent. It can be an important factor, as Dr Townend notes, in supplying industry with senior staff at the managerial as well as the technical level, and the educational potential of the associations is not the least reason for justifying the continuance of support from the Department of Scientific and Industrial Research. There may well be scope for further specific development of the training potential of the associations without interfering with their primary and main function of co-operative research. It should be clear however that if they are to render their full contribution to industrial development, they must be assured not only of wise and far-sighted leadership, but also of sustained financial support, probably on a more generous scale than the resources at present available to the Department of Scientific and Industrial Research have yet permitted.

ROCKETS AND SATELLITES

Manual on Rockets and Satellites

Edited by L. V. Berkner, in association with Gilman Reid, John Hancsian, Jr and Leonard Cornier (Annals of the International Geophysical Year, Vol. 6). Pp. xx+508. (London and New York: Pergamon Press, 1958.) 160s.

THERE is little doubt that this volume of the Annals of the International Geophysical Year contains the most comprehensive account yet published of the researches being carried out and the methods and techniques being used in the fields of rockets and satellites. Any book dealing with such

a young and rapidly growing subject will inevitably date rather quickly, and it so happened that the launching of the first Russian Earth satellite occurred at a very late stage in the preparation of this work. The preliminary account of the Russian results, and the rapid switch in the emphasis of the American satellite programme from the *Vanguard* to the *Explorer* series, are dealt with rather briefly in annexes. It is perhaps fortunate that we have on record here, written before it was overtaken by events, the American plan for the scientific programme intended for the *Vanguard* satellites.

Viewed as a whole the volume cannot fail to be an invaluable source of reference to workers in the field. The upper atmosphere research rocket which still has a vital part to play is not neglected, but the greater part of the book is devoted to Earth-satellite programmes and plans. Those whose interest is more general will gain an insight into the complexities of planning and the widespread co-operation needed in a space research programme, in addition to a sober review of the many new avenues of scientific research now being opened. The volume takes the form of a series of scientific papers, covering subjects as diverse as the design of instruments for many rocket- and satellite-borne experiments, and the organization of volunteer visual observing teams, both in the United States and in the U.S.S.R. It is indeed pleasing to find an international flavour throughout, with significant contributions from the U.S.S.R.

The book is handsomely produced and illustrated, as is to be expected for the price. One must hope that the end of the International Geophysical Year itself will not prevent the compilation of further authoritative international volumes in these expanding fields.

MICROCOSM TO MACROCOSM

Matter, Earth and Sky

By Prof George Gamow Pp xi+593 (London Macmillan and Co., Ltd, 1959) 50s net

EXUBERANT and encyclopædic are the only terms to describe this interpretation of the material universe, most appropriately dedicated to "Aspiring Youth". In the days of stone-turning and avenue-exploring, barriers had to be either surmounted or torn down. Prof Gamow himself was the first to realize that with the right kind of approach nothing so drastic is needed, and that they can be gently tunneled through. There is certainly a barrier between the experience of the ordinary individual and the physicist's interpretation of it. In this book, without demanding excessive penetration on the part of the reader, the author has successfully brought into the open the truths that occupy the inner levels of the well.

The style follows the author's usual successful formula—saying what comes naturally. There are some old friends, including C. G. H. Tompkins, translated to an American setting, but still on a communal Cambridge bicycle. The illustrations are excellent, original and relevant—even those that are put in just for fun, like the one showing an 'experiment' on the thermal expansion of a body, which looks rather unkind. Scientists are pictured with a richly human touch—Otto Hahn registering sheer amazement at the fission of uranium, Compton

strumming his banjo with effect, and Bohr in orbit on a motor-cycle.

The book is divided into three sections. The first, on "Matter and Energy", deals with the elementary physics of the surroundings, relating everyday observations to fundamental principles. This ranges widely from simple mechanics to computers and satellites and rocketry and relativity. The second, entitled "Microcosm", starts with the kinetic view of matter in terms of molecules, and covers atomic and nuclear physics, and a good deal besides. The chapter on the chemistry of life, which goes very fully into protein structure, and discusses Watson and Crick's model of the structure of deoxyribonucleic acid and its implications for the possible working of heredity, is important both for its contents and its influence on the young reader who may (though not if he has got so far through the book) tend to regard physics as a little remote from living. The third part, "Macrocosm", deals with the Earth and its history, the planets, the evolution of the stars, the origin of the elements and of the galaxies, and the recent theory of continuous creation.

So much could not have been achieved in a single book without very careful planning of the sequence of material, and much skill has been devoted to placing the discussion of a fundamental topic in relation to the general framework. Electrolysis, for example, appears in the second part, where the electrical nature of matter is treated. This means that it is a book to be read through, without dodging back to the beginning for explanations.

It is a splendid book, and highly to be recommended to the general reader and for the library. Although very good value for money, its price unfortunately places it high up in the gift-book class. The unkind experiment mentioned above supposes the co-operation of a good-natured relative, and any aspiring youth who can get such a one in an expansive mood would be well advised to clamour for this book as a present instead.

G. R. NOAKES

SURVEYS IN 'APPLIED' MATHEMATICS

Some Aspects of Analysis and Probability

By Irving Kaplansky, Marshall Hall, Jr, Edwin Hewitt and Robert Fortet (Surveys in Applied Mathematics, Vol 4) Pp xi+243 (New York John Wiley and Sons, Inc., London Chapman and Hall, Ltd, 1958) 72s net

THIS book is the fourth of John Wiley's "Surveys in Applied Mathematics", its production was sponsored by the United States Office of Naval Research and by the editorial board of "Applied Mechanics Reviews", its authors are described as being, and indeed are, "internationally recognized authorities in the areas of applied mathematics covered by their surveys". Hall writes on combinatorial analysis, and Fortet on probability theory, while functional analysis and abstract harmonic analysis are surveyed respectively by Kaplansky and Hewitt. An English reader, accustomed to the rigid division between applied mathematics (where nothing is proved) and pure mathematics (where nothing is useful) may well find the classification puzzling. Only the probabilist will be untroubled by it, his subject, having an axiomatic foundation and yet deriving

all its inspiration from practical problems, has no place in the traditional classification, he will be quite happy in the applied mathematical club so long as the topological algebraists are there to keep him company.

Kaplansky's article (32 pages) is the shortest in the book, but is supported by a magnificent bibliography of 113 entries, nearly half of them concerning papers by Russian authors, he gives a remarkably clear and concise account of many topics of current interest in the theories of Banach spaces, locally convex spaces and Banach algebras.

Hall's survey of combinatorial analysis will be of value not only to algebraists but also to statisticians interested in the existence and construction of designs and to the industrial mathematician concerned with linear programming. For the latter there is a fascinating chapter on the theorems of Philip Hall, König and Ramsey, and their applications, these include the transportation problem, the travelling salesman problem, and also such curiosities as the following (Erdős and Szekeres, 1935) "There exists an integer valued function $N(n)$ of the integer variable n such that every set of N points in the plane, no three on a line, will contain n points forming a convex n -gon".

Hewitt's long article on abstract harmonic analysis presents a connected account of a difficult and important field, which is the more valuable because a large number of the most important papers reviewed here were published in Russian. Readers of the older text-books on Lebesgue integration encounter theorems of two kinds: those which make essential use of the group structure of the real line, and those which do not. Those which do not (for example, the Lebesgue convergence theorems) properly belong to measure theory, while those which do (for example, theorems about convolutions, and the whole of the Fourier theory) can nearly all be generalized to the situation in which the real line is replaced by a (say, abelian) locally compact group and Lebesgue measure is replaced by Haar measure, and this is the situation with which abstract harmonic analysis is concerned.

Fortet gives a most valuable account of a number of special topics in probability theory, of which the most characteristic is development of techniques for handling random elements of general type. A probability space is a non-vacuous set Ω a Borel field \mathcal{F} of measurable subsets of Ω , and a totally finite measure μ on \mathcal{F} normalized so that $\mu(\Omega) = 1$. A random variable $x(\cdot)$ is a mapping from Ω to the real line such that all counter-images of real intervals are \mathcal{F} -measurable, and an n -dimensional random variable is defined similarly. The classical theory was concerned exclusively with finite sets of such random variables: the modern theory of stochastic processes is concerned with infinite sets of random variables, suitably parametrized, and the theory of general random elements is concerned with (in the first instance single) random variables $x(\cdot)$ where now the range of the mapping $\omega \rightarrow x(\omega)$ lies not on the real line nor in n -dimensional euclidean space, but in some more general topological-algebraic structure. For example, Mourier and Fortet have studied random variables taking values in a Banach space, and Gelfand has studied random (Schwartz) distributions. In a sense the distinction between stochastic processes and general random elements is artificial for if $\omega \rightarrow x(t, \omega)$ (for each t in some parameter set T) is a set of random variables constituting a

stochastic process, then $\omega \rightarrow x(\cdot, \omega)$ can be thought of as a general random element, and conversely most of the general random elements one wishes to consider in practice (random ergo-distributions, random energy-spectra, etc.) can be reduced to systems of numerical random variables. But the direct treatment of a random variable of general type, where possible, offers many attractions, and there can be no doubt that this branch of the subject will attract considerable attention during the next few years.

The publishers are to be congratulated both on the quality of the surveys included in this volume and on their decision to publish this group of four surveys together.

D G KENDALL

FUTURE MARINE BIOLOGICAL RESEARCH

Perspectives in Marine Biology

A Symposium held at Scripps Institution of Oceanography, University of California March 24-April 2, 1958. Edited by A. A. Buzzati Traverso. Pp. xvi+621. (Berkeley and Los Angeles: University of California Press, London: Cambridge University Press, 1958.) 75s. net.

"APPROXIMATELY 90 to 95 per cent of all biologists are engaged in terrestrial biology. These biologists have a tendency to consider Marine Biology as a somewhat secondary biological annex." P. Drach (p. 603 *et seq.*) further states that general biology can never be properly balanced if based predominantly on terrestrial forms, however important they are to our welfare, a view shared by many of the contributors. The expansion of marine biology is reflected by the wide range of subjects presented at a symposium planned to focus attention on forthcoming fields of marine research. It is significant that a number of contributions come from non-marine biologists. Forty-one papers with subsequent discussions, are arranged in four sections: ecology, physiology and biochemistry; behaviour, evolution and genetics.

Ecological papers by P. Drach, L. Zenkevitch, G. Thoren, A. C. Hardy and others, while emphasizing that more field observations on animal communities are required, show the urgent need for new design and international standardization of instruments and techniques for quantitative sampling. Field observation is so much stressed that K. M. Rao's plea, echoed elsewhere for laboratory observation and experiment on marine equivalents to the guinea pig and fruit fly stands out from the rest. D. P. Wilson's studies on the ability of organisms to detect factors at present defy analysis, and so select a particular substrate, are stimulating. Further emphasis on this need for study on microconstituents is given by S. K. Kon (vitamins and external metabolites), D. I. Arnon (micronutrients) and I. Provasoli (growth factors of marine algae). E. Baldwin's paper on biochemical perspectives and the need for more biochemists in marine research is timely.

Papers on reef building corals (C. M. Yonge), productivity, patchiness and succession in plankton (W. Rodhe *et al.*, R. Margalef, A. C. Hardy, L. Tonelli and V. Tonelli), cell chemistry (E. S. G. Barron, A. Szont Györgyi), biological clocks (C. S. Pitten

drigh, F A Brown, jun) show the variety of future problems That the section on behaviour consists of four papers as compared with twelve or thirteen of the other sections emphasizes our lack of knowledge W H Thorpe's excellent discussion of ethology indicates the vast amount of data awaiting discovery by simple observation assisted by aqualung, television and camera, and T H Waterman's contribution on underwater polarization patterns suggests many new ideas about plankton behaviour

If the biochemist is rare in marine biology how much more the geneticist Yet D L Ray shows that many species are suitable for genetical study, while papers by V L Loosanoff and Y Matsui point the way to controlled shellfish breeding and farming Geographical distribution, races, speciation of pelagic forms where there appears to be no barrier to gene flow, are challenging problems to all

This book is not just a list of problems for the future Most contributors base their speculations on accounts of present work, much of it unpublished Many contributions are of immediate concern and it is regretted that it has taken more than two and a half years to produce a book that one might expect—and hope—will soon be out of date Errors are few, the chief being the transposition of legends to text-figures 2 and 12 in Hardy's paper, while the last two lines to the legend of text-figure 1 of Bogorov's paper should read "continuous line indicates quantity of phytoplankton and broken line quantity of zooplankton" That the contributions are contained in 621 pages is largely due to the small type, but it remains easy to read and the tables and figures are well set out Non-marine biologists would do well to read this book for much of it has general biological implications

J A ALLEN

HETEROCYCLIC CHEMISTRY

Heterocyclic Chemistry

An Introduction By Prof Adrien Albert Pp viii+424 (London The Athlone Press, University of London, 1959 Distributed by Constable and Co, Ltd) 45s net

Six-Membered Heterocyclic Nitrogen Compounds with Three Condensed Rings

By C F H Allen, in collaboration with G M Badger, Bruce Graham, G A Reynolds, James H Richmond, John R Thirtle, J A Van Allan and C V Wilson (The Chemistry of Heterocyclic Compounds a Series of Monographs, Vol 12) Pp xxii+624 (New York Interscience Publishers, Inc, London Interscience Publishers, Ltd, 1958) 196s

CHEMISTS in general and students in particular have long been in need of a book of reasonable size on heterocyclic chemistry, but the digestion, selection and presentation of the subject have apparently daunted chemists, for Morton's book, published in New York in 1946, has been the only work of note to appear for many years This is not surprising, for our present detailed knowledge of heterocyclic chemistry must exceed in volume that of aliphatic or of aromatic chemistry, and the infinite variety of heterocyclic compounds must cause this difference to become ever greater A work by Prof Albert is therefore warmly welcome, and it is exceptionally interesting to see how he has approached

the task of giving a concise account of this subject in 375 excellently printed pages

He has certainly broken completely away from the orthodox treatment, in which each class is usually discussed largely in the order syntheses, reactions, and finally structure on the basis of these two sections Instead, Prof Albert makes primarily an electronic structure approach to the various classes, and also discusses their physical properties, particularly spectra, ionization constants, oxidation-reduction potentials, and dipole moments in considerable (and very valuable) detail, relegating much of the synthetic side to smaller print This makes absorbing reading to the more advanced chemist, but one wonders whether students will both grasp and then continue to visualize the main bulk of heterocyclic compounds as "π-Deficient N-Heteroaromatics", "π-Excessive N-Heteroaromatics", and "π-Excessive O- and S-Heteroaromatics", which form the titles of the author's three main chapters?

The author has dealt with the problem of condensing the sheer bulk of material partly by confining references to original literature to papers published since 1930, on the ground that these papers will provide sufficient references to earlier work The result can be unfortunate, for an account of fundamental work is often followed solely by a recent reference, which may record comparatively trivial modifications or extensions of the earlier work consequently the student may often lack the means to honour "the memory of the pioneers of heterocyclic chemistry" to which the book is dedicated It is a pity, furthermore, that although two distinct series of volumes on heterocyclic chemistry are still appearing, references are given almost solely to Eldorfeld's series, and the larger Weissberger series is almost ignored

The reviewer notes with interest the categorical statement that purines synthesized by building a pyrimidine ring on to an iminazole ring "have always introduced a hydroxy- or amino-group in the 6-position" (p 198) Mann and Porter, in 1945, synthesized by this method a number of 1,7-dialkyl-purines which did not contain these groups in this position

The fresh approach, the clear lucidity of the presentation, and the author's personal enthusiasm have produced a book which chemists will read with great interest

The other volume, the twelfth to be published in the Weissberger series, is devoted solely to the chemistry of compounds having three six-membered rings fused together, the only hetero element being one or more nitrogen atoms The vast amount of information, carefully classified and coded in about 600 pages, vividly illustrates the reviewer's earlier comment on the expanse of our knowledge of heterocyclic chemistry The book deals with the chemistry of aza- and polyaza-anthracenes, -phenanthrenes and -benzonaphthenes, the amount of work entailed becomes apparent when one recalls that the monaza-phenanthrenes alone form a group of five isomers Furthermore, tables are provided enumerating all the known simple and substituted members of each class up to 1952 This vast accumulation of knowledge has required the services of several chemists, and it concludes with an excellent chapter on "The Ultraviolet Absorption Spectra of Polycyclic Heterocyclic Aromatic Compounds" by Prof G M Badger, of the University of Adelaide This volume forms an outstandingly valuable addition to the Weissberger series

F G MANN

Puzzle-Math

By Dr George Gamow and Dr Mervin Stern. Pp 110 (London Macmillan and Co, Ltd, 1958) 8s 6d net

BOOKS of the 'mathematics for fun' type are often neither very mathematical nor very funny but those who know some of Dr Gamow's earlier writings will expect this volume, in spite of its catchpenny title, to combine amusement with instruction, and they will not be disappointed. The thirty-three problems are entertainingly set out, and solved by honest mathematical processes, involving little or no manipulative technique. There are some chestnuts—the three travellers with dirty faces, the fly between two approaching trains—but many of the problems are new or not widely known. Is a motorist likely to be held up longer at a level crossing if the track is double than if it is single? When we ring for a lift why does it seem to come in the wrong direction more often than not? A bright student might easily be led to a better appreciation of the fundamental logic of mathematics by reading this cheerful little book. T A A BROADBENT

Transactions of the International Conference on the Use of Solar Energy

The Scientific Basis, held at Tucson, Arizona, U.S.A., October 31 and November 1, 1955 (Sponsored by University of Arizona, Tucson, Arizona Association for Applied Solar Energy, Phoenix, Arizona, Stanford Research Institute, Menlo Park, California) Vol 1 The Available Energy Measurement of Radiation Pp xvi+135 Vol 2 Thermal Processes, Part 1 Section A, Flat Plate Collectors Pp ix+145 Vol 2 Thermal Processes, Part 1, Section B, High Temperature Solar Furnaces Solar Power Pp i+146-204 Vol 3 Thermal Processes Part 2, Solar House Heating Solar Water Heating Solar Stoves Solar Distillation Pp x+168 Vol 4 Photochemical Processes Pp xii+187 Vol 5 Electrical Processes Pp xii+132 (Tucson, Arizona: The University of Arizona Press 1958) 12 50 dollars the set

THESE Transactions containing 85 scientific papers totalling 887 pages, represent one of the most valuable publications on solar energy research. It is therefore all the more regrettable that although the conference at which these papers were presented was held late in 1955 publication has been delayed until the end of 1958, and moreover that there is no record of the valuable discussions that took place at the conference.

The conference discussed the scientific basis of solar energy research and was followed by the World Symposium on Applied Solar Energy at Phoenix, Arizona. The papers at the latter conference which dealt preferentially with applications, were published in 1956, and the proceedings were reviewed by the writer (*Nature*, 178, 229 1956), who also described in some detail the general features of both conferences soon after the meetings (*Nature*, 177, 110 1956).

The present review is therefore restricted to consideration of a few aspects which have since been emphasized as important by the trend of solar energy research in the interval that has elapsed since presentation. Interest in the flat plate type of collector used for water heating continues but research is concentrated on the simplification of design and the use of metallic oxide surface coatings

to restrict re-radiation of long wave length and thus enable higher temperatures to be attained. The high cost of the silicon photo-cell which was then newly developed, has as prophesied been reduced to economic competition with electricity from dry cells and is coming into general use for portable radio and telephone equipment, not excluding such objects as space satellites. The solar furnace sponsored by the French Government and described by M Trombe in Vol 2 is the most active achievement at present and similar furnaces have been sponsored by the governments of other countries for testing materials to resist the thermal shock encountered in high speed rocket flight and space travel.

The Transactions are essential to those embarking on solar energy research, or wishing to ascertain the state of knowledge up to very recently. Although there have been some remarkable developments since the conference, this set of volumes which has been compiled by Prof Carpenter of the University of Arizona Observatory, constitutes a record of permanent value. H HERWOOD

The Fundamentals of Statistical Reasoning

By M H. Quenouille (Griffin's Statistical Monographs and Courses No 3) Pp 169 (London Charles Griffin and Co Ltd, 1958) 34s

A GOOD short book on the basic principles and theory of statistical inference, expository of those parts of the subject on which statisticians are now generally agreed and objectively critical of some of the more controversial lines of thought, would be of great value. Such a book appears to have been Mr Quenouille's aim, but he has had indifferent success. Few subjects are in greater need of careful choice of every word, yet all too often the writing here is ambiguous or lacking in clarity. For example the opening paragraph of a chapter on testing hypotheses tends to obscure the important distinction between decision theory and scientific inference that Fisher and Barnard have so usefully emphasized in recent years. Later in the same chapter 'restriction' of errors of both the first and the second kind is said to be essential to a significance test of (surely "of deviations from" would be clearer) a null hypothesis.

The first four chapters rapidly survey the concepts of probability, elementary distribution theory, estimation and hypothesis testing. The second half of the book is of a different order of difficulty and of much greater interest. Here is an introduction to maximum likelihood and fiducial inference that could well form the basis of a more substantial text and could stimulate further research. Mr Quenouille has a gift for devising the illuminating example. He has evidently devoted much thought to fiducial distributions and one wishes that he would undertake the systematic and critical account of this topic that must supplement Fisher's more intuitive approach if it is to attain its proper recognition. Unfortunately, the present book is again unsatisfying not only because of limitations of space but also because too often the reader cannot tell what is part of standard theory, what is a new contribution from the author (possibly deserving more explanation or more detailed reference to other publications) and what is a tentative suggestion for future exploration. However, although one may question the wisdom of including some of this material in an introductory book, undoubtedly the more advanced student will value it. D J FISHER

The Nature of Experience

By Sir Russell Brain, Bt (The Riddell Memorial Lectures, Thirteenth Series, delivered at King's College in the University of Durham, 12, 13 and 14 May 1958) Pp viii+73 (London Oxford University Press, 1959) 8s 6d net

ACCORDING to the trust deed, the Riddell lecturer is required to discuss "the relation between religion and contemporary development of thought". It is interesting to look back over past titles, and to see how successive speakers have interpreted their task. In this context, how well these discourses—the thirteenth—fit into the series, and maintain their tradition.

The theme is the field of perception, which the author explores with the object of attaining a view sufficiently comprehensive to restrain, if possible, the excessive specialization which is the outstanding characteristic of modern thought. The three lectures are entitled, (1) "Vision and Fantasy", (2) "The Nature of Perception", (3) "Symbol and Image". Some useful notes and references follow at the end.

Sir Russell is a leading neurologist, and one would expect to find a telling picture of mental processes, in the event, this knowledge is linked with rare aesthetic insight.

The first lecture reviews the conventional sense-impressions and their many contrasts with the structure of matter as the physicist knows it. The author believes that the qualities perceived are constructs of our own brains. Of particular interest is the account of abnormal states produced, for example, by mescaline. The second lecture contains a well-balanced review of the objections which have been raised against the writer's theory. In the last lecture, perhaps the most difficult, art is taken "as the embodiment of feelings in perceptual form", and thus embraces that subjective element deep in human nature which raises it, at times, to an image of the Divine.

F I G RAWLINS

Kingdom of the Octopus

The Life-History of the Cephalopoda. By Frank W Lane. Pp xx+287+48 plates (London Jarrolds Publishers (London), Ltd, 1957) 30s net

MR LANE'S book provides a collection of superb photographs for which the amateur naturalist and professional zoologist must be equally grateful. The full bibliography, clearly representing an immense amount of hard work, will be of value to the teuthologist, making available a number of obscure references and enabling him to examine for himself the provenance of the many curious and often entertaining legends and observations embodied in the text, and thus to make his own estimate of their scientific value.

The text has the inevitable failings of one written by an author who has no (and does not claim to have) specialist knowledge of the subject, and for whom it is therefore hard to assess the relative importance of the different facts and concepts which he has collected. Without such evaluation, however, verbally accurate statements can become misleading, and this fault is intensified, in Mr Lane's book, by a tendency to dramatic presentation which results in important aspects of the subject receiving less full treatment than relatively trivial but striking details. A similar weakness is to be found in the references

made to authors in the text. Mr Lane is most careful to quote his sources, but, too often, equal weight is apparently given to the long-established findings of famous zoologists, to isolated observations scarcely yet verified, and even to statements, not necessarily accurate, introduced casually in the writings of specialists on other fields.

These failings will not diminish the interest which the rich anecdotal material and fine illustrations will rouse in the general reader, but, as a result of them, the book is scarcely suitable for the use of the student who seeks accurate and balanced information, and is not a book to be used for professional teaching without constant checking.

ANNA M BIDDER

Die gesunden und die erkrankten Zahngewebe des Menschen und der Wirbeltiere im Polarisationsmikroskop

Theorie, Methodik, Ergebnisse der Optischen Strukturanalyse der Zahnhartsubstanzen samt ihrer Umgebung. Von Prof W J Schmidt und Dr A Keil. Pp 386 (München Carl Hanser Verlag, 1958) 48 DM

THIS book is undoubtedly a classic of its kind by authors who are world authorities in this particular field. It deals in the greatest detail with the normal structure of the calcified tissues of the teeth of man and animals, and then proceeds to a consideration of their structure in disease. The study of the calcified tissues of the teeth has always presented considerable difficulty. The two methods which have been used most are microradiography and polarized light. It seems a pity that no attempt has been made in this book to consider microradiography, but there is no doubt that the use of polarized light as here described and the interpretations given make it a very delicate method for this work. Much difficulty has been caused in the past by faults in interpretation arising from form birefringence and the possibility of birefringence arising from the organic matrices of some of these structures, but these are now all explained in detail, giving a proper scientific basis for further study.

This is the only authoritative work on the subject. It is beautifully produced and very well illustrated. No department, dental or zoological, dealing with the structure of normal or diseased teeth can afford to be without it.

A I DARLING

Hundred Years of the University of Calcutta

Supplement. Pp xviii+732+95 illustrations (Calcutta University of Calcutta, 1957) n p

THE Centenary History of the University of Calcutta was reviewed in these columns a little more than a year ago (*Nature*, 180, 1152, 1957). This massive supplement adds a large volume of material, including descriptive accounts of the 274 colleges which are or have been affiliated with the University, similar accounts of the development and present state of the institutes and departments of the University, a select list of research publications, a list of University and College teachers in 1956, and a record of the speeches and ceremonies with which the centenary was celebrated in January 1957. There are nearly one hundred attractive photographs, chiefly of college buildings. This is the largest University in the Commonwealth—probably in the world—putting itself on record for posterity.

R S AITKEN

RADIATION MEASUREMENTS TO 658,300 KM WITH PIONEER IV

By PROF JAMES A VAN ALLEN and LOUIS A FRANK

State University of Iowa, Iowa City

Introduction

THE present report comprises (a) the radiation observations obtained with the US deep-space probe *Pioneer IV*, (b) a comparison of these observations with those of *Pioneer III* and of the first Soviet cosmic rocket and (c) an interpretative discussion.

The *Pioneer IV* programme was conducted under the same auspices as those for *Pioneer III*. The radiation detectors and the payload assembly were developed, calibrated and tested co-operatively by the Jet Propulsion Laboratory of the California Institute of Technology and by the State University of Iowa. The four stage rocket vehicle and associated aspects of the enterprise were handled jointly by the US Army Ballistic Missile Agency and the Jet Propulsion Laboratory, and the launching was conducted at the Atlantic Missile Range, Cape Canaveral, Florida.

The radiation 'package' was very nearly identical to the one flown on *Pioneer III* except for one essential change—the Anton type 213 Geiger tube was encased in an additional shield comprising a closed end cylinder of lead of thickness 4.0 gm/cm² and an inner cylinder of stainless steel of thickness 0.6 gm/cm² (Fig. 1). On the basis of extensive laboratory calibrations at the State University of Iowa, the respective Anton 302 Geiger tubes in *Pioneers III* and *IV* had identical characteristics (that is, effective dimensions, shielding, etc.) to within ± 10 per cent (see ref. 1 for further detail).

The purposes of the radiation experiments in *Pioneer IV* were as follows: (a) a re-survey of the

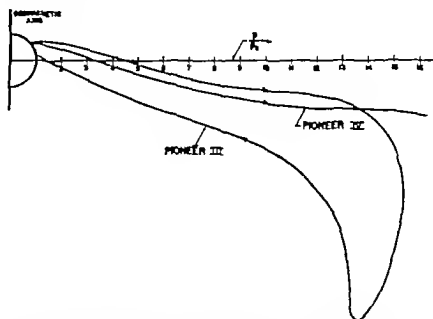


Fig. 2. Plots of the projection of the trajectories of *Pioneer III* and *Pioneer IV* on a geomagnetic meridional plane (centred dipole model). Unit of distance $\rho_E = 6,371$ km.

intensity structure of the zones of trapped radiation around the Earth with special interest in temporal changes since December 6 and 7, 1958, (b) a crude determination of the absorptivity of the trapped radiation as a function of position in order to increase knowledge of its composition and spectral character (c) a re-determination of the effective extent of the geomagnetic field, (d) a search for magnetically trapped radiation in the vicinity of the Moon, (e) a re-determination of the cosmic ray intensity in interplanetary space (f) a search in interplanetary space for 'blobs' of plasma containing particles sufficiently energetic to be detected by the present equipment.

Flight of Pioneer IV

Launch from Cape Canaveral, Florida (28° 7' N 80° 7' W) at 05 11 UT on March 3, 1959.

Burn-out velocity ('space fixed') 11 08 km/sec.

The positional co-ordinates as a function of time were measured by the Jet Propulsion Laboratory tracking array to an uncertainty of some ± 5 km throughout the region of the trapped radiation and to a slowly increasing uncertainty thereafter. Table 1 lists representative values of the co-ordinates and Fig. 2 gives a plot of the trajectories of *Pioneers III* and *IV* in the vicinity of the Earth.

Telemetry

The array of Jet Propulsion Laboratory telemetry stations comprised receivers at Cape Canaveral, Florida (5 ft dish), near Mayaguez, Puerto Rico (10-ft dish) and at Goldstone Lake, California (85-ft dish), as before. In addition there was the valuable Jodrell Bank 250 ft dish through the courtesy of Prof A C B Lovell. The following is a summary of flight periods during which usable radiation observations were obtained.

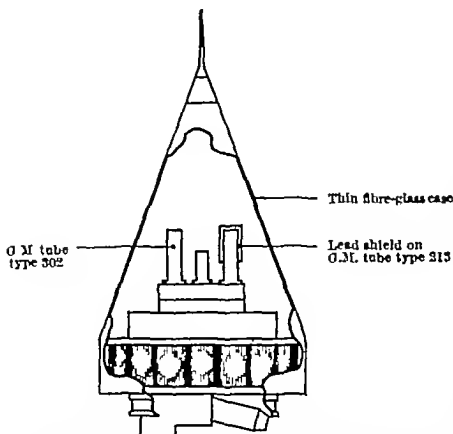


Fig. 1. Physical arrangement of radiation detectors in conical payload of *Pioneer II*. Base diameter 23 cm. Total payload weight 6.1 km. The arrangement of *Pioneer III* was identical except for omission of the shield over the 213 tube.

| | |
|-------------------------|-------------------------|
| (a) Cape Canaveral | (d) Jodrell Bank |
| March 3 05 11-05 23 U T | March 3 06 31-12 24 U T |
| (b) Puerto Rico | March 4 07 52-08 08 |
| March 3 05 14-05 52 U T | 08 23-08 43 |
| 07 23-15 32 | 10 42-12 52 |
| (c) Goldstone Lake | March 5 05 41-12 58 |
| March 3 11 53-21 03 U T | March 6 05 42-12 59 |
| March 4 12 34-21 15 | |
| March 5 12 40-21 12 | |
| March 6 12 53-15 00 | |

From the point of view of the radiation experiment, the only serious loss of data occurred in the period 05 52-06 31 U T on March 3

Beginning at about 14 20 U T on March 6, the strength of the radio signal fell rapidly and no usable data were received after 15 00 U T. In view of the rapidity of the decline (in spite of a trivial rate of change of distance) and of its occurrence at about the end of the expected life-time of the batteries, it is presumed that loss of signal at about $x + 82$ hr was due to exhaustion of the mercury batteries in the power supply of the payload. The radial distance from the centre of the Earth was 658,300 km at 15 00 U T.

Radiation Observations

Due apparently to a high- g shock which was recorded during the launching phase, the high scaling factor (2^{17}) element of the 302's scaling circuit did not function in flight. This failure gives some cause

Table 1 REPRESENTATIVE VALUES OF POSITIONAL CO ORDINATES OF *Pioneer IV*
(By courtesy of Jet Propulsion Laboratory)

| Date and hour (U T) | Geo-graphical latitude | Geo-graphical longitude (E) | Radial distance from centre of Earth | Radial distance from centre of Moon |
|---------------------|------------------------|-----------------------------|--------------------------------------|-------------------------------------|
| March 3 | | | (km) | (km) |
| 05 16 | 28 03° | 289 38° | 6,670 | 376,902 |
| 05 20 | 24 49 | 310 24 | 7,484 | 374,585 |
| 05 25 | 18 51 | 327 98 | 8,894 | 371,731 |
| 05 30 | 13 16 | 330 29 | 10,518 | 369,030 |
| 05 35 | 8 90 | 346 79 | 12,221 | 366,532 |
| 05 40 | 5 55 | 352 00 | 13,040 | 364,193 |
| 05 45 | 2 88 | 355 74 | 15,646 | 361,998 |
| 05 50 | 0 72 | 358 48 | 17,326 | 359,927 |
| 05 55 | -1 07 | 0 52 | 18,977 | 357,960 |
| 06 00 | -2 57 | 2 04 | 20,596 | 356,084 |
| 06 10 | -4 95 | 3 98 | 23,739 | 352,556 |
| 06 20 | -6 77 | 4 92 | 26,767 | 349,272 |
| 06 30 | -8 20 | 5 18 | 29,691 | 346,184 |
| 06 40 | -9 37 | 4 97 | 32,522 | 343,255 |
| 06 50 | -10 34 | 4 41 | 35,271 | 340,460 |
| 07 00 | -11 16 | 3 58 | 37,947 | 337,779 |
| 07 30 | -13 03 | 359 98 | 45,804 | 330,280 |
| 08 00 | -14 34 | 355 31 | 52,812 | 323,400 |
| 08 30 | -15 31 | 349 99 | 59,667 | 316,982 |
| 09 00 | -16 07 | 344 25 | 66,236 | 310,917 |
| 10 00 | -17 20 | 331 92 | 78,696 | 299,593 |
| 11 00 | -18 00 | 318 88 | 90,452 | 289,070 |
| 12 00 | -18 61 | 305 41 | 101,662 | 279,139 |
| 18 00 | -20 53 | 220 44 | 161,788 | 226,753 |
| March 4 | | | | |
| 00 00 | -21 39 | 132 74 | 214,953 | 180,855 |
| 06 00 | -21 89 | 44 07 | 264,261 | 138,707 |
| 12 00 | -22 23 | 314 91 | 311,064 | 100,511 |
| 18 00 | -22 46 | 225 44 | 356,113 | 70,343 |
| 23 00 | -22 59 | 150 71 | 392,608 | 60,149* |
| March 5 | | | | |
| 00 00 | -22 61 | 135 74 | 399,796 | 60,624 |
| 06 00 | -22 08 | 45 89 | 442,117 | 79,376 |
| 12 00 | -22 72 | 315 95 | 483,204 | 113,528 |
| 18 00 | -22 74 | 225 97 | 523,322 | 153,434 |
| March 6 | | | | |
| 00 00 | -22 75 | 135 95 | 562,660 | 195,942 |
| 06 00 | -22 76 | 45 90 | 601,348 | 239,979 |
| 12 00 | -22 77 | 315 83 | 639,476 | 285,112 |
| 18 00 | -22 77 | 225 75 | 677,116 | 331,132 |

* Nearest approach to the Moon (approx.)

for uneasiness concerning the proper operability of all other elements of the payload. But we have been quite unable to find any evidence for any other malfunction and believe that the results reported below are trustworthy.

In Fig 3 is plotted the true counting rate, R , of the 302 Geiger tube as a function of time. Errors are insignificantly small except where error bars are drawn. The constant counting rate beyond 11 10 U T continues without significant variation to the outermost limit of observations. Also shown is the equivalent counting rate of the heavily shielded 213 Geiger tube. Normalization of the counting rates of the two tubes was done in pre-flight laboratory tests by subjecting them (both unshielded) to identical exposure in a beam of hard X-rays. The quasi-d.c. output of the 213 tube was measured by the audio-frequency of the subcarrier oscillator to which its amplifier was connected. A substantial temperature correction was necessary and was made by comparison with another, similarly located oscillator the input of which was digital and the temperature coefficient of which was similar. The temperature of the inner portion of the payload rose from a launching value of 15°C to an asymptotic value of $41.5 \pm 1.0^\circ\text{C}$ with a time constant of about 3 hr. The 302 system had zero temperature dependence over this range. In the lower left-hand corner of Fig 3 is plotted as a dashed line the ratio of the equivalent counting rate of the (shielded) 213 tube to that of the 302, this ratio is the apparent transmission, T , of the shield. The absolute value of T is uncertain by some ± 25 per cent of its value due to a combination of systematic errors.

In the time-period 06 31-06 53 U T the true counting rate of the 302 may lie either on branch A or on branch B . Such an ambiguity is intrinsic to the characteristic curve of apparent rate versus true rate of the system (cf ref 1) and can be resolved only by auxiliary data. The corresponding transmission curves are labelled A and B , respectively. Further discussion is deferred to the next section.

In Fig 4 the observations with the nearly identical 302 tubes of *Pioneer III* and *Pioneer IV* are shown as a function of radial distance from the centre of the Earth, ignoring differences of longitude and latitude.

Discussion and Interpretation

The most striking features of Fig 4 are the immensely greater quantity of trapped radiation in the outer zone on March 3, 1959, than on December 6, 1958, and the detailed structure present, especially in the 60,000-90,000 km region. It may also be noted that the observations by Vernov *et al*² with the Soviet cosmic rocket show that the situation on January 2, 1959, was similar to that on December 6 and 7, 1958. It is very suggestive that there was a substantial magnetic storm commencing at 02 15 U T on February 25 and that there were aurorae of strong intensity on February 25-28 and on March 1³. A special study of this event by Trotter⁴, of the High Altitude Observatory, makes it appear likely that at least three sequences of geophysical events starting on February 25, March 26 and April 23, respectively, were due to a solar M region. In any event, it is noteworthy that the flight of *Pioneer IV* was preceded by five consecutive nights of strong auroral activity, whereas the periods preceding the flights of *Pioneer III* and of the Soviet cosmic rocket were especially

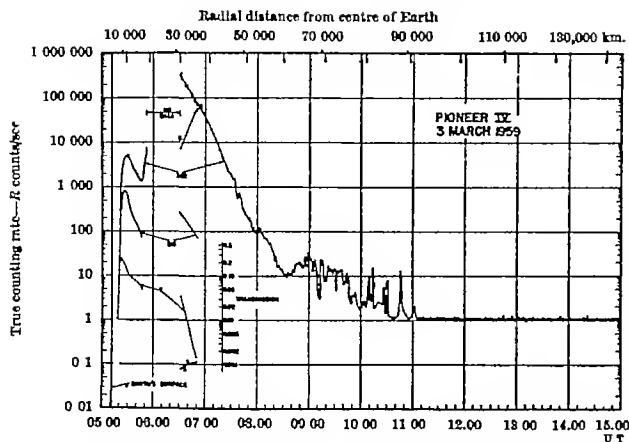


Fig. 3 The counting rate observations during the early part of the flight of *Pioneer IV* (see text for further description of data)

quiet geophysical periods. Hence we suggest that the great temporal differences shown in Fig. 4 constitute the direct observation of the changes which occur in the outer radiation zone of trapped radiation following strong corpuscular emission from the Sun. If this view be accepted then it appears that the *Pioneer IV* observations provide the most persuasive, direct evidence thus far available for the solar origin of (at least) the outer radiation zone.

The inner peak of the *Pioneer IV* data (at 11 000 km) is about three times as intense as that of *Pioneer III*, but reference to Fig. 2 and to a large scale corrected plot as in Fig. 5 of ref. 1 shows that the inner zone was not significantly different on the occasions of the two flights. From this fact it may be concluded that the inner zone lying as it does in the region of strong geomagnetic field is relatively well isolated from direct solar influence.

The A-B ambiguity referred to in the preceding section in connexion with Fig. 3 (and Fig. 4) has not been conclusively resolved, but the following discussion strongly favours branch A as the correct one. The work of Vornov *et al.*⁸ makes it appear likely that in the outer zone the effects recorded by a detector under more than 1 gm/cm² of absorber are due to bremsstrahlung from the bombardment of the outer skin of the payload by electrons of energies less than 100 keV and with a spectrum steeply rising toward lower energies. If this be so then we note that transmission curve B of Fig. 3 not only has a quite unreasonable steepness but at its inner end has a value at least an order of magnitude greater than that measured in the laboratory with X-ray beams generated by elec-

trons of such energies. But transmission curve A is also together consistent with this radiation situation.

Adopting branch A and making use of our absolute X-ray calibrations of the 302 tube we find that the omnidirectional flux of electrons of energy greater than about 20 keV was of the order of $1 \times 10^{11}/\text{cm}^2 \text{ sec}$ at 30,000 km radial distance on March 3, 1959.

Also it is evident that the omnidirectional flux of electrons of energy greater than 200 keV did not exceed $1 \times 10^9/\text{cm}^2 \text{ sec}$ of electrons of energy greater than 2.5 MeV did not exceed $1 \times 10^8/\text{cm}^2 \text{ sec}$, and of protons of energy greater than 60 MeV did not exceed $1 \times 10^7/\text{cm}^2 \text{ sec}$.

The observations of *Pioneer IV* in the inner zone are unambiguous and show that about 30 per cent of the radiation

recorded by the 302 in the lower fringe of the zone also penetrates an additional 4.0 gm/cm² of lead and 0.6 gm/cm² of steel. The radiation becomes rapidly and progressively softer as one goes outwards from the Earth (Fig. 3). On the basis of two recent rocket investigations into the lower fringe of the inner zone⁹ and of our extensive *Explorer II* and *Pioneer III* observations¹⁰, we propose the following tentative composition of the trapped radiation present in the heart of the inner zone (altitude about 3 000 km on the geomagnetic equator): (a) electrons of energy greater than 20 keV—maximum unidirectional intensity $\sim 2 \times 10^9/\text{cm}^2 \text{ sec}$ steradian; (b) electrons of energy greater than 600 keV—maximum unidirectional intensity $\sim 1 \times 10^7/\text{cm}^2 \text{ sec}$ steradian; (c) protons of energy greater than 40 MeV—omnidirectional intensity $\sim 3 \times 10^6/\text{cm}^2 \text{ sec}$. The

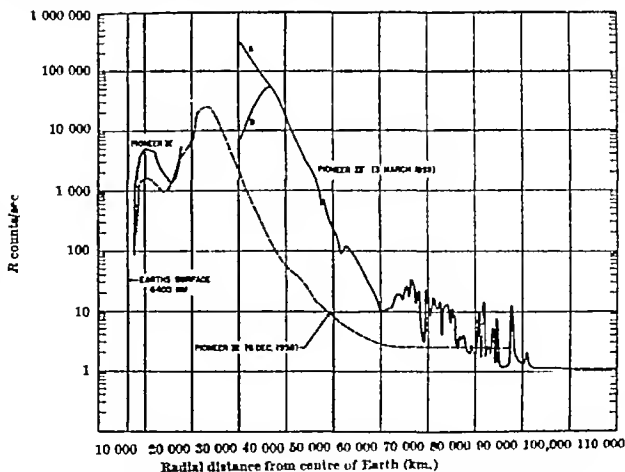


Fig. 4 A comparative plot of the intensity data of *Pioneer III* and *Pioneer IV* (same scale of radial distance but ignoring differences of latitude and

latter two of these three figures are probably trustworthy to a factor of 2, the first one to a factor of 5. These results favour the neutron albedo hypothesis of origin of the inner zone of Vernov and others (cf discussion of ref 8), in respect to both the electron and proton components. A valuable discussion of the proton component has been given recently by Hess⁹. Some residual doubt may be felt as to the adequacy of the source function. It should also be noted that there is a rapidly developing body of knowledge on the sporadic, though relatively frequent (order of once a month) arrival of solar protons having energies up to several hundreds of MeV and intensities up to several orders of magnitude greater than that in the quiet cosmic ray beam¹⁰⁻¹³.

The conclusive identification of protons in the lower fringe of the inner zone⁷ and the resemblance of their spectrum there to that expected on the neutron albedo hypothesis⁹ has been accepted by many workers as conclusive evidence for the adequacy of this hypothesis. The quantitative considerations of Hess have also added strongly to this point of view. But it should be remarked that others, including Morrison, Gold and the present authors⁸, have some uneasiness in accepting a trapping-lifetime of several years, as is necessary for the success of the neutron albedo hypothesis. Thus, it is comforting to find that there is now an alternative source of protons (that is, direct solar emission) of suitable energy and intensity, provided a valid mechanism can be discovered for their admission into the inner zone. The reader is also cautioned to await observations during the oncoming period of minimum solar activity for illuminating evidence on temporal changes in both inner and outer radiation zones. Such a programme of observation is being undertaken by this laboratory.

Radiation Intensity Beyond 92,000 km

Pioneer IV provided a total of 45 hr of observation of the counting rate of the 302 Geiger tube in the range of 92,000–658,300 km from the centre of the Earth. (The counting-rate-meter circuit of the 213 was not sufficiently sensitive to provide a reading at any time during this portion of the flight.) The mean counting rate was calculated over each interval of time during which 256 (2⁸) counts were recorded. The distribution of counting rates in the 695 such intervals (each of about 4 min duration) has been studied in detail and it has been found that during no one of these intervals did the counting rate differ with statistical significance from the overall mean value of 1.090 ± 0.003 counts per sec.

A broader scale survey of the mean counting rate during larger segments of the trajectory was obtained by tabulating the times at which 'flips' of the major scaler (2¹³ = 8,192 counts per major 'flip cycle') occurred. The constancy of the counting rate during observed periods encouraged us to also 'count through' the unobserved periods of time, during which the payload was below the effective horizons of the receiving stations. During the longest such period six major flips were missed, and during the other two such periods four major flips were missed if it be assumed that the counting rate did not differ markedly when under observation and when not under observation. The results of this process are shown in Table 2. The trustworthiness of the tabulated counting rates during unobserved periods rests on *a posteriori* evidence as follows. On the assumption that the unobserved counting rates did not differ

Table 2 SUMMARY OF DATA FROM 302 TUBE BEYOND 92,000 KM BY FLIPS OF MAJOR SCALER (8,192 counts per flip cycle)

| Serial No of flip | Time of flip and station, day, hr min, sec | Δt sec | Mean counting rate (sec) ⁻¹ | Radial distance to centre of Earth (km) | Radial distance to centre of Moon (km) |
|-------------------|--|----------------|--|---|--|
| 0 | 3/12 18 19 JB | | | | |
| 0 | 3/12 18 22 PR | | | | |
| 1 | 3/14 23 13 PR | 7,401 | 1.094 ± 0.012 | 104,920 | 270,240 |
| 0 | 3/12 18 22 GL | | | 120,740 | 257,130 |
| 1 | 3/14 23 10 GL | 7,488 | 1.094 ± 0.012 | 147,440 | 230,080 |
| 2 | 3/16 20 18 GL | 7,508 | 1.082 ± 0.012 | 107,020 | 222,150 |
| 3 | 3/18 34 18 GL | 7,500 | 1.092 ± 0.012 | 185,880 | 205,040 |
| 4 | 3/20 30 15 GL | 7,407 | 1.093 ± 0.012 | | |
| 5 | Not observed | | | | |
| 6 | Not observed | | | | |
| 7 | Not observed | | | | |
| 8 | Not observed | 52,020 | 1.090 ± 0.005 | | |
| 9 | Not observed | | | | |
| 10 | Not observed | | | | |
| 11 | 4/11 16 15 JB | | | 305,450 | 104,800 |
| 12 | 4/13 20 55 GL | 7,480 | 1.095 ± 0.012 | 321,340 | 02,750 |
| 13 | 4/15 27 07 GL | 7,572 | 1.082 ± 0.012 | 337,150 | 81,030 |
| 14 | 4/17 33 18 GL | 7,571 | 1.082 ± 0.012 | 350,030 | 73,140 |
| 15 | 4/19 38 40 GL | 7,522 | 1.080 ± 0.012 | 366,420 | 65,620 |
| 16 | Not observed | | | | |
| 17 | Not observed | 37,386 | 1.090 ± 0.005 | | |
| 18 | Not observed | | | | |
| 19 | Not observed | | | | |
| 20 | 5/00 01 46 JB | | | 440,610 | 79,340 |
| 21 | 5/08 06 13 JB | 7,467 | 1.007 ± 0.012 | 454,010 | 88,010 |
| 22 | 5/10 12 23 JB | 7,570 | 1.082 ± 0.012 | 470,990 | 102,420 |
| 23 | 5/12 16 32 JB | 7,449 | 1.100 ± 0.012 | 485,110 | 115,320 |
| 24 | 5/14 22 33 GL | 7,501 | 1.083 ± 0.012 | 499,230 | 128,950 |
| 25 | 5/16 27 21 GL | 7,448 | 1.100 ± 0.012 | 513,040 | 142,810 |
| 26 | 5/18 30 55 GL | 7,414 | 1.105 ± 0.012 | 525,090 | 155,280 |
| 27 | 5/20 35 15 GL | 7,460 | 1.098 ± 0.012 | 540,350 | 171,510 |
| 28 | Not observed | | | | |
| 29 | Not observed | 37,620 | 1.089 ± 0.005 | | |
| 30 | Not observed | | | | |
| 31 | Not observed | | | | |
| 32 | 6/07 02 15 JB | | | 607,950 | 247,650 |
| 33 | 6/09 08 41 JB | 7,586 | 1.080 ± 0.012 | 619,840 | 261,600 |
| 34 | 6/11 13 48 JB | 7,507 | 1.090 ± 0.012 | 634,630 | 279,200 |
| 35 | 6/13 20 57 GL | 7,620 | 1.074 ± 0.012 | 647,000 | 205,890 |

Overall mean for 35 intervals, 1.090 ± 0.002 counts/sec
Overall mean for 17 observed intervals, 1.090 ± 0.003 counts/sec
PR, Puerto Rico, GL, Goldstone Lake, JB, Jodrell Bank

markedly from the observed ones, it is found in Table 2 that the unobserved counting rates differed by less than 1 per cent (that is, to within statistical uncertainty) from the adjacent, observed ones. The precision of this agreement in all three of the cases under consideration gives one a strong feeling of assurance that the counting rate of the 302 did not differ significantly at any time in the interval 92,000 to 658,000 km (March 3, 11 10 UT, to March 6, 15 00 UT) from its mean observed value of 1.090 ± 0.003 counts per sec. Several valuable conclusions follow from this analysis and are described in subsequent sections.

Paucity of Energetic Plasma in Interplanetary Space during March 3–6, 1959

On the basis of Table 2 and the foregoing discussion, it appears that, to high accuracy, the apparatus did not encounter any solar plasma containing particles sufficiently energetic to register efficiently on the 302 tube during some 76 hr of interplanetary flight.

Since the burden of evidence for the origin of the outer radiation zone of the Earth requires that plasma fly outwards from the Sun sporadically, it must be concluded that there happened to be a notable absence of such plasma during this period. This finding is especially striking in view of the strong geophysical activity during the preceding week. An alternative view is that the acceleration of the components of the plasma to sufficiently high energies to be registered efficiently by our equipment occurs

only in the geomagnetic field. The 302 tube in the present arrangement had an efficiency of about unity for protons of energy greater than 30 MeV, an efficiency of the order of unity for electrons of several MeV energy, and an efficiency of the order of 10^{-4} to 10^{-6} for electrons in the hundreds to tens of keV energy range (by way of their bremsstrahlung).

Hence during the 70 hr in question the time integrated flux of the higher-energy electrons and protons could not have exceeded $100/\text{cm}^2$ in an isolated burst during any one of the 0.95 observed 4 min intervals, could not have exceeded $1,000/\text{cm}^2$ in an isolated burst during any one of the three unobserved periods which had a duration of some 10 hr each, and could not have exceeded $2 \times 10^3/\text{cm}^2$ if distributed (with quite unbelievable uniformity) over the 70 hr period. The corresponding figures for 00 keV electrons, for example, are 4×10^4 times as great.

Lack of Influence of the Moon

Pioneer II's closest approach to the centre of the Moon was 00,149 km at about 23 00 τ on March 4 (Table 1). The telemetered signal was not being received at that time (see section on "Telemetry," and Table 1). But observations were obtained as close as 61,700 km and Table 2 and the accompanying discussion make it exceedingly unlikely that any significant change of counting rate occurred at any place in the vicinity of the Moon. The quantitative discussion of the preceding section is applicable here also. The geometrical shadow of the Moon on the apparatus was, of course, negligible. Hence this result suggests as an upper limit to the Moon's magnetic moment a value comparable to that of the Earth. This high an upper limit is, of course of little interest in the light of other probably more definitive knowledge which favours a much smaller value.

The Soviet cosmic rocket passed much closer to the Moon than did *Pioneer IV*, but unhappily the radiation intensity was unreadable at that range.

None the less, the determination of the Moon's magnetic moment by investigating its trapped corpuscular radiation on near approaches remains a technique of potential value. It will doubtless be wise to use a detector of the lowest feasible energy threshold and of the highest feasible sensitivity.

Re-determination of Interplanetary Cosmic-ray Intensity

On the basis of Table 2 and of our best present values of absolute geometric factor and efficiency of the 302 Geiger tube, we find for the interplanetary value of the omnidirectional cosmic ray intensity $J_0 = 1.8 \pm 0.3/\text{cm}^2 \text{ sec}$ during the period March 3-6 1959.

It may be noted that this value is one-half of that measured¹ on December 6 and 7, 1958, with *Pioneer III*. On the basis of a recent re-study of *Pioneer III* data, Snyder¹⁴ presents evidence that *Pioneer III* did not reach a sufficiently great distance to be entirely free of the influence of the geomagnetic field.

The *Pioneer IV* observations to very much greater distances (out to 103 Earth radii) are not subject to this uncertainty. Hence, we have considerably greater confidence in the new value quoted above though it should be understood that the counter will record protons of energy as low as 30 MeV and electrons of energy as low as 2 MeV. In any event, the measurement provides a solid upper limit to the total primary cosmic ray intensity in the general

astronomical vicinity of the Earth during early March 1959.

Using balloon borne equipment of discriminating character McDonald¹⁵ finds primary unidirectional cosmic ray intensities (corrected to zero atmospheric depth) at geomagnetic latitude 55° on July 2, 1958, as follows:

- Protons of energy greater than 230 MeV $0.000 \pm 0.0070/\text{cm}^2 \text{ sec steradian}$.
- Particles of energy greater than 158 MeV/nucleon 0.0149 ± 0.0012 .
- Sum of (a) and (b) 0.1099 .

An interesting comparison results from multiplying McDonald's sum of $0.11/\text{cm}^2 \text{ sec steradian}$ by 4π to obtain an estimate of the omnidirectional intensity of primary cosmic rays remote from the Earth. The result is $J_0 = 1.38/\text{cm}^2 \text{ sec}$. In so far as McDonald has been able to eliminate fast downward moving albedo his implied J_0 has the nature of a lower limit.

Vernov and Chudakov² report a value of $2.3 \pm 0.1/\text{cm}^2 \text{ sec}$ on January 2, 1959.

Effective Extent of the Geomagnetic Field

Our original interpretation of the *Pioneer III* observations¹ included the conclusion that the geomagnetic field loses its ability to trap charged particles at about 10 Earth radii. Snyder's discussion makes it appear that this was too small a value. The *Pioneer IV* observations (Fig. 4) indicate that geomagnetic trapping is significantly present out to as far as 14 Earth radii at least on a specific occasion. The loss of geomagnetic trapping efficiency is of course a loosely defined concept and there are doubtless marked fluctuations in the radiation regions at the outer fringes of the Earth's field.

Terrestrial Ring Current of Dolginov and Pushkov

Measurement of the scalar magnetic field intensity with the magnetometer in the Soviet cosmic rocket on January 3 1959, provided results of very great interest¹⁶ in the present connexion. The observed scalar field intensity fell gradually and progressively further below the curve representing the extrapolation of the surface field (using an eight-coefficient harmonic expansion and assuming a curl free field outside the solid Earth) in the radial distance range 14,000-21,000 km. At 21,000 km, the experimental curve was some 709 gammas below the 'theoretical curve (about 1,200 gammas). At greater radial distances the experimental curve rose toward the theoretical one and approximated to it beyond 20,000 km. These results imply a westward flowing ring current having the maximum value of the apparent current density at about 21,000 km radial distance from the centre of the Earth. By comparison with Fig. 4 of the present article it is seen that the most intense portion of the ring current lies in the inner side of our outer peak of radiation intensity and indeed in just the region in which the gradient of the volume density of charged particle kinetic energy has its greatest value. The understanding of the detailed relationship between the Dolginov-Pushkov ring current and the trapped radiation now becomes one of the most challenging and timely problems of geophysics.¹⁷

It may be speculated that the modification of the geomagnetic field by the ring current at about 3 Earth radii influences the structure of the radiation zones and perhaps contributes to the existence of the slot between the two zones.

Although the difference in the radiocarbon ages of the cranial bones and mandible is less than might have been expected in view of their contrasting states of preservation, it should be borne in mind that whereas a bone that has been buried in the ground for a few centuries may have become porous and 'sub-fossil' (with some absorbed fluorine), a bone of equal antiquity that has been preserved in air, for example on the floor of a dry cave, in a building or in a reliquary, may have retained the composition of 'recent' bone

Summary Radiocarbon dating has confirmed that the Piltdown skull (human) is Post-Pleistocene, probably less than 800 years old, and that the Piltdown mandible (orang-utan) is younger rather

than older, although possibly several centuries old. It is shown that these findings are not inconsistent with the skull being in 'sub-fossil' condition whereas the mandible (of very different origin) has the preservation of 'recent' bone

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⁴ See, for example, Martin, R., "Über Skelettkult und verwandte Vorstellungen", *Mit. Geogr. Ethnogr. Gesell. Zürich* 1920, Taf. 4, Fig. 6

⁵ Everett, A. H., Second Quarterly Report on the Bornean Cave Exploration, Rep. Brit. Assoc., Sheffield, 144 (1879)

DISORGANIZATION OF THE SECONDARY STRUCTURE IN PROTEINS EXPOSED TO IONIZING RADIATIONS IN THE SOLID STATE

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LITTLE is known of the chemical and physical changes which occur when proteins are exposed to ionizing radiations under conditions where the effect is due to ionization within the protein molecules, that is, by 'direct' action. Detailed physical chemical studies have only been made on protein irradiated in solution when the reaction is indirect and due to free radicals. Most investigations of the direct effect have been confined to following the effect on their biological properties. It has been known for nearly fifteen years (cf. Lea¹) that the inactivation of dry enzymes by ionizing radiations is exponential with dose, which suggests that one event leads to loss of activity. The amount of energy which has to be supplied before this single reaction occurs is normally between 50 and 200 eV per molecule, depending on the enzyme. Quantitatively this suggests that nearly every primary ionization must be effective in destroying the biological activity. A primary ionization in an organic substance brings with it far-reaching chemical changes which usually affect several groups, but it seems highly improbable that the inactivation of all enzymes can be attributed to the chemical modification of a few amino-acid residues.

Biochemical studies² have shown that for many enzymes only a small part of the protein molecule is necessary, and that a large proportion of the amino-acid residues can be modified without loss of activity. Energy transfer processes which were recognized in organic macromolecules³ cause preferential attack of some groups, but the effect is not sufficiently selective to provide a mechanism for the inactivation of all enzymes by a single random event.

In a detailed study of the changes produced by irradiating solid crystalline bovine serum albumin (Armour Laboratories) containing 4-6 per cent of water with 2 MeV electrons, in the absence of oxygen we have found that the first effect of irradiation is to disorganize a large part of the molecule. This alteration in structure is not dependent on covalent chemical changes which follow ionization, but is the

result of a breakdown of many secondary valency bonds brought about by a single event which occurs on average for every 45 eV deposited and can therefore be associated with a primary ionization. The occurrence of a process of this type was predicted by Platzman and Franck and provides a mechanism for the inactivation of heat-labile enzymes of all types by ionizing radiations.

Opening up the Molecule

On irradiation the sedimentation behaviour of the bovine serum albumin in the ultracentrifuge changes⁴, and the decrease in normally sedimenting material follows an exponential relationship (Fig. 1), with a D_0 (dose required to change 63 per cent of all molecules) of 6.5×10^6 rads. This corresponds to an energy of 45 eV per molecule, which has to be supplied to affect on average one molecule. Change in sedimentation implies an alteration in molecular weight or in frictional resistance determined by the internal structure of the molecule. Light-scattering measurements show that with a dose sufficient to alter the sedimentation of 75 per cent of the molecules, the average molecular weight of bovine serum albumin rises only from 69,000 to 90,000. The ultracentrifuge measurements therefore indicate that a single event which occurs on average for every 45 eV of energy supplied changes the shape of the molecule. The assumption that the material sedimenting normally is native protein that has not been affected at all by radiation is confirmed by chromatography.

Evidence that radiation 'opens up' the molecule is provided by changes in the chemical reactivity of the constituent amino-acid residues. Bovine serum albumin contains seventeen disulphide groups per molecule, but at the isoelectric point none of these can be reduced to -SH groups⁵, or oxidized with peracetic acid to sulphonic acid groups⁶ under standard conditions. These groups are sterically inaccessible, but at pH values away from the isoelectric

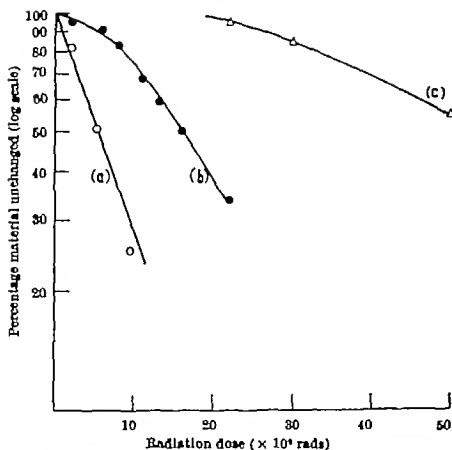


Fig. 1. Effect of irradiation of 2 MeV electrons on some physical properties of bovine serum albumin. a, Fraction of bovine serum albumin showing changed sedimentation behaviour in the ultracentrifuge; b, fraction of bovine serum albumin insoluble in water; c, fraction of bovine serum albumin insoluble in $M/15$ phosphate buffer (pH 7).

point, or following denaturation, some become available for reaction. Exposure to 4 M guanidine hydrochloride at the isoelectric point makes available 70 per cent of the total present and this is further increased at alkaline pH values. On the other hand, a maximum of only 50 per cent are revealed by heat denaturation*.

Irradiation of the solid protein progressively increases the number of disulphide bonds available up to a maximum of 50 per cent (Fig. 2) (at the highest doses some of these are destroyed but within the dose range studied this is negligible). From the irradiated bovine serum albumin a fraction can be separated which is no longer soluble in water, and dissolves only in salt solution. In the water soluble fraction an increasing proportion of the disulphide bonds (up to 30 per cent) is revealed, and by applying a correction, on the basis of the ultracentrifuge measurements, for the presence of unchanged native material, the number of available groups in the molecules affected by radiation can be calculated (Fig. 2). This first radiation change can be described as an opening up of the molecule which changes the frictional properties but not the molecular weight, and reveals five disulphide bonds normally hidden. Since this change is associated with a single reaction which occurs when an average of 45 eV have been left in the molecule it can probably be ascribed to the production of one primary ionization.

Changes following a Multi Hit Dose Relationship

Another radiation effect is to render the protein insoluble in water while remaining soluble at high and low pH values and in salt solutions. To avoid 'trapping', the insoluble fraction is determined by measuring the protein which comes out of solution on dialysing out the $M/15$ phosphate buffer (pH 7) in which the irradiated protein is completely soluble. Fig. 1 shows that in the production of insolubility there is a pronounced threshold with dose and it fits

accurately a 'two hit curve'. This protein has a greatly increased light scattering molecular weight with average values ranging up to 350 000, but is highly polydisperse. These aggregates are not broken up, that is, the average molecular weight is unchanged, by solvents breaking hydrogen bonds or disulphide bonds and the cross links joining the molecules in the aggregates do not therefore involve either of these bonds. An interpretation consistent with all the facts is that a second ionization still further disorients the secondary structure of the molecule and thereby changes its solubility behaviour enabling cross links to be formed between molecules. In this extensively modified protein following the second ionization approximately half the disulphide bonds are available.

Further irradiation does not reveal any more disulphide bonds, but it does render the protein insoluble even in salt solution (curve C, Fig. 1). This heavily irradiated material dissolves only in 4 M guanidine hydrochloride. Probably extensive chemical alterations now involving about 5 per cent of all the amino acid residues made extensive intermolecular hydrogen bonding possible.

Chemical Changes

Chemical analysis of the irradiated protein for nine amino acids shows that the disappearance of amino acids (the nature of the products was not established) was linear with dose but that the sensitivity of the constituent amino-acids varies. Cysteine and dicarboxylic acids were the most sensitive, the aromatic and the basic amino acids came next in sensitivity and proline was the least affected by radiation of those studied. However the total range was less than a factor of three for example 10^4 rads affected 18 per cent of the cysteine, 13.5 per cent of the histidine and 8 per cent of the proline. Thus after a dose sufficient (that is, 45 eV/molecule) to open up the protein (only one molecule in five will have a single cysteine residue changed, one in six one histidine residue, and only one in two will have lost a carboxyl group).

The possibility that main chain polypeptide bonds are broken was tested by looking for low molecular

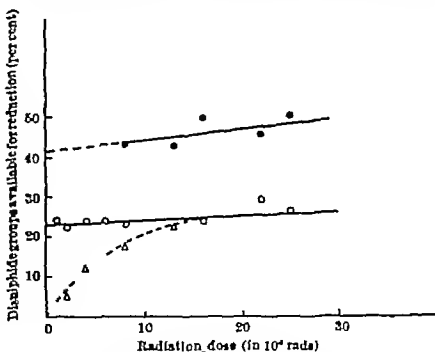


Fig. 2. Effect of radiation on the number of disulphide bonds in bovine serum albumin which can be reduced at the isoelectric point with β -mercapto-ethylamine. — Δ — For water-soluble fractions (that is including the molecules that have not been affected by radiation). — \bullet — for the insoluble fraction after correction for unchanged protein on the basis of the ultracentrifuge data. — \bullet — for fraction insoluble in water but soluble in salt solution.

weight fragments which could be recovered by dialysis of solution of heavily irradiated protein in 4 M guanidine hydrochloride. To guard against the possibility that broken fragments do not become detached because they are linked to the main molecule by disulphide bridges, the irradiated protein dissolved in guanidine hydrochloride was oxidized with peracetic acid, which breaks all disulphide bonds under these conditions. As no dialysable fragment could be found even after a dose of 2.5×10^5 rads it can be concluded that main-chain breaks play no part in the disorganization of the secondary structure.

Other chemical changes due to irradiation are the formation of carbonyl groups⁷ and of additional SH groups, as well as of a new amino-acid which has the same chromatographic behaviour as α -amino-*n*-butyric acid.

The presence of oxygen during the irradiations did not alter the first stage of 'opening up' or the destruction of amino-acids. However, the protein is rendered insoluble in water at lower doses and the greater radiation sensitivity of dry enzymes in oxygen⁸ may be due to the increased tendency for aggregation, or the production of main-chain breaks, which is facilitated by oxygen.

Mechanism of Enzyme Inactivation

Although bovine serum albumin has been studied by us in greatest detail, irradiation of solid trypsin, lysosyme and γ -globulin produces a very similar sequence of events, and we believe that the pattern outlined above applies generally to globular proteins. We interpret the changes which occur in a protein molecule by an ionization produced within it by an atomic particle as a two-stage process. First, the introduction of a positive charge disrupts the secondary structure over a large part of the molecule and introduces a new configuration. Secondly, the group in the molecule that has become ionized undergoes a chemical change. The latter are not randomly distributed and energy transfer processes increase the probability of damage in certain amino-acid residues. But these effects are not very selective and there is no indication that one particular type of side-chain will be altered in every protein molecule that had suffered an ionization. This precludes the possibility that loss of activity can be due to these chemical effects, and it seems much more plausible to relate inactivation to the initial disturbance of secondary structure as this is an immediate consequence of the ionization. An explanation is provided why ionizing radiations are much more effective (on a dose basis)

in inactivating enzyme⁹ than ultra-violet light or the indirect action of ionizing radiation (that is, H and OH radicals). Both these processes attack the protein chemically and alter side-chains, but they cannot disorganize the secondary structure directly.

We suggested tentatively¹⁰ that the sudden introduction of a positive charge breaks down induced dipoles and that the resulting temporary opening of hydrogen bonds allows the protein molecule to adopt a configuration having a lower free energy. The difficulty is to provide a mechanism by which the electric disturbance spreads over a significant part of the protein molecule. Platzman and Franck¹¹ were led from purely theoretical considerations to postulate that an ionization within a protein molecule changes the internal hydrogen bonding. They have discussed the probable range of the electrical disturbance in considerable detail and conclude that some fifteen to twenty hydrogen bonds can be severed in this way. Not enough is known of protein structure to predict whether the breakage of this number of hydrogen bonds is sufficient to produce the observed disorganization.

We wish to thank Mr W H T Davidson, of the Research Laboratories of Tube Investments, Ltd, for carrying out the irradiations, and Dr D Rosen for the ultracentrifugation.

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ORIENTATION OF ANIMALS TO POLARIZED LIGHT

By DR. H. KALMUS

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WORK done or published during the past year concerning the orientation of animals—mainly arthropods—to the plane of polarization of light indicates the emergence of two different and, up to a point, contradictory approaches to these visual reactions. What may be called the orthodox view, gradually developed since von Frisch's original dis-

covery in 1948 of the ability of bees to orientate themselves with respect to the plane of polarization, has been ably summarized in a review article by Stockhammer¹. He considers the various types of arthropod eyes to be analysers and, in particular, thinks that the analysing faculty is not situated in the dioptric parts but depends upon special arrangements

of visual pigments in the receptor cells which, like a polarizing screen, would combine the properties of analysis and absorption.

Quite different conclusions have been drawn by Baylor and Smith (*Apis*)³, Bambridge and Waterman (*Mysidium*)², Burdon-Jones and Charles (*Littorina*)⁴, as well as by Kalmus (*Aedes*, *Drosophila*, *Thaumato myia*)⁵, who considered that the orientational behaviour of these various animals in the presence of polarized light might be explained either by purely external mechanisms, for example, by brightness patterns resulting from unequal scattering or reflexion from environmental objects, or by similarly unequal refraction from some faces of the dioptric apparatus, such as the surface of the eye. Neither of these interpretations requires analysing arrangements in the receptors.

The hypothesis that the rhabdomers of insect ommatidia are absorbing analysers is supported by the electro-physiological results and electron microscopical work quoted by Stockhammer¹, it has been further strengthened by the beautiful electron micrographs of insect eyes by Fernández Morán⁶, confirming that each rhabdome is built-up of numerous rod-shaped or tubular units which are oriented in regular array with their long axes more or less at right angles to the long rhabdome axis. In an opposite pair of rhabdomers in any ommatidium the rods or tubules show a similar orientation, but in adjoining rhabdomers their orientation differs. The orientation of the rods in the rhabdoms of neighbouring ommatidia may follow a regional pattern. At the level of the basement membranes 7-9 single sheathed nerve fibres exist in every ommatidium, indicating that separate signals might originate and be transmitted from each rhabdome. Some of Morán's figures show indeed a striking similarity to the 'star' model of an ommatidium, which von Frisch proposed many years ago for its analysing properties and provided it can be shown that the dichroitic visual pigment is incorporated into the rhabdome pattern in a regular and orientated manner, a physical basis would seem to exist for the assumption that the rhabdomers of insect eyes are indeed analysers. Thus equipped, the eyes of a bee should be able to distinguish between various areas in the blue sky which, during the day time, are fairly characteristic in their degree of polarization and direction of the plane of polarization, and which, according to von Frisch's experiments, they learn to recognize and navigating bees might use this information, rather as they use the position of the Sun when it is directly visible to them.

A transversal arrangement of rod-shaped structures seems to be of wide occurrence in the rhabdomers of arthropods, and a similar organization, found in the visual elements of the squid *Loligo*⁷ may occur in the molluscs. But in the rods and cones of vertebrates, the orientation of the structures to which the visual pigments are presumably attached is quite different and unsuitable for the detection of the plane of polarization of light impinging in the physiological direction.

Reactions to polarized light striking the rounded surface of some types of bulgy eyes at a skew angle can be expected to produce specific orientational effects in the absence of retinal analysers. Castilo (quoted by Stockhammer¹) has shown that a primitive type of such orientation occurs even in the absence of eyes, for example in fungi the cylindrical sporangiothecae of *Phycomyces* growing upwards

in a culture respond unequally to light of equal intensity but different planes of polarization. If light from two such sources strikes a sporangiotheca from opposite directions it will bend showing that the horizontally polarized light has a stronger effect than the vertically polarized light provided that the former is not the weaker in intensity by more than 10-15 per cent. In compound eyes, perception of polarization in oblique rays of light is only possible if the optical isolation of the individual ommatidia is not absolute, and if some light initially deviating from the ommatidial axis can produce visual effects. Such a situation is admitted by Stockhammer (quoting Waterman) to exist in *Limulus*, but denied by him for *Drosophila*, *Cladocera* and *Mysidium*. It may nevertheless occur in some commoner situations, for example, when insects fly under large areas of strongly polarized light from the sky bordering directly on dark areas in their visual field.

Selective reflexion of polarized light by structures in the environment of an animal provides another means of orientation, by producing brightness patterns. Such patterns being objective can be made visible to the human eye. In Baylor and Smith's⁵ experiments, bees were released into a flat chamber covered with clear glass and illuminated only by plane polarized light from above. Those bees which crossed the box tended to run preferentially at right angles to the plane of polarization when the bottom of the chamber was covered with some dark and reflecting material whereas over a white paper they did not show any directional preference. Under unpolarized light preferential directions of running were observed over a directionally biased dark reflecting surface. Bees running under a source of polarized light over the dark bottom of the chamber showed orientation even when the light could not strike their eyes directly, regardless of whether they were running on the dark surface or upside down on the glass. A periscope like arrangement showed that the intensity of the light reflected at sighting angles of 10-30° from the dark surface under polarized light varied greatly in different directions, and it is in fact easy to demonstrate that reflexion of polarized light from such a surface at low angles is strongly directional.

Making use of optomotor responses, I showed⁸ that various dipterous (*Aedes*, *Drosophila*, *Thaumatomyia*) and other insects followed the rotation of a 'Polaroid' sheet under vertical illumination only when they were moving on or over dark reflecting material, but did not react against a bright background. The existence of an objective brightness pattern in the light reflected at low sighting angles was again demonstrated and movement of this pattern can explain the optomotor responses.

Bambridge and Waterman² showed that orientational responses to polarized light of the marine crustacean *Mysidium gracile*, previously reported by them occur only when the water containing the animals is made turbid by the addition of yeast. No significant results were obtained in carefully purified sea water. The orientational responses of *Mysidium* under a vertical source of polarized light thus seem dependent upon the discrimination by these crustaceans of differences of intensity in light scattered horizontally.

Burdon-Jones and Charles⁴ have shown that photonegative winkles of the species *Littorina littorea* move along the plane of polarization of light from an overhead source when it strikes them directly from above, even when the animals are allowed to

crawl on a small ball in such a way that no light is reflected from the substrate. The snails, however, orientate themselves equally well when their eyes are shielded from direct light and the only light they can see is reflected from the substrate. Photopositive individuals orient themselves at right angles to the plane of polarization. Burdon-Jones and Charles believe that in either situation the snails orient themselves with respect to a pattern of light and shade, perhaps arising from the Fresnel laws of refraction of plane polarized light, and that the animals do not possess any special powers of analysis whereby they could discern the polarized light in another way.

Our knowledge of orientational behaviour in polarized light is as yet too scanty and insufficiently integrated to permit of a general resolution of the apparent contradictions, and in fact it is not at all certain that similar mechanisms operate in all situations where polarized light has been shown to produce orientational effects. Some suggestions might, however, be useful. One might distinguish between phototactic responses of animals which are correlated with the plane of polarization of light and the more complex perception and consequent utilization of polarization patterns in the blue sky as inferred for the bee by von Frisch. Indirect directional effects of overhead sources of polarized light striking certain structures in the natural or experimental environment or in the dioptric apparatus and resulting in objective brightness patterns might frequently provide a sufficient explanation for the orientational behaviour of animals whether they in fact possess retinal receptors with analysing properties or not. On the other hand, it is rather difficult to see how orientation with respect to small areas of blue sky could occur without

such receptors. However, in many situations brightness gradients and polarization patterns in various parts of the blue sky are associated, and bees might in fact orient themselves to the former. Furthermore, reflexion patterns caused by sunlight will often have their maximum brightness in the same azimuth as the Sun itself and the same applies to polarized light from a small area of sky reflected in a substrate. Thus the position of the Sun might be perceived by a bee directly or, when the Sun is invisible, its azimuth might be inferred from a brightness maximum in an area of the sky or a reflecting background. The reactions of *Littorina* in the different conditions described above conform with such an explanation and might perhaps be taken to support this speculation.

Another aspect of the orientation to polarized light might be mentioned finally, namely, its role in the life of the animals. It is probably safe to assume that many of the observed reactions are merely experimental artefacts. However, it is possible that, in other instances, orientation to sources of polarized light—however it works—may be of great ecological importance. Progress in this field will depend on the careful weighing of evidence from such diverse techniques as electron microscopy, electrophysiology, photometry and not least from observations of the animals concerned.

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³ Bainbridge, R., and Waterman, T. H., *J. Exp. Biol.*, 35, 487 (1958)

⁴ Burdon-Jones, G., and Charles, G. H., XVth Intern. Cong. Zool., Sect. XI, paper 10 (1959)

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OBITUARIES

Sir Ian Clunies-Ross, C.M.G.

SIR IAN CLUNIES-ROSS, chairman of the Commonwealth Scientific and Industrial Research Organization (Australia), died on June 20 in Melbourne, Victoria, in his sixty-first year. He was born at Bathurst, New South Wales, and educated at Newington College, Sydney. He graduated as bachelor of veterinary science from the University of Sydney in 1921 and was awarded the degree of doctor of veterinary science of that University in 1928. After graduation he was awarded a Walter and Eliza Hall Veterinary Research Fellowship and undertook postgraduate studies at the London School of Tropical Medicine and at the Molteno Institute, University of Cambridge. In 1928 he went to Japan for parasitological studies at the Institute of Infectious Diseases at Tokyo Imperial University.

In 1925 Clunies-Ross was appointed lecturer in parasitology in the University of Sydney, and in the following year Council for Scientific and Industrial Research parasitologist. When the C.S.I.R. McMaster Animal Health Laboratory was established in 1931 through the munificence of Sir Frederick McMaster, Clunies-Ross was appointed as the first officer-in-charge. He held this position until 1937, when he was appointed Australian representative, and later chairman, of the International Wool Secretariat in London.

Early in his career Clunies-Ross specialized in veterinary parasitology—a much-neglected subject in Australia at that time. He saw clearly its great economic significance, especially to the sheep and wool industry, and applied himself to it so effectively that he quickly became one of the world's leading scientists in that field. Although most of his work dealt with helminthiasis of sheep, his interest ranged widely among parasitological problems of other domestic animals and of man. He brought to all his work a broad outlook and a depth of scientific understanding which inspired his colleagues and immediately won the confidence of the livestock industries. Between 1923 and 1937 he published some sixty articles as sole author and a further fifteen as senior author; in addition, he was co-author of a text book on the parasitic diseases of sheep.

Realizing at the outset that the clarification and definition of the multiple and diffuse problems of ovine helminthiasis were essential if effective means of therapy and prophylaxis were to be devised, he instigated widespread surveys of the incidence and distribution of the major worm parasites of sheep, and of the associated climatic and other factors which determined their clinical significance. Thus, for the first time a sound basis was laid for studies on epidemiology, host-parasite relationships and selective anthelmintic treatment. He and his colleagues fol-

lowed up with great vigour and enthusiasm the advantage this clearer understanding of the problem gave them, and progress flowed from it rapidly.

Among his many outstanding contributions, Clunies Ross was the first to record the effect of copper sulphate on closure of the oesophageal groove in sheep. This opened up a new approach to anthelmintic treatment. It was he who, by well planned field trials, removed the fears of graziers that more intensive stocking of sheep on improved pastures would result in heavy losses from parasitism. This led him to investigate the effects of improved pastures on the quantity and quality of wool production. It was widely held that the wall being of the Merino and the quality of its wool depended on extensive, highly selective grazing, and that intensive grazing on the narrow range of species in sown pastures would result in coarse and inferior fleeces. Clunies Ross clearly demonstrated that not only can Merino sheep tolerate intensive grazing but also that they respond to the higher nutritional levels of sown pastures by producing much heavier fleeces with little change in fibre diameter.

Clunies Ross was an inspiring research leader. He had the capacity to see problems clearly, to ask the crucial questions and to find ways of answering them effectively by laboratory or field experimentation. His interest in veterinary research, however, and his choice of problems was always greatly influenced by his genuine love of animals. This is well exemplified by the work in tick paralysis of dogs, which was one of his most original and successful investigations. He was then living in a part of Sydney where many hundreds of pet dogs died annually from the disease. He was so moved by their suffering and by the distress of their owners that, in addition to all his other work, he took it upon himself to study this problem also. Within three years he elucidated the epidemiology of the disease traced its cause to a toxic factor in the salivary gland of the engorging female tick (*Ixodes holocyclus*), and prepared an antitoxic serum of high curative value. This was typical of him, his interest was not in gaining new knowledge for its own sake but for the use which could be made of it. Having once gained it, he used to the full his great gifts as a writer and public speaker to explain its significance to all who could apply it with advantage.

Clunies Ross's active personal research had to be laid aside when he joined the International Wool Secretariat. Although he was appointed professor of veterinary science in the University of Sydney in 1940, he had little opportunity for scientific work as he was called upon to serve during the war years as director of scientific personnel in the Commonwealth Directorate of Manpower and with the Department of War Organization of Industry as an adviser on the pastoral industry. The War interrupted his scientific career, but it gave him opportunities to use his unique knowledge of Australian agriculture and his outstanding powers as a speaker and publicist to encourage and assist the remarkable growth of science and education in Australia during the years which followed. In 1946 he joined the Executive Committee of the Council for Scientific and Industrial Research and in 1949, when the Council was reorganized as the Commonwealth Scientific and Industrial Research Organization, Clunies Ross became its first chairman. He continued to maintain his close interest in the wool industry and played a large part in procuring the funds which enabled CSIRO to build up a major effort in sheep and

wool research and wool textile research. Throughout the pastoral industries his many friends had confidence in his judgment, and with their help and with the backing of the Government he had the satisfaction of seeing towards the end of his life, a large body of scientists working enthusiastically on many problems of great national importance. The major contributions which CSIRO has made to the agricultural development of Australia have been largely due to his outstanding and inspiring leadership.

Clunies Ross had many interests outside his scientific work. The field of education was one in which he played a big part, and he was outspoken on the need for retaining breadth and liberalism in education. He stressed repeatedly the dangers inherent in the increasing specialization of modern scientific and technological careers. He played a large part in persuading the Government to set up the Murray Committee on Australian universities and made a major contribution to its outstanding report. He was deputy chancellor of the University of Melbourne and a member of the Council of the Australian National University. For many years he was active in the work of the Australian Institute of International Affairs and was well known as a public speaker on foreign affairs. He was particularly interested in the relations between Australia and its northern neighbours. As chairman of the International House of the University of Melbourne a hall of residence in which Australian and overseas students live together, he was instrumental in making the idea a reality.

Clunies Ross was made C.M.G. in 1954, and in the same year he was created a knight bachelor. He was a Foundation Fellow of the Australian Academy of Science. He was awarded the honorary degrees of doctor of laws by the University of Melbourne, and doctor of science by the Universities of New England and Adelaide. He is survived by Lady Clunies Ross, three sons and one daughter.

At the memorial service held in Scots Church, Melbourne, shortly after his death Prof. J. D. McCaughey, Master of Ormond College University of Melbourne, made a fitting tribute to his memory. He expressed in those simple terms the feelings of his many friends and colleagues throughout Australia and overseas. "But in and through these achievements, it is Ian Clunies Ross the man whom we remember with admiration, with respect and with affection to-day. His capacity for work must have been enormous to die at sixty is young yet into those years was packed an astonishing variety and depth of interests. He lived a heavily committed life, yet, I suppose, that many of us in this Church think of him, with gratitude, as one who had time for friendship. He accepted us with a smile. It must have been given to few who have lived so fully yet to be loved by so many."

F. W. G. WHITE
D. A. GILL

Dr V. Korenevsky

DR V. KORENEVSKY who died suddenly on July 9, was born in 1880 in Russia and graduated from the Imperial Military Medical Academy in St. Petersburg in 1903. After military service in Manchuria during the Russo-Japanese War he worked in Vetchnikov's department at the Pasteur Institute in Paris and in Pavlov's laboratory in St. Petersburg.

In 1911 he was appointed professor of experimental pathology in the Imperial Military Medical Academy and remained there until the Revolution. His disagreement with the policy of the newly formed Soviet Government made it necessary for him to leave St Petersburg and he escaped to south Russia, where he served as a doctor with the White Army for about a year. After the defeat of the White Army he made his way to England and in due course became naturalized.

During 1929-45 he was a member of the staff of the Lister Institute. Afterwards he established the Oxford Gerontological Research Unit, with the support of funds provided by Lord Nuffield, and remained there until his retirement in 1952.

The bulk of Korenchevsky's work between the Wars was primarily endocrinological and was concerned with studies of the effect of sex and thyroid hormones, separately and in combination, not only on the reproductive organs but also on the other organ systems of animals of different ages. His work was characterized by a very close attention to detail, the use of first-class histological techniques and insistence on the need for healthy experimental material. Korenchevsky regarded this work as a necessary preliminary to provide a rational basis for use of hormones in mitigating some of the degenerations which occur with ageing.

Dr Korenchevsky will be especially remembered, however, for his pioneer achievements in stimulating interest in the field of gerontological studies. His own concern with the problems of ageing went back to the early years of the century when he visited Russian infirmaries for old people, and during his stay with Metchnikoff in Paris he worked on the

effects of gastro-intestinal autointoxication. He always remained convinced of the value of Metchnikoff's theory, and he reaffirmed his belief in the importance of autointoxication as an ageing factor in several recent publications.

By the late 1930's he felt that the change in the climate of opinion, for which he had been waiting, had come and that vigorous efforts to emphasize the need for gerontological research might at last be effective. He therefore set out with the intention of developing an International Association of Gerontologists which would be responsible for investigations in all branches of the subject. His efforts were just beginning to bear fruit when the outbreak of the War in 1939 brought them to an end for the time being.

After the War, his retirement from full-time active laboratory work allowed him to extend his campaigning even more vigorously. He was an outspoken advocate of the importance of gerontology, and in his missionary ardour he sometimes appeared intolerant of the ideas of others. But any irritation engendered by his interventions were always more than outweighed by their stimulant effect, and it was clear to everyone that he was never seeking any personal advancement but only the benefit to his chosen subject which recognition might bring. The results of his lifetime of strenuous effort will be found not so much in his large series of careful scientific publications as in the numerous national societies for the study of problems of ageing throughout Europe and the Americas, in the International Association of Gerontology and in the enhanced status which the subject has now acquired.

P L KROHN

NEWS and VIEWS

Chief Scientist to the Ministry of Power

Dr C M Cawley, CBE

DR C M CAWLEY, CBE, has been appointed chief scientist to the Ministry of Power in succession to Sir Kelvin Spencer, who has retired from the public service. Dr Cawley, who is fifty-two, has been at the headquarters of the Department of Scientific and Industrial Research for the past six years, where he has been responsible for administering general policy in relation to the work of the Department's research stations, and to grants made by the Department to the universities and other bodies, for the promotion of research and the training of research workers. He is a University of London graduate with first-class honours in chemistry and joined the Scientific Civil Service in 1929, serving on the staff of the Fuel Research Station until 1953. He will take up his new appointment at the Ministry of Power in the early autumn.

Ministry of Supply Appointments

Dr N J L Megson

DR N J L MEGSON has been promoted to be deputy chief scientific officer and appointed director of materials, research and development (air) at the Ministry of Supply Headquarters. Dr Megson studied chemistry at the University of Birmingham under Prof G T Morgan. He obtained his BSc in 1923 and his MSc in 1925. He joined the Chemical Research Laboratory, Department of Scientific and

Industrial Research, in 1927, as head of the Synthetic Resin Section and carried out fundamental and applied work on various aspects of polymers, particularly in the phenolic resin field.

On the outbreak of war he was appointed to the Ministry of Supply as advisor on plastics and later became assistant director in charge of the Advisory Service on Plastics, Rubber and Paints, concerned with development and application of new and special materials for a variety of Service equipment. In 1949 he was awarded the degree of DSc by the University of Birmingham for a thesis entitled "Polymer Investigations". He became head of the Chemistry Department, Royal Aircraft Establishment, in 1951, responsible for research and development of non-metallic materials associated with aircraft and airborne equipment. Dr Megson is the author of fifty or sixty publications, including a book, "Phenolic Resin Chemistry", and he has recently been awarded the Gold Medal of the Plastics Institute. He succeeds Dr H Sutton, whose direct contribution to and sponsorship of work on light metals for aircraft construction has brought him deservedly wide appreciation.

Dr B G Dickens, CBE

DR B G DICKENS, who has been promoted to be chief scientific officer and appointed as director general of atomic weapons in the Ministry of Supply, brings to that post wide knowledge of

operational problems and experience of weapon development. He obtained a first-class honours degree in physics in the University of London and entered the Civil Service in 1932. He served at the Royal Aircraft Establishment until 1936 and was then transferred to Air Ministry Headquarters. He was attached to the Royal Air Force Station at Biggin Hill as the scientific officer associated with the now well known air defence experiments which were initiated by Sir Henry Tizard and his committee. When he returned to the Air Ministry he was still closely concerned with air defence problems and in addition became joint secretary of a committee under Sir George Thomson to advise the Government on the practicability of an atomic bomb. He was for a time responsible for arranging the officially sponsored work in various universities. In 1941, he was put in charge of the newly formed Operational Research Section Bomber Command, which analysed the Command's operations from all aspects and made contributions to the knowledge available to the Command staff, which led to increased efficiency and improved operational methods. After the War at Air Ministry Headquarters he assisted in the establishment of the peace-time organization of operational research in the Royal Air Force. During 1948-1952 he was director of technical personnel administration in the Ministry of Supply where his main work was the planning of recruitment of technical staff particularly in the fields of guided weapons and atomic weapons. He returned to the Air Ministry as deputy to the scientific adviser, whose duties were to advise the Air Staff on the influence of the new weapons on strategy and tactics and to direct operational research. He was then appointed director of guided weapon research and development in the Ministry of Supply, where he was responsible for much of the Ministry's research and development work on guided weapons for all three Services. In a reorganization in 1958 his work was concentrated on the development of the British intermediate range ballistic missile.

Mr P A Hufton

Mr. P A Hufton has been promoted to become chief scientific officer and appointed head of the Aerodynamics Department at the Royal Aircraft Establishment in succession to Mr L F Nicholson, who is the new director general of scientific research (air), Ministry of Supply. Mr Hufton graduated in engineering at the University of Manchester in 1933 and obtained his M.Sc. degree a year later. He joined the Aerodynamics Department of the Royal Aircraft Establishment in December 1934 and after working for a short period on low speed research transferred to the Aerodynamic Research Flight where he remained until March 1946. Before the War, he worked part time with C N H Look at the National Physical Laboratory on propeller theory and experiments. During the War he was responsible for take off and landing research, particularly for heavily loaded aircraft, rocket assisted take-off, development and flight testing of high lift devices, and work on carrier landings for the Royal Navy. In the spring of 1946 he moved to the Aeroplane and Armament Experimental Establishment at Boscombe Down as superintendent of performance. He returned to the Aerodynamics Department, Royal Aircraft Establishment, Farnborough, in October 1953, in charge of the Supersonics Division and moved to the Royal Aircraft Establishment at Bedford as head of the Aerodynamics Division in September

1957. A year later Mr Hufton became chief superintendent of the Royal Aircraft Establishment at Bedford in succession to Mr L H G Sterne.

Chemistry at the Royal College of Science and Technology, Glasgow

Prof F S Spring, F.R.S.

Prof F S Spring, who is retiring from the chair of chemistry in the Royal College of Science and Technology, Glasgow, graduated at the University of Liverpool under Sir Ian Heilbron and received his first appointment in 1930 in the University of Manchester, where he remained for sixteen years. After Sir Ian Heilbron moved from Liverpool to the chair of organic chemistry in Manchester he and Spring worked in close collaboration over a number of years and made notable contributions to our knowledge of the chemistry of the sterols, vitamin D and the triterpenes. During this period Prof Spring's work was particularly associated with the structure of ergosterol and calciferol, and with the β amyrin group of triterpenes. Prof Spring was elected to the Freeland chair of chemistry at the Royal Technical College (now the Royal College of Science and Technology) in Glasgow in 1946. Here he has developed a flourishing school of research in the chemistry of the triterpenes and of certain heterocyclic systems. Prof Spring was a Tilden Lecturer of the Chemical Society and was elected a Fellow of the Royal Society in 1952.

Prof P L Pauson

Dr. PETER LUDWIG PAUSON who has been appointed to succeed Prof Spring graduated at the University of Glasgow with first-class honours in chemistry in 1940 and proceeded to Sheffield as holder of a Henry Ellison Research Fellowship. There he worked under R D Haworth on purpurigallin and was awarded the degree of Ph.D. in 1949 having already shown his versatility by giving good service as temporary assistant lecturer in inorganic chemistry. He spent the next four years in the United States first as assistant professor at Duquesne University, Pittsburgh, then as Research Fellow successively at the University of Chicago and at Harvard. It was then that he discovered the novel sandwich compound, diacylopentadienyl-iron, usually known as ferrocene. The interest aroused by this substance and its relatives was such that, less than four years later Dr Pauson could publish a timely review article on work in this field, with eighty-eight references. He returned in 1953 to the University of Sheffield, where he now holds the post of reader, vigorously pursuing the investigation of these remarkable substances, both as quite exceptional cases of metallic co-ordination and as organic aromatic systems of a new type.

Nuclear Physics at the University of the Witwatersrand

Prof J P F Sellschop

Dr. J P F SELLSCHOP has been appointed to the chair of nuclear physics at the University of the Witwatersrand as from July 1. He will continue to be director of the University's Nuclear Physics Research Unit to which position he was appointed in 1950. Prof Sellschop who at the age of 20 became the youngest professor in the University, is at present in Britain carrying out research at the Atomic Energy Establishment at Harwell for six months. He is a member of the Research Advisory Committee of the

Atomic Energy Board and represented the Union at a seminar on atomic energy and its educational problems which was held in Saclay, France, under the auspices of the International Atomic Energy Agency in July. Prof Sellschop was also an official delegate to the second International Conference on the Peaceful Applications of Atomic Energy in Geneva last year. Born in Luderitz, South West Africa, Prof Sellschop received his early education at Christian Brothers' College, Pretoria. He then became a student at the University of Pretoria and received the B.Sc. degree there *cum laude* in 1950. After working at the National Building Research Institute in Pretoria for two years he was awarded an H.B. Webb scholarship and enrolled in the Merensky Institute of Physics at the University of Stellenbosch and in 1952 received the degree of M.Sc. *cum laude*. He then joined the Bernard Price Institute of Geophysical Research, later successfully reading for the Ph.D. degree in the nuclear physics group of the Cavendish Laboratory, Cambridge, as holder of a postgraduate scholarship awarded by the Shell Company of South Africa Ltd. in 1954.

Microbiology at Sheffield

Prof S. R. Elsdon

DR SIDNEY REUBEN ELSDEN has been appointed to the newly created chair of microbiology in the University of Sheffield, as from October 1. Dr Elsdon was educated at the Cambridge and County High School for Boys and the University of Cambridge. He graduated B.A. in 1936 and obtained first-class honours in both parts of the Natural Sciences Tripos. During 1937-38 he worked under Dr Marjory Stephenson in the Department of Biochemistry at Cambridge and was then appointed assistant lecturer, and later lecturer, in physiology in the University of Edinburgh. In 1943 Dr Elsdon joined the scientific staff of the Agricultural Research Council's Unit of Animal Physiology at Cambridge. He went to Sheffield in 1948 as senior lecturer in microbiology in the Department of Bacteriology and in 1952, when the University created a separate Department of Microbiology, Dr Elsdon was appointed head of the new Department. He has also been honorary director since 1952 of the Agricultural Research Council's Unit of Microbiology, which is housed in his Department. Dr Elsdon's Department has received generous support from the Rockefeller Foundation, and the Agricultural Research Council Unit has also received a grant from the Kellogg Foundation.

New Commonwealth Institute Building

PLANS for a new building for the Commonwealth Institute were made public on June 17. The new premises, which will replace the present accommodation in the Colcutt building in South Kensington, will be erected on a 3½-acre site at the southern end of Holland Park, fronting Kensington High Street, at an estimated cost of £725,000. Work will start next spring and is scheduled for completion in 1962, when the removal of the Institute from its present building will be necessitated by Government plans for the expansion of the Imperial College of Science and Technology. The new Institute will consist of a main exhibition block with a wing on the western side. In the wing will be housed offices, a restaurant, a reception centre and dining space for visiting school parties. A large reception room for the Commonwealth Students' Club and for confer-

ences and social occasions, a reference library and reading-room, a cinema to seat between 450 and 500, and a gallery specially designed for temporary art and other exhibitions are also included in the plans. The architects are Messrs Robert Matthew and Johnson-Marshall. The Commonwealth Institute is the major centre in the United Kingdom for information about the Commonwealth nations and their Dependencies. Founded as the Imperial Institute in 1887, it has occupied its present accommodation in the Colcutt building since 1893. The name was changed from 'Imperial' to 'Commonwealth' Institute by the Act of 1958.

The British Non-Ferrous Metals Research Association

THE opening of the latest addition to the laboratories of the British Non-Ferrous Metals Research Association by Sir Alexander Fleck on May 13 is a further step in the progress of an Association which has grown in activity and reputation ever since it was first established some thirty years ago. This reputation in the field of non-ferrous metallurgy is acknowledged not only in Britain but also abroad. The restoration of the laboratories after serious war damage suffered serious delays, and with the increase in the Association's work and the resulting congestion, the decision was taken in 1957 to complete the building plans which had been formulated some twenty years earlier. The block now opened adds some 12,500 sq ft of floor space, bringing the total to about 53,000 sq ft. It contains now corrosion laboratories, a large new metal finishing shop, extensions to the physics laboratories and to the foundry. Together with these a new council chamber and badly needed offices for the senior staff add considerably to the administrative amenities.

The Metropolitan-Vickers Nuclear-Metals Laboratory

IT was with the view of ascertaining the effects of irradiating metals that Metropolitan-Vickers Electrical Co. Ltd. decided to extend the existing facilities of the Research Department by building a Nuclear-Metals Laboratory. The Laboratory is equipped for the examination and testing of irradiated components and materials ranging up to a complete fuel element having an activity of the order of 10 kc. It is provided with two large concrete caves, and a train of five interconnected lead-walled cells is used to receive large irradiated objects. Essentially the caves are constructed of barytes concrete blocks. The air in the caves is arranged to be maintained at a slightly lower pressure than that in the open laboratory, thus ensuring that no air-borne radioactive dust can escape. Remote control manipulators enable the operations to be carried out inside the caves from outside the walls. The new laboratory will primarily be engaged on work for the Associated Electrical Industries—John Thompson Nuclear Energy Co., Ltd., and on work under contract for the U.K. Atomic Energy Authority. The scope of work will be concerned not only with investigations into the irradiation effects on constructional materials such as graphite and steel of various types, but also with establishing the behaviour of metals such as magnesium, zirconium, beryllium, etc., and of thermal and electrical insulation materials. A highly organized health physics service is maintained to safeguard the operating staff against all the hazards involved.

Sponsored Research in Great Britain

FACILITIES for sponsored research in Great Britain were increased by the formation in 1957 of the Arthur D Little Research Institute which has laboratories at Inveresk, Midlothian. The Institute is a non-profit-making organization registered in Great Britain as a company under the Friendly Societies Act, and although the two concerns are separate, it operates in close association with a similar group in the United States, Arthur D Little, Inc., of Cambridge, Mass. The Institute has now issued its first annual report from which readers may gain some idea of the scope and objects of the new venture. With Lord Bilsland as chairman of the Board of Directors, and with Dr F N Woodward as director of research, the Institute has been concerned with several projects, all of which are being treated with special reference to the fundamental scientific background. The results will normally be given open publication when the work is complete and interim accounts of the various projects are given in this annual report. These projects include investigations of the sodium derivatives of sucrose and of their condensation with a variety of organic halogen compounds, studies on the mechanism of the formation of isotactic polymers, the development of rapid methods for assessing the effectiveness of potential corrosion inhibitors, studies on the mechanism of inhibition of corrosion by electrochemical methods, and investigations into the modification of wood cellulose by chemical methods. In addition, the report refers to lectures, publications and other scientific activities organized by the staff of the Institute. It will be of great interest to all those who wish to know more about this new development in sponsored research and its place in the general organization of research in Great Britain.

Nuclear Studies in the United Kingdom

THE Science Department of the British Council has issued its third list (May 1959) entitled "Nuclear Studies". This is a concise catalogue of courses in pure and applied sciences concerned with the use and development of nuclear energy. It is issued primarily as a guide for the overseas student who wishes to undertake specialized formal training in the United Kingdom. Consequently it includes only full time courses, generally of one week or more in duration, and is not concerned with research topics or with the courses which may be regarded as forming part of a normal first degree course. Although the list has appeared too late for application to be made for many of the courses during the academic year 1959-60, it serves to direct inquiries for courses in 1960-61. Further information can be obtained from the Science Department of the British Council, 65 Davies St., London W 1.

Building Research in New Zealand

IN recent years, a number of fields of investigation relating to the building industry in New Zealand have been pursued independently in various organizations and laboratories in which the main interests have been in quite different fields. The Dominion (Chemical) Laboratory has investigated paints and local building materials, the New Zealand Forest Service has carried out work on timbers both indigenous and exotic, suitable for building, the Pottery and Ceramics Research Association has investigated the appropriate use of brick constructions

for earthquake conditions, and the Dominion Physical Laboratory has done some valuable work on methods of domestic heating, thermal insulation and related physical problems. But there has been no co-ordination between these diverse efforts, nor any institution wholly devoted to problems of the building industry.

This anomalous state of affairs is now to be abolished with the establishment of a Building Research Bureau, which is being sponsored by a joint committee of the New Zealand Master Builders Federation and the New Zealand Institute of Architects. Dr Lyndon Bastings has been appointed the first director. It is intended initially to set up a library and an information service, but as funds allow, it is hoped that laboratories and other practical facilities will follow in due course. The address of the new Bureau is Construction House, 66 Murphy Street, Wellington, N 1, New Zealand.

Postgraduate Courses at the Imperial College of Science and Technology, London

ADVANCED postgraduate study has long been a special feature of the work of the Imperial College of Science and Technology, University of London. As new types of technology emerge—of which nuclear power and soil mechanics are notable recent examples—they open up possibilities of study which must remain outside the scope of any course for a first degree but which are properly within the field of university teaching. The postgraduate courses at the College have been greatly increased in number in recent years to meet the wide range of technological development. Postgraduate courses provide the opportunity for students including many who have already spent a year or more in industry, to further their knowledge in a particular specialized field and at the same time to learn from experts their experience of the application of this knowledge in industry. Details of the courses are set out in an impressive handbook published by the College (*Postgraduate Courses, 1959-60*, Pp. xi+111, London: Imperial College of Science and Technology, 1959); the list should give considerable satisfaction to all who are concerned with Britain's place in the world of technology. Many of these courses have been accepted by the Department of Scientific and Industrial Research as suitable for the tenure of advanced course studentships. Grants for the courses related to agricultural science are awarded by the Ministry of Agriculture Fisheries and Food. The courses are assisted by industry in particular a number of firms support the work of the advisory committees in concrete technology and technical optics and provide bursaries for the respective courses.

Sandwich Course in Executive Development

THE Department of Commerce and Management of Sheffield College of Technology is to provide a sandwich course in executive development commencing in November 1959. The purpose is to provide for the young manager and potential manager a fully integrated plan of executive development, by bringing together in one scheme both education for management within the College and general and vocational managerial experience in his working environment. Full time attendance at the College will be required for approximately fifteen weeks during each year of the course and will be spread over a period of two academic years. Only students already engaged in industry and individually

sponsored by their employers will be accepted into the course. Further information can be obtained from the Head of the Department of Commerce and Management, 1, Melbourne Avenue, Sheffield, 10

Developmental Biology

THE first number has recently appeared of a new journal, *Developmental Biology*, published by the Academic Press, and produced by an editorial board consisting of Prof J Brachet, Prof E Hadorn, Dr P Weiss with Prof M V Edds of the Department of Biology, Brown University, as managing editor (*Developmental Biology*, Vol 1, No 1, April 1959 Pp x+124 Volume 1 (6 issues) 14 dollars New York and London Academic Press, Inc., 1959). The manuscripts in English should be sent to *Developmental Biology*, Department of Biology, Brown University, Providence, Rhode Island, U S A those in French to J Brachet, Laboratory of Animal Morphology, University of Brussels, Brussels, Belgium, and those in German to E Hadorn, University of Zurich, Switzerland. Many of the classical divisions of biology no longer correspond to the way in which research is organized and thought develops in biology to-day. The formation of this journal is an attempt to produce some degree of rationalization by bringing together studies of all aspects of development and growth. This is well exemplified by the contents of the first number, which contains articles dealing with the chick embryo, with *Drosophila* larvae, with the ribonucleic acid involved in differentiation of a fern and with the function of SH groups in morphogenesis. In the editorial to the first number the editors say that they are prepared to accept articles written from a wide variety of points of view, for example, analytical or descriptive, technical or theoretical, using either a molecular approach and/or an organismal approach. Micro-organisms, plants and animals are all equally regarded as relevant to the problems of developmental biology.

Native Life in Angola

THE Portuguese Companhia de Diamantes de Angola is noted for the interest it takes in archaeology and the native cultures of the region in which it operates. Business firms are not usually directly concerned with interests of a cultural nature outside their own money-making projects, and this makes it all the more remarkable that the Angola Diamond Mining Co. has published already a large number of splendid volumes, full of illustrations which deal with many aspects of the past and present history of the country. A recent volume (Companhia de Diamantes de Angola (Diamang) Servicos Culturais Dundo-Lunda-Angola Museu do Dundo Publicações Culturais No 37 *Flagrantes da Vida na Lunda* Introdução de José Osório de Oliveira Pp 192 (Lisboa Companhia de Diamantes de Angola 1958)) is a superb publication of large format containing no less than 148 full-page illustrations of the countryside and its inhabitants. We can see basket-makers at work, fishing scenes, a moment in a divination ceremony, a Lunda chief with his robes and ceremonial insignia, etc. The first 44 pages are devoted to an introduction by Dr José Osório de Oliveira, there being Portuguese, French, and English versions. An account of some of the cultural activities of the company is given and also of the country and its people. On the last page the author writes "The honour attributed to the leaders of 'Diamang' in having anticipated in Africa

that which the experts convoked by UNESCO counselled is nothing more than justice, for one cannot fail to look upon the company as the keystone of local native life." This is true, and furthermore, both archaeologists and anthropologists all over the world have reason to thank the Company for the Dundo Museum and many other contributions to learning.

Summer Tanager

FOLLOWING a series of depressions and strong westerly winds, an unusual bird was observed on Bardsey Island on September 11, 1958. It was somewhat smaller than a song thrush, olive green above and deep yellow below, with a heavy blunt bill and peculiarly short legs. Subsequent observations suggested that the bird was a summer tanager, *Piranga rubra*, which had not previously been recorded in any European list, the few red feathers on the head and the back suggested that the specimen was a young male. Details of the observation and of the highly successful work carried out at Bardsey Bird and Field Observatory during 1957 are described in the annual report of that Observatory for 1957, which can be obtained from W M Condry, Eglwysfach, Machynlleth, Montgomeryshire.

Chromosome Numbers in *Solidago*

IN further studies of the genus *Solidago*, J R Beaudry and D L Chabot (*Canad J Bot*, 37, No 2, 1959) have observed the chromosome numbers in 25 taxa of the genus. In all, the chromosome numbers of 42 taxa have now been published. The basic number of the genus is nine. Thirty-three taxa are diploid ($2n = 18$), five are tetraploid ($2n = 36$), three are aggregate taxa containing both diploid and tetraploid cytodesmes, and one is hexaploid ($2n = 54$). Polyploidy has thus contributed to the evolution of the genus *Solidago* but it seems that most of the species have differentiated gradually. *S. decemflora* DC of western North America differs from *S. nemoralis* Ait of the same continent by morphological characters, its geographical distribution, and its chromosome number, the first taxon being tetraploid and the second diploid, the two are thus good species and not merely varieties of the same species. *S. rigida* is considered to be an aggregate, consisting of two entities which are distinguished not only by their morphology and geographical distribution but also by their chromosome numbers, the eastern one (*S. rigida* L.) is tetraploid, whereas the western one (*S. parvirigida* Beaudry) is diploid. The bog and marsh goldenrods, *S. Purshii* and *S. uliginosa*, also possess different chromosome numbers, the first being diploid and the second tetraploid.

Soil Fungi in the Belgian Congo

J MEYER has given a comprehensive account of soil and litter fungi in the Belgian Congo (region of Yangambi) (Publications de l'Institut National pour l'Étude Agronomique du Congo Belge Série Scientifique, No 75 "Moississures du Sol et des Litières de la Région de Yangambi (Congo Belge)", par J Meyer Pp 211+4 planches Bruxelles Institut National pour l'Étude Agronomique du Congo Belge, 1959 190 Belgian francs). In this work, the author has recorded his taxonomic observations on the very considerable number of fungi observed or isolated, leaving the questions of sociology, synecology, etc., to be dealt with later. The generally

accepted classification of soil fungi into native or cosmopolitan species, and exotic fungi (soil myadara), is followed, but the author notes that the exotic organisms require further sub division into two groups namely preferant species (*espèces préférentes*) implying having precedence or priority, and exclusive species. The nature of the vegetation, and the fruits, leaves and branches which fall from it to form the litter, carrying down air borne organisms by which they have become infected, influences the nature of the exotic fungal flora. So also do rhizosphere relationships. Hence the author considers that the work of the soil mycologist must necessarily suffer limitations if it fails to take into account the nature of the vegetation and its litter that is to say, properly envisaged, the phenomenon to be investigated is that of vegetation-litter-soil. In this initial study, some 251 species are listed described and many of them illustrated. Of these 101 came from the soil (13 Phycomycetes, 31 Ascomycetes, and 147 Deuteromycetes) and 60 were observed directly on debris. The Hyphomycetes have been classified according to Hughes's system (1953).

Precambrian Geology of South western Australia

THE Precambrian geology of south western Australia has recently been reviewed by A. F. Wilson (*J. Roy. Soc. Western Australia* 41 57 1958), who provides a new tectonic geological map of a quarter of a million square miles of this region on a scale of 20 miles to the inch. This is the first attempt to integrate all known trends of granites, gneisses and 'greenstones' and on the map these and charnockitic rocks are distinguished for the first time. The well known north north westerly trend of the Goldfield area is found to extend in a general way throughout much of the region. The strike of the granites conforms to the regional strike of the metamorphic rocks but magmatic emplacement is suggested locally. Granitization contacts are also common and filter press differentiation phenomena are known. Geochemical and petrographic features suggest that many gneisses are similar in composition to grey wacke rocks, but that the granites would need to have been subject to some kind of metasomatism to have been produced from such a source. Charnockitic rocks are found over a very large area and seem to have developed in at least four different ways and in two main periods—one early and the other late Archaean. It would appear from radioactive age determinations that the bulk of south western Australia is of early Archaean age and that a late Archaean period of metamorphism has affected parts of the south and south-east, and also possibly the western margin of the shield which is down faulted beneath the Perth basin.

Perkin Centenary Trust Awards

THE Perkin Centenary Fellowship has been awarded to Mr. Brian Whitear, a research chemist in the laboratories of Messrs. ICI Ltd. Mr. Whitear will work at the University of Southampton, under the supervision of Prof. R. C. Cookson, on photochemical reactions of coloured substances. Perkin Centenary Scholarships have been awarded to the following: Mr. Ronald R. Cox (tenable at the University of Birmingham), Mr. B. T. Lawton (tenable at the Royal Technical College, Salford); and to Mr. D. J. Pearson (tenable at the Bradford Institute of Technology).

University News

Hull

THE annual report 1957-58, of the University of Hull notes the establishment of the grade of senior lectureship, to which eight lecturers have been promoted and also another large deficit on the halls of residence. Residence fees have been assessed to provide a surplus, and if costs do not rise appreciably an overall deficit should be avoided during the next three years. The first stage of the new library building is expected to be completed in the summer of 1959 and a provisional building programme of an estimated capital cost of £204,000 has been approved by the University Grants Committee for the years 1960-63 including a new physics building, a hall of residence on the University site, an arts and social science building, and extensions to Ferens Hall. The completed programme will cost nearly £2 million and will provide places in Hull for about half the 2,000 students expected in the University in the 60s. The Senate's report includes brief notes on research work in progress, an account of the work of the Department of Adult Education and a list of publications during the year arranged under departmental headings.

Announcements

H.R.H. THE DUKE OF EDINBURGH has accepted an invitation to become the first Honorary Fellow of the Illuminating Engineering Society.

PROF. J. H. MATTHEWSON, of the Institution of Transportation and Traffic Engineering, University of California, will give two lectures at the Road Research Laboratory, Langley Hall, Langley, Slough Bucks., on 'Experiments on Automobile Collisions' (September 9) and 'A Simulator for Research on Driver Behaviour' (September 16). Both lectures will commence at 3.30 p.m. Tickets can be obtained (free) on application to the Director of Road Research, Road Research Laboratory, Harmondsworth West Drayton, Middlesex.

SIR JAMES DENBY ROBERTS has been appointed chairman of the Joint Committee of the Agricultural and Medical Research Councils and the Development Commission on Biological (Non Medical) Problems of Nuclear Physics in succession to Lord Rothschild, who retired earlier this year. This Committee was formed to sponsor and co-ordinate research on the effects of radioactive substances on plants and animals, and is responsible for the supervision of monitoring fall-out in foodstuffs and other biological materials. Sir James is chairman of the Scottish Society for Research in Plant Breeding and is particularly interested in farming in the Highlands.

IT is announced that the Commonwealth Scientific and Industrial Research Organization (Australia) has formed a new Division of Mineral Chemistry, replacing the Minerals Utilization Section of the Organization's Chemical Research Laboratories. The Division's research under the leadership of Mr. R. G. Thomas will be concerned with the chemical transformation of minerals into a wide variety of useful products.

A COLOURED wall-chart illustrating in section the Metro-Vickers Type EM6 electron microscope has recently been produced primarily for the use of technical colleges and teaching institutions. Supplies have been reserved for lecturers and science teachers and requests for copies should be addressed to the Publicity Department of Metropolitan Vickers Electrical Co. Ltd. Manchester.

INDUSTRIAL RESEARCH ASSOCIATIONS IN BRITAIN

RESearch for Industry, 1958", which reports on work done by the industrial research associations in the Government scheme, this year adopts a new pattern which has much to commend it. It includes the report of the Industrial Grants Committee of the Council for Scientific and Industrial Research which comprises a review of grant policy during 1957-64 (see p. 211 of this issue), and a review of the achievements during the past five years of the ten research associations to which new or revised terms of grant were recommended during the year. Apart from brief notes on any outstanding features of the work of other research associations during the period, the bulk of the report comprises a list of existing associations, giving their officers, total income and publications during the year and a brief note on the scope of the present work of each association. There is also an assessment by Dr D. T. A. Townend of the place of the research associations in the evolution of scientific endeavour, and a report entitled "New Ideas, New Products, New Processes" on how co-operation research serves the textile industries. In this report, which covers the work of several research associations, the point is made that one-fifth of an association's resources is only adequate for fundamental research if the total resources are big enough.

Of the research associations which received new or revised terms of grant during the year, stress is laid on the basic research into the composition of gelatin and glue, the structure of the gelatin molecule, the properties of solutions and gels and the conversion of collagen into gelatin being carried out by the British Gelatine and Glue Research Association, the economic value of the work of the British Hat and Allied Felt Makers' Research Association, the achievements of the British Hydromechanics Research Association in the design and utilization of pumps and in high-pressure hydraulic machinery and in hydraulic model testing. The Furniture Development

Council has conducted a basic investigation into factors affecting the strength and rigidity of cabinet construction, developed test methods for furniture lacquers and worked on a new, economical material—wood chipboard. The Heating and Ventilating Research Council began its first major research project in 1956-57—an investigation of problems arising from the intermittent heating of buildings, with the view of ascertaining possible fuel savings by choosing in advance equipment and programme of the daily heating cycle in relation to the thermal characteristics of the building and installation. The Lace Research Association has carried out much work on new types of yarn and on problems arising in dyeing and dressing synthetic fibre materials, and is engaged in a basic study of the bobbin and carriage, which is the central feature of major types of lace machines.

Basic research carried out by the British Flour-Millers' Research Association includes a complete analysis of the amino-acid composition of flour and of the changes which occur when it is made into bread. The Research Association of British Rubber Manufacturers has extended its cover to plastics, notably polyvinyl chloride and polyethylene, and has been investigating the basic physical characteristics of rubber and plastics and the influence of service conditions such as temperature on these characteristics. An outstanding piece of chemical research increased knowledge of how traces of certain metals, notably copper and manganese, can cause premature deterioration of important classes of rubber products, especially rubber-proofed fabrics. The British Coke Research Association has developed instruments such as an isothermal bomb calorimeter for accurate determination of the calorific value of solid and liquid fuels and an electromagnetic semi-microbalance for use in fundamental studies relating to carbon.

AGRICULTURAL RESEARCH IN BRITAIN

ACORRESPONDENT, commenting in a Scottish farming paper on the Report of the Agricultural Research Council for 1957-58, complained that he could find no reference to research on grass tetany. Because of its current seriousness, he felt that some of the four million pounds that the Council administers should be allocated directly towards research into this problem. If he had read the report with deeper understanding he would have realized that such a criticism was not really justified. For example, at the Rowett Research Institute there are in progress fundamental studies on the physiology of rumen digestion with particular reference to young grass which is high in potash and nitrogen. The work is not labelled grass tetany or hypomagnesaemia, but it is in fact just the sort of work that will lead to a better understanding of the metabolic diseases of livestock which are still very largely unsolved. Agricultural research has long since passed from its old phase of an empirical approach to outstanding problems, and this is well illustrated by this report,

for the main emphasis is on fundamental studies necessary for a better understanding of the vital mechanisms of plants and animals.

Another illustration of this approach is provided by the investigations, mainly at Rothamsted Experimental Station and at the University of Durham, into the biology of the potato root eelworm. Studies have been made of diffusate from potato roots which stimulates hatching of the cysts, and investigations are proceeding at several centres into the chemistry of this material, with the view of obtaining a means of causing hatching in the absence of the host plant.

A feature of the report is the very considerable emphasis which is given to the several aspects of poultry research, which for a number of years was something of a Cinderella so far as the Council was concerned. The industry, with an annual output of £200 millions, is second in importance in Britain to dairying, and it also is one of the most heavily subsidized. It is very important that the industry

should be more efficient, and especially is this true in respect of disease control for wastage is a very heavy source of loss. To day there are two poultry research institutes, one wholly and the other partly financed by the Council, while there is a considerable amount of poultry research being supported at other centres. One pleasing aspect of the breeding work is the attention that is being given to methods which will be within the compass of the small breeder, who is in imminent danger of being squeezed out by the large organizations producing hybrid chickens.

Possibly the most notable advance from the point of view of the farmer relates to the control of husk in cattle, which is caused by the lungworm *Dictyocaulus viviparus*. This work has been undertaken by the University of Glasgow Veterinary School and was started in 1952. The successful outcome of this work is that double vaccination, using doses of larvae that have been partially inactivated by irradiation with X rays gives an effective field control of a disease which has been a serious source of loss to farmers. The cost to the cattle industry has not been confined to deaths and loss of thrift but has included also the

cost of housing and hand feeding susceptible animals in order to avoid infection. Now that farmers have an effective control of the disease, it will be possible for them to put calves out to pasture and thereby considerably lower the cost of rearing. X irradiation opens up enormous possibilities in the control of other endo-parasitic infections and further work is proceeding on this side.

One final point about the Council's activities—though the greater part of its funds go to research institutes such as Rothamsted Experimental Station and the National Institute for Research in Dairying the universities are by no means neglected. Apart from a number of research units there were ninety-four separate projects at sixteen universities which were receiving grants in March 1958. It seems that fears expressed a few years ago that the big institutes would monopolize research in agriculture and the sciences basic to agriculture are groundless, for it is obviously the Council's policy to encourage workers at the universities who have, among their other duties, the task of training research workers to staff the institutes.

SELF-REGULATION IN LIVING SYSTEMS

THE first Ottawa symposium on self regulation in living systems, held in October 1958 (see *Nature*, 183, 730; 1959), led to requests for a second meeting with particular emphasis on problems of stability in self regulating systems. This meeting was held at the National Research Council laboratories in Ottawa on March 11. As on the previous occasion a very wide range of professions was represented, and the attempt was made to increase our understanding of the behaviour of living systems by analogy with known physical and mathematical techniques and concepts.

The opening paper outlining the nature of the problem, was by a physiologist, Dr A. S. V. Burgin (McGill University, Montreal). Burgin emphasized that all physiological problems are multifactorial in character, and that in a real biological system it is impossible to isolate a single variable. A real need exists for more adequate mathematical techniques to deal with such problems. However, at present simplifying assumptions are essential in order to reduce problems to manageable form. Thus we may, for example, consider the blood circulatory system as made up of two pumps—namely, the right and left ventricles of the heart—connected in series with each other and with the blood vessels of the body. The problem here is how the outputs of the two pumps are maintained equal to one another. It is found that over a wide range of input pressures the output flow is proportional to this pressure, and in this way automatic regulation is achieved. It appears that blood pressure is controlled by sensors acting via the base of the brain to cause dilation or contraction of capillaries in the circulatory system. In these cases, and, for example, in the problem of maintenance of body temperature, the mechanisms by which the actual operating values are determined remain largely unknown at present. It was also pointed out that there are definite time cycles within the body for which at present no explanations have been given. Following Burgin's paper there was considerable discussion as to whether the dependence

on temperature of the rate of chemical processes might provide an adequate mechanism for the maintenance of an internal temperature standard.

Dr A. C. Smith (Computing Centre, University of Ottawa) presented some analysis of the properties of idealized control systems, using the method of the Laplace transformation. The analysis, however, was limited to strictly linear systems, and it was felt that the non linear problem is in fact of great importance to physiologists and others. The conclusion reached in the analysis was that optimum control conditions obtain when the control action depends upon both the variable under control and its time derivative. This conclusion agreed with the general experimental observations of the physiologists present. In the discussion the influence of time delay or phase of negative feedback on the stability of systems was of primary interest. Physiological systems discussed in this connexion included problems of neurological instability and the recent work, reported in the literature, on the relation between stammering and delays in the reception of aural signals. The galvanometer amplifier using a light beam and photocell to provide a high degree of negative feedback offers a simple mechanical system showing some of the important features. If the time delay in the response of the cell is appreciable the galvanometer amplifier system may build up to a state of oscillatory instability. It should be emphasized that the polarity of the feedback is still nominally negative if the feedback is connected up in the opposite sense (positive feedback) then the galvanometer amplifier becomes entirely unstable, and obviously so!

An outline of some modes of operation of digital computers by Dr Bradford Dunham (Research Laboratory, International Business Machines Corporation, New York) opened the way for analogies to be drawn with living systems. In programming a computer a specific problem must be given a precise mathematical formulation and then translated into machine language. Under these conditions

say that the machine will either perform activities requiring no 'judgment', or it may be adapted to include activities requiring 'judgment' provided that the programme contains some means for evaluating consequences. We can then go further and consider problems which are rather inexact, or poorly defined, with the condition that the answer(s) to the problem (which may be very difficult to find) must be easy to check or recognize as correct when arrived at. In order to do this, the machine changes its own programme in some successive manner and at the same time evaluates the effect of these changes. It certainly appears that this technique of 'machine search' can be regarded as a learning process (perhaps even more ?) in that the machine itself attempts to arrive at the correct way to tackle a problem.

Dr F L McNaughton (Montreal Neurological Institute) made some remarks on stability in relation to the human system, pointing out first that we are still far from an adequate understanding of how the brain works. Experiments in which people were isolated from their environment result in hallucinations in the experimental subject and some distortion of perception when the period of isolation is ended, a clear interdependence of nervous system and environment is indicated. When this adjustment of man to his environment breaks down he shows the symptoms of disease. Broadly speaking, it appears that only damage or disease in the general receptor or motor areas of the brain produce immediately identifiable external symptoms. Considerable parts of other areas of the brain may be removed or quite drastic surgery carried out, with what appear to be only transient after-effects in many cases. In discussion, the close analogy between the apparent organization of the human brain and the problem of 'machine search', mentioned above, was pointed out. It has been found that in machine 'learning' of this

type, the initial and final stages of the programme (which might perhaps be likened to 'receptor and motor areas') are critical in the solution of the problem, but otherwise many alternative programmes appear to be possible.

Dr G Glinski (Department of Electrical Engineering, University of Ottawa) spoke on the general problem of stability and adaptability of multi-loop feedback control systems. Systems of this type are much closer to living systems than the simpler control systems discussed earlier since a number of variables are involved in controlling a single output. In addition, there may be feedback to one or more inputs and it is also possible to take into consideration some interaction between input variables.

In the previous symposium, Dr A C Burton (University of Western Ontario) presented some demonstrations on the significance of visual perception. The present symposium concluded with a short demonstration by Dr Burton of interaction between visual inputs. This followed an experiment first performed by Mach in which an interaction between neighbouring receptors in the eye leading to a sharpening of the contrast between light and dark regions is shown quite dramatically by the apparent presence of intensified dark and light bands in the penumbra region of a straight edge when projected on to a lantern screen.

Following the meeting, a panel discussion took place on the Canadian Broadcasting Corporation system under the chairmanship of Sir Robert Watson-Watt, in which Drs Burgen, Dunham and MacDonald took part. During this spontaneous discussion the significance of 'learning' by machines was explored further. It is probable that a further symposium will be held—perhaps this time in Montreal.

D K C MACDONALD
DOUGLAS L MARTIN

THERMONUCLEAR PROCESSES

A CONVENTION on "Thermonuclear Processes" was held in the Great Hall of the Institution of Civil Engineers on April 29-30. The convention was organized by the Institution of Electrical Engineers in conjunction with the British Nuclear Energy Conference. A total of twenty-two papers were read, half of which were concerned exclusively with the engineering problems arising out of research into controlled thermonuclear reactions. The remaining papers were largely re-statements of results given at the Geneva Conference on the Peaceful Uses of Atomic Energy last year, albeit presented in a form more suitable for a predominantly engineering audience. However, some new results were given, particularly in the papers submitted by the United States and the U S S R.

The mechanism of energy loss remains the outstanding question in connexion with the toroidal stabilized pinch or *Zeta*-type discharge. At the Geneva Conference, Dr S A Colgate of the University of California claimed that the entire energy loss during the first 7-8 μsec of the discharge life-time in his small torus was due to runaway electrons with an energy of about 2 keV striking the walls. Later, Drs Hughes and Kaufmann of Associated Electrical Industries, Ltd, Aldermaston, published results obtained with the *Sceptre* apparatus showing that

impurity ions were drifting around the torus with the unexpectedly high velocity of 10^8 cm/sec. The angular momentum of the deuterium plasma deduced from these measurements was in agreement with the notion of runaway electrons as the chief source of loss. This happy unanimity was destroyed by the release of two further results during questions at the Convention. First, a search had been made on *Zeta* for the Doppler shift in impurity spectra indicating drift motion and none had been found. Secondly, the group at Los Alamos under Dr J A Phillips working with *Perhapsatron S4* had some evidence to show that the whole of the energy loss from their torus was due to radiation in the vacuum ultra-violet region. Clearly more work will have to be done before the problem is finally resolved.

Mr G B F Niblett of the Atomic Weapons Research Establishment, Aldermaston, described some new experiments on the rapid compression of plasma. In this work a fast-rising axial magnetic field is created inside a linear discharge tube by means of a long single-turn copper coil coupled to a condenser bank. The resulting ring discharge ionizes the gas and is rapidly collapsed by the rising magnetic pressure. The heating principle is the same as that of the fast linear pinch first reported by Kurchatov at Harwell in 1956, but the changed geometry avoids

electrode effects and is expected to be hydromagnetic ally more stable. A ringing discharge with a frequency of about 200 kc/s was produced in a $1\frac{1}{2}$ in bore tube. A rotating mirror photograph of the discharge in nitrogen showed successive contractions of the discharge corresponding to the oscillations of the coil current. In other measurements, the radial oscillation of the hollow cylindrical shell of plasma when confined between two magnetic fields was observed. It was suggested that these oscillations might be used to heat the plasma.

A paper presented by Mr. J. D. Jukes of the Atomic Energy Research Establishment, Harwell, analysed a system for extracting electrical energy directly from any fusion reactor which uses the principle of magnetic confinement. To extract the energy the plasma is taken through a compression cycle by varying the confining magnetic field. During the compressed state, energy accumulates in the plasma due to the heating of the nuclear fuel. When expanded the plasma temperature is low so that fusion reactions occur infrequently and the plasma cools, losing energy by bremsstrahlung radiation. In this way, waste heat is removed from the plasma and a closed Carnot cycle can be achieved. Since the neutrons produced in the fusion reactions are unaffected by the magnetic field, only the energy released in charged particles can be extracted in this way. Mr. Jukes concluded that it should be possible to withdraw about one third of the available energy from proposed fusion devices directly as electrical energy.

Dr. C. M. van Atta of the University of California Radiation Laboratory presented a survey of the very large American programme in this field which costs 40 million dollars a year and employs three hundred professional staff. A new experiment demonstrating the propagation of torsional Alfvén waves through plasma was described. To produce the plasma a linear discharge carrying a current of 20 k amp in an axial magnetic field of 10 kilogauss is used. The waves are generated by applying an alternating radial electric field between one of the electrodes and the conducting wall of the tube. The measured velocity of propagation increases linearly with the axial magnetic field strength and is in close agreement with theory if the ion density is assumed to correspond to all the gas initially in the tube being ionized. This work is being done by Dr. J. Wilcox at the Radiation Laboratory, Berkeley. Among other experiments reported in this paper were hydrodynamic stability studies by Dr. S. A. Colgate using high current pulses through sodium, and similar studies by Dr. H. P. Furth using plasma and a variety of magnetic field configurations.

An important consideration in the magnetic mirror method of confinement is the accuracy of the assumption that the magnetic moment of a spiralling charged particle is a constant. The principle of mirror confinement is based on the adiabatic invariance, and since a confined particle may undergo many millions of reflexions from the mirrors during its containment, the accuracy required is of a high order. In experiments by Dr. E. Lauer of Berkeley, positrons with energies of the order 1 MeV resulting from the β decay of radioactive neon were shown to be contained between magnetic mirrors for 10^4 reflexions. The distance between the mirrors was 1 m and the Larmor radius of the electrons 0 cm.

Dr. I. N. Golovin of the Institute of Atomic Energy, Moscow gave an account of research into magnetic mirror systems in the Soviet Union. He

described an experiment on the adiabatic invariance of the magnetic moment similar in principle to that reported by Dr. van Atta. In this case electrons from the radioactive decay of tritium were used and confinement for up to 10^4 reflexions had been demonstrated. Work had also been done to find the effect of azimuthal asymmetries in the magnetic field on the number of reflexions. It was found that until the azimuthal variations in the magnetic field strength exceeded about 10 per cent there was no effect on this containment. The remainder of Dr. Golovin's paper was devoted to a discussion of the work on *Ogra*, the large Russian mirror machine. He stated that *Ogra* was built to study plasma instabilities and was designed to produce a hot plasma with a density of 10^{12} ions/cm³ if no instabilities were encountered. The principle of injection in this machine is that of dissociation of the input beam of 200 keV molecular ions through collisions with the residual neutral gas in the volume. By balancing the favourable process of dissociation against the unfavourable one of charge exchange, it can be shown that a dense plasma will only be formed if the input beam current exceeds a certain value, the so-called burn out current. The burn-out current for *Ogra* was calculated assuming that the background neutral gas density was determined by the ionization of neutral gas by fast ions and by the release of neutral gas from the walls through the impact of fast particles. A figure of the order 200 m amp was obtained for the formation of a hydrogen plasma. Another assumption in the calculation was that the path length of an injected molecular ion moving in the magnetic field and failing to make a collision should be not less than 10^4 cm before it returns to the injector. This length depends critically on the magnetic field configuration and the ion gun alignment, and one of the first tasks with the machine will be to optimize these. A very low initial pressure is also required and to date the lowest value achieved has been $\sim 3 \times 10^{-6}$ mm mercury. In view of the size of the vacuum chamber, 1.5 m bore and 20 m long, this represents a considerable technical achievement. The present ion source gives 150 m amp of molecular ions at 100 keV. Up to the moment only a 30 m amp beam of ions has been injected into the machine and the burn out condition has not been achieved. Impressive photographs were shown of the beam spiralling in the magnetic field.

During question time Dr. K. W. Allen of the Atomic Weapons Research Establishment, Aldermaston, raised the subject of the order of magnitude difference in the relevant charge exchange cross sections as measured by Fedorenko in the U.S.S.R. and by Barnett in the United States. Replving, both Dr. van Atta and Dr. Golovin declared their faith in the measurements carried out in their respective countries, but Dr. van Atta hoped that the work would soon be repeated in a third and preferably neutral country. Other points raised during discussion periods concerned the importance of the spectral region 10 Å–400 Å for plasma measurements, the power lost by synchrotron radiation from the electrons in a magnetically confined plasma and the need for more work on surface bombardment effects.

Finally, Sir George Thomson called for more refined experiments, with purer plasma and more homogeneous magnetic fields. He concluded by declaring his faith in the ultimate solution of the problem of obtaining economic power from fusion reactions.

R. BICKFORTH

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NEW RESEARCH LABORATORIES

ON May 13 Sir Alexander Fleck, chairman of Imperial Chemical Industries, Ltd., opened a new laboratory block for the British Non-Ferrous Metals Research Association at Euston Street in London. The laboratories have gradually been extending on this site since 1930 and now contain about 53,000 sq ft of floor space and house a staff of about 180. They serve the needs for co-operative research of practically all branches of the non-ferrous metals industry, and the 40-50 research projects in progress cover the production, properties and uses of the commoner non-ferrous metals, certain aspects of the metallurgy of the metals concerned with nuclear energy, and metal finishing.

The new laboratory was made possible by the generous response to a building fund on the part of the Association's membership of more than 600 firms and of the Department of Scientific and Industrial Research, which has treated contributions as grant earning. The main features of the new block are a much-enlarged foundry, new corrosion and physics laboratories and a new electroplating shop. Alterations to existing buildings have enabled a new creep testing laboratory to be built which will allow the capacity to be doubled to more than 100 units, the rehousing of many different types of fatigue testing machines in one room, and the provision of more space for the General Metallurgy Section. This, among other things, gives the Section more room for vacuum apparatus for the determination of gases in metals.

In the foundry, moulds are now made in one well-equipped bay and poured in an adjacent melting and casting shop. The melting equipment consists of five gas-fired lift-out crucible furnaces, a gas-fired bale-out furnace for research into die-casting problems, a 600-lb low-frequency induction furnace for studying the performance of refractory linings, and also an electric resistance furnace and a high-frequency furnace each capable of melting charges of up to 20 lb of copper or nickel alloys in vacuum or special atmospheres.

From the inception of the laboratories the value of physical methods of analysis has been realized and the Association's work in developing spectrographic analysis of metals to its present state of efficiency is well known. Recently, the X-ray fluorescence method of analysis has aroused considerable interest and it appears extremely promising for analysing the major constituents in alloys and for the analysis of ores and slags. Its potentialities are being studied, using a spectrometer designed by the Physics Section and built in the Association's workshops. In the Chemistry Section emphasis is on the physico-chemical methods of analysis, including polarography, spectrophotometry and the use of the flame spectrophotometer.

The Physics Section has two X-ray diffraction sets and a variety of special-purpose cameras for crystal orientation studies, the identification of phases in compounds and other tasks. An electron diffraction camera is available for studying oxide and other thin films on metal surfaces.

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the metal industry, and several studies are being made of problems in this field. They include the use of eddy currents for rapid inspection of tubes and rods for flaws, an investigation into emissivity variations of hot metal surfaces which affect the performance of radiation pyrometers, and the development of a novel thermo-electric gauge for measuring, non-destructively, the thickness of electro-deposits.

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Many modern plating solutions contain organic additions which affect the smoothness, brightness and mechanical properties of the coatings in a beneficial way. Exactly how these organic agents do this is not known, and typical addition agents prepared with tracers, such as carbon-14 and sulphur-35, are being used to study the mechanism of the process.

In the Corrosion Section one laboratory is employed solely for sea-water corrosion studies, the current work being concerned mainly with the attack on heat-exchanger tubes handling heavily polluted estuarine waters in power stations, oil refineries and in ships. Some of these tests are at controlled potentials to simulate the effects of applied cathodic protection. The influence of marine atmospheres is assessed by exposure at a site on Hayling Island and the laboratory roof site is used mainly for inland tests. Stress corrosion tests are carried out at both these sites and there is also a special high-humidity room for this purpose in the corrosion laboratory.

One of the main uses of non-ferrous metals is the handling of supply waters, and the effect of water composition on the resistance to corrosion of various metals is being studied at field stations and also in the laboratories using synthesized waters.

The General Metallurgy Section, besides carrying out the usual metallographic work, heat treatment and constitutional studies, contains a metal-working shop with a 12-in rolling mill, a 500-ton press for extrusion and forging, a small forging hammer and a drawbench. This section of the laboratories is also working on the development of titanium, zirconium and thorium alloys and has argon arc melting equipment appropriate for this type of work. Special apparatus which uses an atmosphere of argon for carrying out long-term creep tests on these reactive metals is housed in the new creep laboratory.

HIGHER EDUCATION IN EAST AFRICA

IN 1954, a delegation, headed by Dr (now Sir) Eric Ashby, was appointed to assist in planning the development of Makerere College, Uganda. In addition to indicating the general scope of the development which it thought appropriate, the delegation also made reference to the broad problem of developing higher education in East Africa as a whole. As a result, a working party, under the chairmanship of Sir Alexander Carr Saunders, visited East Africa in July 1955, to review in greater detail the requirements of higher education. Its findings were published in a White Paper¹, in which the Governments of Kenya, Tanganyika, Uganda and Zanzibar fully accepted the desirability of further university college development, within the scope of a single University of East Africa.

A second working party, under the leadership of Dr J. F. Lockwood, visited East Africa in July 1958 to examine proposals for the creation of new institutions of higher education in particular within the framework of a University of East Africa.

Its report², recently published, contains four main recommendations, which are being considered by the East African Governments. (1) By re-organization and extension, the Royal Technical College of East Africa, in Nairobi, should, without delay, become a university college of a new type in which academic and professional courses of equal standing would have their place with Faculties of Science, Arts, Engineering and Special Professional Studies. (2) That plans should be formed for the establishment of an inter-territorial university college in Tanganyika at Morogoro, to be opened in 1956-57, or as soon thereafter as possible. (3) That a university of East Africa should be created by 1960 and that the university colleges then existing and any which may be founded thereafter, should be associated as constituent colleges of the university. (4) Since the carrying out of these recommendations will guarantee adequate provision for higher technological and professional training for some years ahead, no additional institutions offering facilities for these kinds of training should at present be contemplated.

If these recommendations are accepted the new University of East Africa would have as its constituent colleges, Makerere College, the Royal College of East Africa (the reorganized Royal Technical College) and the new university college in Tanganyika. The report adds: "The inter-racial character of the colleges we take for granted as an indispensable element in their fully liberal nature and outlook. That they should also be wholly inter-territorial was likely for many years to be a vital necessity in terms both of academic need and of finance."

It is suggested that since the college in Nairobi would begin its career as a university college under the same system which now applies to Makerere College, students of the reconstructed college would work for degrees of the University of London, under a scheme of special relationship. The University of East Africa, following its foundation, would grant its own degrees, for which students of all the colleges would read. Since the university college in Tanganyika would probably not begin its teaching until after 1958, students of this college would at the outset, read for degrees of the newly established university.

Though realizing that its proposals are modest the working party stresses that the cost, in terms both of capital and recurrent expenditure, will be high and points out that the several Governments will be unlikely to be able to meet capital expenditure from their own joint resources. "The compulsion of their present circumstances will thus force them to lean heavily on expectations of generous grants from Colonial Development and Welfare funds."

The report concludes with the hope that financial help will be forthcoming, for the individual colleges from non-official sources and pays tribute to generous gifts, which the Gandhi Memorial Academy Society has made to the Royal Technical College.

C. MONTMFR

¹ Higher Education in East Africa. Pp. 123 (Entebbe 1955).

² Report of the Working Party on Higher Education in East Africa. July-August 1958. Pp. 11+43. (Nairobi: Government Printer 1959). 2s. 3.

GLOEOSPORIUM IN APPLE STEM WOUNDS

TWO contributions on *Gloeosporium* in apple stem wounds have recently appeared (*J. Hort. Sci.*, 32, No. 2 1959). R. O. Sharples has reported on an investigation of the response of apple stems to wound infections by the fungus *Gloeosporium perennans*. In anatomical studies relating to the establishment of infections on apple branches he has shown that the defensive mechanism of the host includes the production of suberized barriers by bark phellogens and the blocking of xylem vessels by gum deposition. These responses follow wounding, whether or not the wounds are inoculated with *G. perennans*, but the presence of the fungus delays the response. Accordingly the size and form of lesion induced by inoculation are largely determined by the effect of the fungus in postponing the normal wound healing process.

This effect, and consequently penetration by the pathogen is greatest during the period of host dormancy. Invasion occurs most rapidly through the sieve tubes and the vessels and fibres of the outer xylem, the longitudinal intercellular spread of hyphae through the cortex is slower.

Intra-cellular infection of the pith and medullary ray cells occurs in pruning wound infections. When the progress of the infection is arrested, the phellogen and cambium lay down barriers of callus tissue consisting of parenchymatous outer cells surrounding a core of wound wood. After the lesion has been thus isolated the fungus persists as a saprophyte and eventually forms acervuli on the exposed dead host tissue. A limited spread of infection past the suberized barriers occasionally appears.

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permanent mysteries to some, unable to learn the conventions of each idiom or keep standard comparisons in their heads. The aggregation of many individual values into composite ecological statistics offers no problem to modern computing devices, which also are capable of mapping electronically information fed into them by some scanning apparatus in an aeroplane.

Airborne radar, duplicated perhaps with magnetometers and gravimeters, adds to the sensitivity and completeness of the record. Not only images but also radio waves, power points and carbon dioxide can be 'photographed'. Infra red photography picks up besides the aeroplane on the airfield the heat of the runway and thus the number of planes recently started. The emphasis in modern photogrammetry has thus shifted from the static physical condition to the recordable human transactions.

In brief, there are three chief ways in which such a survey can be used:

(1) To supply general social and economic statistics such as the presence and growth of industry, agriculture, house building, road improvements, conservation and productivity, cross checked with ground social surveys and nationally or regionally collected annual or census statistics.

(3) The planning of policy and of improvements and services is based on these surveys. A deft handling of photographic material should be combined with opinion studies and other studies on the ground such as traffic and migration counts done by mechanical or human agents.

(3) The evaluation of policy, that is, the effectiveness of any constructive activity. This will probably be done increasingly as part of ordinary photogrammetric work, with the help of someone competent in statistics and sociology and with a knowledge of the particular part of the world that is to be studied. At a later stage perhaps, when many different studies have been accumulated and compared, the skilled social interpreter may also be able to make useful deductions from a study of the photographs unaided by ground studies.

* *Silberman L. Zaire* 68 (1955)

* "The Significance of the Canadian-Colombo Plan to the Economic Development of Ceylon" (Planning Technical Services) (Toronto 1958)

* Chicago Aerial Industries have recently done such studies for a telephone and a gas company. Mimeographed reports (1959)

* Green N. E. and Monier, R. B. Reliability and validity of Aerial Reconnaissance as a Collection Method for Urban Demographic and Sociological Information" (Maxwell Air Force Base 1955)

* Duncan O. T. *Population Studies* 27 (1957)

EMISSION OF RELATIVELY HIGH-ENERGY IONS FROM LOW-VOLTAGE ARCS

By E. R. HARRISON

Atomic Energy Research Establishment, Harwell, Berks

SOME interesting effects have been observed with low voltage arcs for which so far no completely satisfactory explanations have been found. The principal effect observed is the emission of luminous rays consisting of ions of the cathode material at energies much greater than the total potential difference across the arc.

In the experiments described below, the arc is formed between a tungsten, molybdenum or tantalum filament, which is separately heated, and a nickel anode at a distance of about 5 cm and is maintained in a rare gas, usually argon, at a pressure of 1–50 mm mercury. The applied potential difference is 40–80 V and the current is 200–500 mA. The arc is thermally constricted or 'punched' to a diameter of approximately 5 mm. In arcs of this kind the electrons, ions and gas molecules are in an approximate thermal equilibrium at a temperature generally of the order of 10^4 °C. The ionization potentials of tungsten, molybdenum and tantalum are lower than the excitation potentials of the rare gases and in the present experiments the arcs therefore tend to consist of ions formed from metal volatilized from the cathode. Spectroscopic analysis of the arc reveals strong W II and W I (Mo II and Mo I) lines but only a few faint argon lines.

The first effect observed is that tungsten is deposited at the point where the arc makes contact with a cool nickel anode. This deposition occurs even when the anode is screened from any material evaporated directly from the hot cathode. The rate of deposition on the anode, as determined by activation analysis, is typically 3×10^{-4} gm/sec amp^{-1} , equivalent to a tungsten ion current of 1.5 mA in an arc of 1 amp. It appears that in hot cathode-cool anode arcs of this type there is an efficient mechanism for

transporting positive ions from the cathode to the anode against the electric field. It is evident that such a transport mechanism is required if the ions in the arc are formed originally from volatilized cathode material in the immediate vicinity of the cathode.

A second effect is observed when the arc is constricted by a small aperture of $\frac{1}{2}$ –1 mm diameter in a nickel diaphragm placed between the cathode and anode as shown in Fig. 1. The cathode is now about 5 cm from the aperture diaphragm, and the anode is about 10–20 cm, or preferentially, the anode has a coaxial aperture of 2–3 mm diameter and is spaced about 5 mm from the first aperture as is shown in Fig. 1. On the anode side of the apparatus the pressure is maintained within the range of 10^{-1} to 10^{-2} mm mercury. As a result of the constriction, impressive luminous white rays are observed projecting from the centre of the small aperture into the low pressure region. Occasionally the rays form a uniform diverging beam as in Fig. 2 but more often

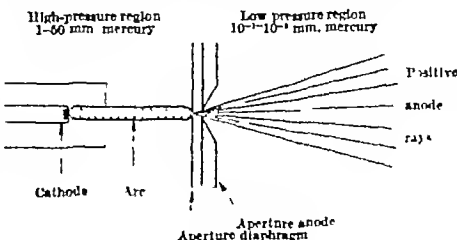


Fig. 1. Apparatus for producing a constricted arc which ejects energetic positive ions through the aperture anode.



Fig 2 Positive tungsten ion rays of approximately 450 eV accelerated by an argon arc of 250 m amp and 80 V

the beam is divided into several individual rays of small diameter which flicker and move in synchronism with the instability motion of the arc. Spectroscopic analysis of the deposit formed by the rays incident on a receiving target shows that the rays consist of tungsten atoms. On changing the cathode material to molybdenum, the deposit formed by the rays is found to consist only of molybdenum, but the luminosity of the rays is unaltered and their colour only very slightly affected.

Electrostatic and magnetic deflexion experiments establish the surprising fact that the rays are positively charged and have energies greater than the potential difference across the arc. The accelerated ions are reasonably monoenergetic and have an energy in the range 100–750 eV, depending on the conditions of the arc. With an aperture reduced to $\frac{1}{2}$ mm diameter and a pressure of 80 mm mercury in the arc, tungsten ion rays with energies greater than 1,000 eV have been observed with a potential difference of only 60 V across an arc of 500 m amp. Rays may also be observed when the pressure is as low as 1 mm mercury, in this case the arc develops only in a limited region adjacent to the aperture in a form reminiscent of a 'ball of fire'. The rays are not so easy to produce when the supporting gas is either helium or neon, possibly because the arc currents in these experiments are limited to relatively small values. With krypton and xenon the rays are produced as readily as in the case of argon.

Difficulty is encountered when attempts are made to measure electrically the current in the tungsten ion rays, not only because of secondary electrons but also because there is apparently an electron flux which is not easily eliminated. Activation analyses of deposits formed by the rays incident on a target show that in a typical case there is a total flux of 0.4×10^{-6} gm/sec $^{-1}$ amp $^{-1}$ equivalent to 0.2 m amp in an arc of 1 amp. This is consistent with the fact that a large fraction of the tungsten migrating towards the anode is deposited around the aperture. More intense fluxes, up to 1 m amp per ampere of arc current, can be achieved by applying an alternating potential difference of 20–50 V between the cathode and an enclosing cylindrical electrode. The flux and luminous intensities do not appear to be critically dependent upon the frequency in the range 10^4 to 10^7 c/s, and it is possible that the increase in intensity is due to the enhanced fluctuation movements induced in the arc.

Potential fluctuations of up to 20 V of the electrodes and movable probes have frequencies of 10^4 – 10^5 c/s with a wide spectrum of 'hash' superimposed. The fluctuations in luminosity of the rays as detected by a photomultiplier are similar to those of the arc and reveal frequencies in the same range as the potential variations. The emission spectrum of the

rays is predominantly W II, or in the case of a molybdenum cathode, Mo II.

A third effect observed is that the rays frequently show a pronounced variation in intensity of luminosity along their length. Thus, if the rays are projected into a region of low pressure of 10^{-3} mm mercury, in a typical case all rays are bright for the first 2.5 cm, the luminosity then becomes faint for about 0.5 cm, and then abruptly increases in intensity and thereafter diminishes slowly up to distances as great as 30 cm.

A completely satisfactory explanation has not been found for all the effects described. The luminosity of the rays is most probably due to charge exchange between the tungsten (molybdenum or tantalum) ions and the supporting gas, the abrupt variations in the luminosity, however, are not understood. The mechanism responsible for producing the positive anode rays is most probably associated in some way with the transport of ions in the arc from the cathode to the anode. The oscillatory or 'hashy' nature of the arc may be an essential self-sustaining feature. Thus, sound waves will be propagated with a phase velocity of $(\gamma k T/m)^{1/2}$, where m is the mass of the atoms of the supporting gas, and one possibility is that the electric fields produced by the separation of the electrons and ions are sufficiently large to cause a fraction of the ions to move with a drift velocity of approximately $(e \lambda E \sin \phi / m)^{1/2}$ in phase with the sound waves, where λ is their mean free path, E is the oscillatory electric field, and ϕ is the phase angle. Experiments designed to detect the propagation of signals along the arc at the phase velocity of sound have not been entirely successful, and the evidence is meagre and unconvincing. Possibly the arc is in a turbulent state, and generates and propagates sound waves only over small distances.

If disturbances of approximately 1 mm wavelength are propagated in the arc, the potential fluctuations suggest that the associated electric fields are of the order of 400 V cm $^{-1}$. In the region of the constriction the oscillatory electric field might be expected to increase inversely as the diameter of the arc, giving a value of 6×10^3 V cm $^{-1}$ if allowance is made for the fact that the arc is smaller than the constricting aperture. It is therefore possible that the ions gain their energy of several hundred electron volts from the oscillatory electric fields in the constricted region of the arc.

Energetic ions of several hundred electron volts have been observed elsewhere⁶ in high-current, low-pressure arcs in magnetic fields used in the DCX experiments. However, the arc conditions are considerably different and the accelerating mechanism is not necessarily of the same kind as that proposed above.

Acknowledgments are made to Mr J D Lawson, Prof A von Engels, Dr P C Thonemann and Dr S A Ramsden for their suggestions and interest, to Mr D H F Atkins for the activation analyses and to Mr F T Burks for the spectroscopic analyses of the ray deposits.

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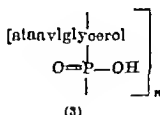
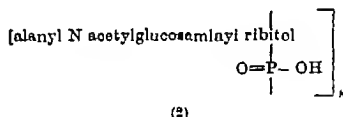
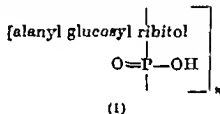
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TEICHOIC ACIDS FROM BACTERIAL WALLS

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NEWCASTLE UPON TYNEComposition of Teichoic Acids from
a Number of Bacterial Walls

INVESTIGATIONS on the function of the nucleotides cytidine diphosphate glycerol¹ and cytidine diphosphate ribitol² led to the discovery of a new group of natural polymers, the teichoic acids, in the walls of certain bacteria³. In *Bacillus subtilis* the teichoic acid is of the type shown in formula (1), whereas that in *Staphylococcus aureus* has the related structure (2), in which the sugar component is glucosamine. That from *Lactobacillus arabinosus* is of the type (1), but some of the ribitol residues bear two glucosyl substituents, whereas others are unsubstituted by glucose. A more detailed discussion of their structure and relationship with cytidine diphosphate ribitol has been given elsewhere⁴.



We had intended to confine the term teichoic acid to those polymers of ribitol phosphate of the general structure (1) or (2) found in bacterial walls. A more extended survey of other organisms (see Table 1) has shown that some bacteria contain a new type of teichoic acid in which ribitol has been replaced by glycerol. Preliminary studies on the hydrolysis of these glycerol derivatives by acids, or by alkali followed by prostato phosphatase, show that they have the structure (3). Visual chromatographic estimation indicates that they represent more than 30 per cent of the wall in some cases. Consequently, the restricted nomenclature originally adopted must now be modified to include all polymers of the types (1), (2) and (3).

The polyol phosphate derivatives in walls of *L. arabinosus* and *B. subtilis* are clearly ribitol teichoic acids of the type (1), and no trace of a glycerophosphate polymer has been detected in these walls. All strains of *Staph. aureus* examined so far contain a ribitol teichoic acid (2) but these walls also contain other traces or in one case a considerable amount of a glycerophosphate polymer. Similarly walls of *Streptococcus faecalis* contain a ribitol teichoic acid of the type (1) and a glycerophosphate polymer.

It is interesting that *L. casei*, *L. delbrückii*, *L. bulgaricus*, *Staph. albus* and *Staph. citreus*, unlike the other lactobacilli and staphylococci examined so far contain glycerol teichoic acid but no trace of a ribitol teichoic acid. The compound from *Staph. albus* and *Staph. citreus* was present in their walls but preparations from whole cells were used for the work on the three lactobacilli and it is not known whether the teichoic acid in these preparations originated from the walls. The compound from *L. casei* is of the type (3) in which alanine is attached to a polymer of glycerophosphate. The amount of hexose in preparations of this material is very small and we have been unable to demonstrate any glycosylglycerol linkages. It seems likely that all the glycerol-teichoic acids in the bacteria listed will be of type (3) but the presence of glycosyl residues is still possible in some cases.

In addition to the organisms discussed here a number of others yielded small amounts of glycerophosphate on acid hydrolysis of their walls. There is evidence that polyols other than ribitol and glycerol are present together with these in teichoic acid preparations from some organisms, and sugars other than glucose or glucosamine may occur.

Extracts prepared from whole cells of all organisms examined contained a glycerophosphate polymer even when no such polymer was present in the isolated walls. It is not known whether this is a teichoic acid of type (3) which has been lost from the walls during their preparation or whether it is associated with other cell structures.

In contrast to the variations in polyol and sugar the only amino acid found in purified preparations of teichoic acid is alanine. This amino acid isolated from teichoic acid from *L. arabinosus* and *Staph. aureus* has the D configuration⁴. It was shown earlier that the alanyl residues are in ester linkage and it is now found that the lability of these residues (half life 5 min at 37°, pH 7.2, 1.1 M hydroxylamine) in neutral salt free hydroxylamine solution is comparable to that of amino acids bound to ribonucleic acid (half life 3 min. at 30°, pH 7.2, 0.8 M hydroxylamine)⁵. The alanine ester linkages are therefore much more reactive than normal amino acid esters which do not react significantly with hydroxylamine under comparable conditions⁷.

Table 1

| | Type of polymer | |
|--|-----------------|---------|
| | Glycerol | Ribitol |
| <i>Lactobacillus arabinosus</i> 17-5 | — | — |
| <i>L. casei</i> (A.T.C. 459) | + | — |
| <i>L. delbrückii</i> (N.C.I.B. 8203) | + | — |
| <i>L. bulgaricus</i> (N.C.I.B. 76) | + | — |
| <i>Staphylococcus aureus</i> II | trace | + |
| <i>Staph. aureus</i> (Duncan) | trace | + |
| <i>Staph. aureus</i> (Oxford) | + | + |
| <i>Staph. citreus</i> | + | — |
| <i>Staph. albus</i> (N.C.T.C. 944) | + | — |
| <i>Bacillus subtilis</i> (vegetative form) | — | — |
| <i>Escherichia coli</i> (Type 1) | trace | — |
| <i>Corynebacterium jeikeium</i> | + | — |
| <i>Streptococcus faecalis</i> (A.T.C. 900) | + | + |

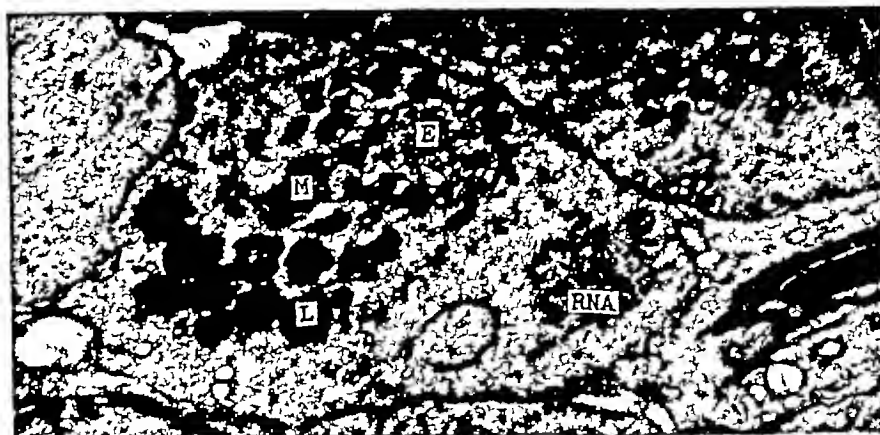


Fig 1 Micrograph showing a late stage in the formation of a residual body. E, endoplasmic reticulum, L, lipoidal body, M, mitochondrion, RNA, aggregate of particles containing ribonucleic acid ($\times c 7,300$)

in spermatid development all the above-mentioned inclusions had concentrated within a small lobe of cytoplasm near the base of the nucleus. Just before the mature spermatid is shed, this lobe of cytoplasm is cast off and becomes spheroidal in shape. The spheroidal bodies which arise in this way clearly correspond to the residual bodies of Regaud. Each residual body is bounded by a membrane derived from the cell membrane of the corresponding mature spermatid. Within, and close to, the limiting membrane lie two or three small groups of granular mitochondria, several lipoidal bodies (sometimes arranged in crescent fashion) and Golgi remnant. The greater part of each residual body is occupied by a comparatively large, eccentrically placed mass of strongly basophilic material.

Soon after the sperms have been shed the residual bodies migrate peripherally. As precisely as could be determined by light microscopy, this appeared to be due to phagocytosis by Sertoli cells. Afterwards, the residual bodies come to lie close to Sertoli nuclei at the border of the tubule.

Changes occur within the residual bodies both during their peripheral migration and while they are at the periphery of the tubule. The first sign of these changes is the appearance of minute vesicles about 0.3μ in diameter which form along the edges of the basophilic material. During their movement towards the periphery the residual bodies become reduced in size, their diameter decreasing from about 10μ to 5μ . Finally, there is a loss in basophilia and then all that can be seen is the limiting membrane, some mitochondria and lipoidal bodies, and the Golgi remnant. After this stage it is impossible to identify the residual bodies with any certainty. However, accompanying and following upon the 'end' stage, lipoidal bodies of about the same size as the residual bodies, and in the same general location, appear within the Sertoli cells. We have studied the residual bodies at this time to see if they become converted into the lipoidal bodies described above. What may be transitional stages have, in fact, been observed, but only very rarely.

Histochemical tests have shown that the basophilic material referred

to above consists of, or contains, ribonucleic acid. The lipoidal bodies which occur within spermatid cytoplasm, and form part of the residual bodies, do not respond positively to Baker's⁵ acid haematin test for phospholipins nor to Schultz's⁶ test for cholesterol. The same negative responses for both tests are also given by the lipoidal bodies within Sertoli cells.

Electron Microscope Observations

Tissue was fixed in 1 per cent osmium tetroxide buffered to pH 7.3⁷. It was then embedded in a 1:3 mixture of *n*-methyl and *n*-butyl methacrylate, sectioned with a glass knife and examined in a

Siemens Elmiskop Ia. Due to the comparatively small size of the residual bodies and the fact that they occur only under certain physiological conditions a great deal of material has had to be examined to find even the more important stages referred to above.

Observations made by electron microscopy are in accord with those made by light microscopy. In addition, finer details have been seen. During late formative stages (Fig 1) the mitochondria are irregular in shape and characteristically cluster around a local concentration of endoplasmic reticulum. Adjacent to these elements is a group of osmiophilic granules which correspond to the lipoidal bodies seen under the light microscope. The Golgi remnant consists of a few paired membranes in parallel arrangement and aggregates of many small vesicles enclosed by two or more membranes. Near the inclusions just described occur one or two particulate masses, spheroidal in general outline and corresponding to the ribonucleic acid granules seen by light microscopy. At a later stage in the formation of the residual bodies the mitochondria are either greatly elongated and constricted in the middle (as though in a process of division) or are small, dense and spheroidal. The endoplasmic reticulum appears to consist of membranes delimiting vacuoles of various sizes. The basophilic material consists of one large mass of fine particles.

Studies by electron microscopy have confirmed quite definitely that the residual bodies are phago-

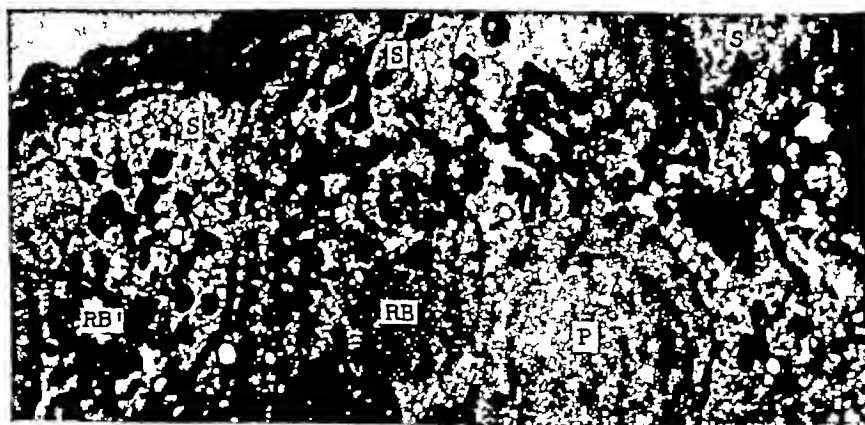


Fig 2 Micrograph showing residual bodies within Sertoli cells at the border of a tubule. Some of the residual bodies (RB) are comparatively intact. Others have been largely absorbed and appear irregular in shape (RB'). P, primary spermatocyte, S, Sertoli cell ($\times c 7,300$)

cytosed by the Sertoli cells. Within any one Sertoli cell, even in ultra thin sections, we have observed up to six residual bodies. Each residual body is enclosed by a variable number (1-4) of fine membranes. When the body reaches the edge of the tubule the limiting membranes are no longer continuous. Residual bodies at the periphery contain the same basic constituents as those seen in the last stages of their formation in the tubulo lumen. Later, the basic phallic material and various other components are absorbed until all that remains is an irregular-shaped body which is intensely osmophilic and presumably lipidal (Fig. 2). About this time a peripheral ring of lipid can be demonstrated in Sertoli cells by the use of appropriate light microscopical techniques.

When the residual bodies come to lie close to the Sertoli nuclei (adjacent to the tubule tissue) changes occur both within the Sertoli cytoplasm and in germ cells. Within the Sertoli cells appears the peripheral ring of lipid mentioned above. Mitochondria either increase in number or become concentrated peri-

pherally. The cytoplasmic matrix (as seen under the electron microscope) becomes very dense. The young spermatids start to elongate and become more deeply enclosed by Sertoli cytoplasm. There is an increase in chromatin content of the nuclei of type B spermatogonia. It is possible that the residual bodies produce in the Sertoli cells some influence that may serve to trigger off the changes in the germ cells as reported above. The residual bodies would then be responsible for the local control of spermatogenesis. This is now being investigated further.

We are grateful to the Wellcome Trust for a grant to purchase an electron microscope and to St Bartholomew's Hospital and Medical College for further financial help.

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GROWTH RESPONSES TO SELENIUM IN LAMBS

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UNTIL recently, selenium as a dietary constituent was regarded as of significance only when it occurred in excess of certain well-defined limits. In selenium poisoning areas about 5 p.p.m. in herbage is considered to be the tolerance limit for livestock¹. It has now been shown²⁻⁴ that selenium in organic and inorganic form has high protective powers against necrotic liver degeneration in the rat and mouse, and exudative diathesis in the chick fed basal diets deficient in vitamin E and containing a high proportion of *Torula yeast*, protection being obtained respectively with 0.04 p.p.m. and 0.1 p.p.m. of selenium in the ration. It has been shown also in the chick that selenium is a required nutrient necessary for normal growth as well as for the prevention of exudative diathesis⁵.

So far as large animals are concerned there is evidence to indicate that sodium selenate fed to pregnant ewes at the rate of 0.1 p.p.m. of selenium in the ration will protect their lambs against muscular dystrophy (white muscle disease)⁶.

Furthermore trials conducted in the South Island of New Zealand⁷ suggest a protective action of selenium when given to the lambs themselves, in naturally occurring outbreaks of a type of muscular dystrophy affecting young lambs.

Arising from the idea that subclinical muscular dystrophy might be one of the factors responsible for the slow growth rate of weaned and unweaned lambs commonly observed in the South Island—a condition known locally as 'ill thrift'—we commenced trials to investigate the possible effects of selenium supplements on the growth rate of various classes of lambs on the College farms. This communication records the observations made to date.

All lambs were individually identified with ear tags, divided at random into treatment and control groups and weighed at intervals of 2-3 weeks. Selenium was given as sodium selenate by subcutaneous injection in sterile water at the rate of 1.0 i.u.m.

selenium every 7-10 days. Lambing commenced about the beginning of August and weaning occurred in the first week of December.

The first three trials involved pure bred Romney, Border Leicester and Corriedale ram and ewe lambs reared on the College home farm. The fourth trial was carried out on Corriedale wether lambs brought on to the College farm from the same farm on which the fifth trial was conducted (Ashley Dene farm).

Mean live weights and gains are set out in Table 1, with the numbers of lambs in each group given in brackets.

Table 1 MEAN LIVE WEIGHTS AND GAINS (lb.)

| Trial 1 | Romneys | 0.10.58 | 22.1.59 | Gain |
|---------|------------------------|------------|---------|-------|
| | Date | 30.5 (94) | 60.4 | 38.0 |
| | Selenium | 31.6 (88) | 60.3 | 34.8 |
| | Control | | | 4.1* |
| | Difference in 105 days | | | |
| Trial 2 | Border Leicesters | 19.10.58 | 22.1.59 | |
| | Date | 51.2 (40) | 79.2 | 28.0 |
| | Selenium | 50.3 (47) | 71.9 | 21.6 |
| | Control | | | 6.4* |
| | Difference in 93 days | | | |
| Trial 3 | Corriedales | 21.11.58 | 22.1.59 | |
| | Date | 46.9 (101) | 63.1 | 16.5 |
| | Selenium | 47.4 (50) | 60.0 | 13.5 |
| | Control | | | 3.0* |
| | Difference in 62 days | | | |
| Trial 4 | Corriedale wethers | 11.11.58 | 19.2.59 | |
| | Date | 52.2 (20) | 74.5 | 22.3 |
| | Selenium | 52.2 (20) | 67.6 | 15.0 |
| | Control | | | 6.7* |
| | Difference in 93 days | | | |
| Trial 5 | Corriedale (mixed sex) | 3.11.58 | 2.2.59 | |
| | Date | 40.6 (23) | 78.3 | 37.7 |
| | Selenium | 41.0 (21) | 68.6 | 27.0 |
| | Control | | | 10.7* |
| | Difference in 91 days | | | |

* Significant at 1.0 per cent level

Analysis of variance shows that the differences in gains in live weight are highly significant ($P < 0.01$) in all trials. The magnitude of these responses varies considerably, being greater in general in the lambs from the Ashley Dene farm. The response is rapid, evidence of increased growth being observable in all groups in 2-3 weeks after treatment commenced.

Further, it appears to be a continuing one, although the duration of some of the trials is obviously short.

Explanation of the mode of action of selenium in producing a growth response under these conditions must at the present time be rather speculative. There can be little doubt now that traces of selenium are required by the animal for normal metabolism, that vitamin E and selenium are interrelated in their metabolic functions, and that vitamin E cannot completely replace the need for selenium. The growth responses in lambs may therefore be taken as an indication of a specific selenium deficiency, one manifestation of which is a slowing up of growth, and another a predisposition to muscular dystrophy and possibly other conditions in which the metabolism of vitamin E is involved.

This concept is in conformity with the known distribution of naturally occurring outbreaks of exudative diathesis in chicks and white muscle disease in lambs¹⁰, both of which, in New Zealand, are almost entirely restricted to the South Island.

In this respect it is of interest to note that the groups of lambs giving the greatest response (trials 4 and 5) came from flocks in which losses from white muscle disease had occurred earlier in the season before these trials commenced (4 out of 600 for trial 4 and 7 out of 51 in trial 5).

At the other extreme, in the pure-bred lambs on the College farm, only one death occurred from white

muscle disease, there were no other signs of the disease in the 580 lambs born this season, nor has there ever been any history of the disease on this farm. Selenium responses have therefore been obtained, not only in lambs from areas where white muscle disease is common, but also where it has been extremely rare.

On the other hand, the College farm has had a history of so-called 'ill-thrift' of varying degrees of severity over the past three years. Just what part, if any, selenium deficiency plays in the 'ill-thrift' syndrome in this area is not as yet clear. That it may be a factor of some importance is indicated by the data presented in these trials.

This is a preliminary report only and final results will be published elsewhere.

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CARBOHYDRATE — AMINO-ACID INTER-RELATIONS IN BRAIN CORTEX IN VITRO

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IT is now well known that when radioactive glucose is metabolized by brain cortex *in vitro*, radioactive amino-acids are formed¹⁻³. A mince of the brain of one-day old mice when incubated with glucose uniformly labelled with carbon-14 incorporates radioactivity in all amino-acids of brain protein with the exception of threonine¹. Rat brain cortex slices can convert ¹⁴C-glucose into labelled glutamic, aspartic and γ -aminobutyric acids³. When ¹⁴C-glucose is injected intraperitoneally into one-day-old mice, radioactivity is found in aspartic and glutamic acids and in alanine in the brain proteins². It is evident that glucose, during its normal metabolism in the brain, produces intermediates—presumably the α -ketonic acids—that undergo conversion to amino-acids largely at the expense of organic nitrogen already available in the brain cell. Such amino-acids must play a part not only in the various biosynthetic operations of the nerve cell but also in the maintenance of ionic balance in the cell. It is therefore of importance to understand more fully than is known at present the precise relations existing between sugars and amino-acids in the brain, and the manner in which these relations may be affected by substances that influence brain metabolism. Among such substances are potassium ions, which have long been known to exert profound effects on the metabolism of nerve cells. Cationic balance is a factor of fundamental importance for the metabolism of brain, both aerobically⁴ and anaerobically⁵.

We have therefore carried out experiments to ascertain the effects, on the formation of amino-acids from glucose in the brain cortex *in vitro*, of those concentrations of potassium ions that produce optimal stimulation of respiration, of a neurotropic drug such as amytal and of a respiratory inhibitor such as sodium malonate. The experiments have been carried out not only to throw more light on the mode of action of these substances but also to indicate the importance of the consideration of the amino-acids as part of the over-all metabolism of sugars in the nervous system.

The experimental work was carried out with the conventional Warburg manometric apparatus. Slices of rat brain cortex weighing approximately 90 mgm were incubated in a medium of the following composition: sodium chloride, 128 mM, potassium chloride, 5 mM, calcium chloride, 3.6 mM, magnesium sulphate, 1.3 mM, disodium hydrogen phosphate, 10 mM brought to pH 7.4 with N hydrochloric acid. The final volume was 1.0 ml and each flask contained 5 mM glucose uniformly labelled with carbon-14 with an activity of 10⁶ counts/min when counted on aluminium planchets at infinite thinness. 0.1 ml of 20 per cent potassium hydroxide was used as carbon dioxide absorbent. Incubations were carried out in oxygen at 37° C for 1 hr, after which the tissue slices were homogenized in 8.0 ml of 80 per cent ethanol, centrifuged and the supernatant evaporated at 30° C in a current of air. The dried

extract was dissolved in 0.5 ml of water and 400 μ l was chromatographed two-dimensionally on Whatman No 1 paper. The solvents used were *sec* butanol/80 per cent formic acid/water (70:11:17 v/v/v) for the first phase, and phenol/water/ammonia (1 lb phenol:110 ml water:17 ml ammonia spec grav 0.88) for the second phase.

The radioactive spots were localized by radioautography and the radioactivities of the spots were measured quantitatively using a Tracerlab counter with a mica window 28 mm in diameter and thickness 1.5–1.8/cm². Activities were corrected for background. The counting efficiency by this method was calculated to be 10.8 per cent.

All results are expressed as counts per minute for 100 mgm of wet-weight tissue.

Effects of Potassium Ions on Amino-acid Formation from Glucose and Fructose

The stimulating effects of potassium ions at 105 mM (preferably expressed as mEq/litre (milliequivalents/litre)) on brain respiration, shown many years ago by Dickens and Grovillo¹ and by Ashford and Dixon², take place with the identical substrates, glucose, pyruvate or lactate, which permit responses to applied electrical pulses. The potassium effect has many of the metabolic characteristics of brain tissue in the excited state. It is suppressed by low concentrations of narcotics that have no demonstrable effects on the unstimulated respiration in the presence of glucose which is quantitatively the most important metabolic fuel of the brain^{3,4} and of ganglia⁵. The narcotic suppression of potassium stimulation of brain respiration applies not only to central narcotics⁶ but also to local anesthetics⁷, to chlorpromazine, alcohols and aldehydes^{8,9} and to the newer depressants of the glutarimide type, and focuses interest on the mechanism of potassium stimulation of neuronal respiration. This stimulation seems greatly to resemble that brought about by oscillating electrical pulses^{10,11}, which may produce their effects by ionic displacements, for example, of potassium, calcium or sodium. All the evidence points, in fact, to the similarity in many respects of the biochemical effects of electrical stimulation of the brain cortex slices with those due to the presence, in the incubation medium, of potassium ions at 0.1 molar concentration. Brain homogenates or minces are, as is well known, unresponsive to either forms of activation. Presumably in the conscious animal such stimulation operates by the action of sensory impulses, and high sensitivity to narcotics of the metabolic activity of the stimulated brain cell ensues.

The potassium stimulation of brain respiration is highly sensitive to malonate, whereas unstimulated brain respiration is but little affected by malonate^{12,13}. It is evident^{14,15} that potassium ions activate the citric acid cycle involved in glucose oxidation in the brain or a pace making step closely associated with it.

Results showing the effects of the addition of 105 mM potassium chloride solution to the incubation medium on amino-acid formation in rat brain cortex slices are shown in Table 1. It will be seen that in a normal physiological medium containing 5 mM potassium ions there is a labelling of glutamic acid, aspartic acid, glutamine, alanine and γ aminobutyric acid in the presence of glucose and of fructose both uniformly labelled with carbon 14. The labelling of glutamic acid, with both sugars, is highest among the

Table 1 EFFECTS OF 0.1 M POTASSIUM CHLORIDE ON AMINO-ACID PRODUCTION FROM GLUCOSE AND FRUCTOSE UNIFORMLY LABELLED WITH CARBON 14 IN SLICES OF RAT BRAIN CORTEX. Substrate concentration, 5 mM (10⁶ counts/min.). Incubation time, 60 min. temperature 37°C. Amino acids are expressed as counts/min./100 mgm wet tissue/10⁶ counts/min. uniformly labelled substrate per vessel.

| Amino-acid formed | Glucose 1- ¹⁴ C | | Fructose 1- ¹⁴ C | |
|-----------------------------|----------------------------|-----------------------|-----------------------------|-----------------------|
| | 5 mM K ⁺ | 105 mM K ⁺ | 5 mM K ⁺ | 105 mM K ⁺ |
| Glutamic acid | 8 057 \pm 358 | 5 810 \pm 476 | 4 784 \pm 307 | 942 \pm 21 |
| Aspartic acid | 1 318 \pm 164 | 1 183 \pm 185 | 2 150 \pm 122 | 2 127 \pm 101 |
| Glutamine | 1 280 \pm 112 | 2 80 \pm 200 | (9) | (4) |
| Alanine | 057 \pm 60 | 794 \pm 40 | 374 \pm 63 | 224 \pm 24 |
| γ Amino butyric acid | 906 \pm 142 | 1 401 \pm 164 | 730 \pm 22 | 271 \pm 10 |

All values are given with mean standard errors.

* Glutamine could not be counted when fructose was used as substrate as the fructose spot overlapped that of glutamine.

amino-acids investigated aspartic acid showing the next highest activity. It is noteworthy that the labelling of aspartic acid on incubation with uniformly labelled fructose greatly exceeds that of aspartic acid found after incubation with uniformly labelled glucose.

The most important quantitative effect of the presence of 105 mM potassium ions which increases the respiration of brain cortex slices in the presence of glucose by almost 100 per cent, is to bring about a large increase in the labelling of glutamine (nearly 100 per cent) and of γ aminobutyric acid. The total count of the labelled amino-acids in the presence of glucose uniformly labelled with carbon 14 is increased from 9 287 to 11 331 counts/min. The labelling of glutamic acid or alanine is slightly increased whereas that of aspartic acid is slightly decreased.

It may be noted that the ratios of radioactive glutamate:glutamine and γ aminobutyrate found with potassium stimulated rat brain cortex slices in presence of glucose are 1:0.44:0.27 (Table 1), which approximate to the ratios of these amino-acids normally found in the adult rat brain cortex¹⁶, namely, 1:0.43:0.17.

As it is well known that glutamine is derived from glutamate in brain in a reaction involving adenosine triphosphate¹⁷ the process bringing about the removal of free ammonium ions that are liberated during the functional activity of the brain¹⁸, and that γ aminobutyric acid is derived from glutamate by a decarboxylase normally present in the brain¹⁹, we may consider that the net effect of exposing brain cortex slices in presence of glucose, uniformly labelled with carbon 14 to 105 mM potassium ions, is to increase the total yield of glutamic acid, the excess over the normal appearing as both glutamine and γ aminobutyric acid. This phenomenon may be explained by the fact that the presence of 105 mM potassium ions accelerates the operation of the citric acid cycle in the brain, increasing the rate of turnover of intermediates, among which is a keto glutarate which by transamination with intracellular amino-acids, forms glutamate and thence glutamine and γ aminobutyric acid.

Typical results given in Table 2 lead to the conclusion that the presence of potassium ions accelerates the conversion of pyruvate to acetyl-coenzyme A. The results demonstrate that the presence of 105 mM potassium ions greatly increases the rate of oxidation in brain cortex of both pyruvate 1-¹⁴C and pyruvate 2-¹⁴C to carbon 14 dioxide the latter process being much more inhibited by the presence of malonate than the former. The fact that some inhibition

Table 2 COMPARISON OF THE EFFECTS OF 0.01 M SODIUM MALONATE AND 0.1 M POTASSIUM CHLORIDE ON OXIDATION OF PYRUVATE-1-¹⁴C AND PYRUVATE 2-¹⁴C BY SLICES OF RAT BRAIN CORTEX
Substrate concentration, 10 mM (10⁴ counts/min), incubation time, 60 min temperature, 37° C, aerobic Carbon-14 dioxide evolved expressed as counts/min/mgm dry weight tissue/hr [10⁴ counts/min substrate per vessel]

| Experimental conditions | Pyruvate 1- ¹⁴ C | | Pyruvate 2- ¹⁴ C | |
|--|-----------------------------|-----------------------|-----------------------------|-----------------------|
| | 5 mM K ⁺ | 105 mM K ⁺ | 5 mM K ⁺ | 105 mM K ⁺ |
| Sodium pyruvate only | 1,166 | 2,008 | 481 | 1,040 |
| Sodium pyruvate + 0.01 M sodium malonate | 903 | 1,342 | 258 | 330 |

of the former process by malonate occurs leads to the conclusion that part of the carbon-14 dioxide derived from pyruvate-1-¹⁴C is formed after its fixation and metabolism by the citric acid cycle

Granting that the effect of the presence of 105 mM potassium ions is an increased rate of formation of acetyl-coenzyme A, it becomes at once apparent (see Fig. 1) that the rate of formation of α -ketoglutarate (and thereby the rates of formation of glutamate, glutamine and γ -aminobutyrate) should be increased, whereas that of oxalacetate (and thereby aspartate) may not be increased, as its greater rate of formation is balanced by its greater rate of removal by condensation with the increased quantity of acetyl-coenzyme A that has become available

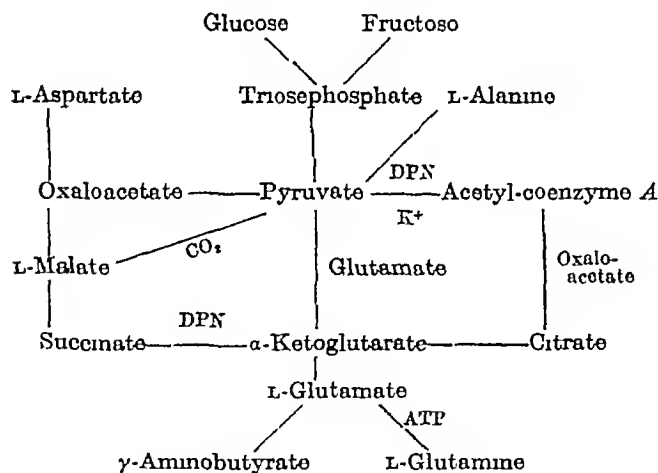


Fig 1

The conclusion that the major effect of increased potassium ions is to increase the velocity of formation of acetyl-coenzyme A from pyruvate in brain cortex makes it possible to understand the mode of action of potassium ions in affecting the formation of amino-acids from fructose uniformly labelled with carbon-14. It will be seen, in the results quoted in Table 1, that in the presence of the normal potassium ion concentration (5 mM), there is a marked increase of labelled aspartate and a marked decrease of labelled alanine as compared with the amounts of these amino-acids formed in the presence of glucose uniformly labelled with carbon-14. When the potassium ion concentration is increased to 105 mM, the outstanding effects are the large falls in the amounts of labelled glutamate and γ -aminobutyric acid. Owing to experimental difficulties, when using fructose on paper chromatograms, it was not possible to make accurate assays of the radioactive glutamine formed

The significant factor to be taken into account in interpreting the results found with uniformly labelled fructose (Table 1) is the much lower affinity of fructose for brain hexokinase than that of glucose.²⁴ The result of this lower affinity is a diminished availability of pyruvate in the brain cortex slices, under the experimental conditions quoted, a fact that accounts for the feeble anaerobic glycolysis exhibited by brain cortex in presence of fructose. Sufficient pyruvate is available, however, to enable the citric acid cycle to operate and to yield a respiratory value of the same order as shown by glucose in presence of brain cortex. The lack of availability of pyruvate, apart from that amount required for the citric acid cycle to operate, is also shown by the much lower ability of brain cortex slices to form lactic acid or to synthesize acetyl choline in presence of fructose as compared with that found in the presence of glucose.²⁵ Although respiratory activities, and presumably, therefore, the amounts of available adenosine triphosphate, of brain cortex slices in the presence of glucose and fructose are approximately the same, the rate of formation of acetyl-coenzyme A in the presence of the former sugar is greater than in the presence of the latter

The lowered availability of pyruvate, in brain cortex slices in the presence of fructose uniformly labelled with carbon-14, results in there being less acetyl-coenzyme A available for condensation with oxalacetic acid formed during the operation of the citric acid cycle. This in turn leads to more oxalacetic acid being available for transamination into aspartic acid than occurs with glucose. On this interpretation, the larger yields of labelled aspartic acid found in the presence of uniformly labelled fructose than in the presence of uniformly labelled glucose is directly due to lack of available acetyl-coenzyme A for the acetylation of oxalacetic acid. The lowered availability of pyruvic acid from uniformly labelled fructose is shown also by the diminished rate of formation of labelled alanine (Table 1) in the presence of this sugar

The effects of an increased concentration of potassium ions on amino-acid formation from fructose may also be understood. The acceleration of conversion of pyruvate to acetyl-coenzyme A by the presence of 105 mM potassium ions leads to an increased rate of respiration, so that more of the limited pyruvate available is converted to carbon dioxide. There is therefore less pyruvate available for conversion to amino-acids. Experiment shows (Table 1) that a total count of 8,056 counts/min for the amino-acids investigated falls to 3,564 counts/min in the presence of 105 mM potassium ions

The limited amount of pyruvate, made available from fructose, leads ultimately to the formation of a smaller quantity of α -ketoglutarate than takes place with glucose, in spite of the increased rate of formation of acetyl-coenzyme A due to the presence of 105 mM potassium ions. This in turn leads to smaller amounts, at equilibrium, of labelled glutamate and γ -aminobutyrate. The quantity of labelled aspartate formed, however, remains approximately constant. This occurs, presumably, because the malic acid enzyme that transforms pyruvate to malate with fixation of carbon dioxide, and thence to oxalacetate and aspartate, is operating optimally. This process is already known to occur with retina²⁶ and with mouse brain²⁰

It is therefore possible to obtain an understanding of the relations existing between glucose or fructose,

and the amino acids derived from these sugars in the brain, both in the presence of normal and high concentrations of potassium ions, on the basis of our present knowledge of the operations of the citric acid cycle in brain of transaminating processes affecting the α ketonic acids, and on the conclusion that the stimulating action of potassium is largely directed to the conversion of pyruvate into acetyl coenzyme A.

The implications of these findings are considerable for they indicate that cationic balance, by influencing the relative velocities of the neurochemical processes affects the formation of substances such as acetyl choline or γ aminobutyric acid, which are now well known to be implicated in the electrophysiology of the nervous system.

Effects of Sodium Malonate on Glucose-Amino-Acid Inter-relations

In the presence of 10 mM sodium malonate the respiration of brain cortex stimulated by potassium is inhibited to the level of the endogenous respiration, which is only slightly affected.

The effects of the addition of 10 mM sodium malonate on the formation of labelled amino acids from glucose uniformly labelled with carbon 14 are shown in Table 3.

Table 3. INFLUENCE OF 0.01 M SODIUM MALONATE ON AMINO-ACID FORMATION FROM GLUCOSE UNIFORMLY LABELLED WITH CARBON 14 WITH AND WITHOUT 0.1 M POTASSIUM CHLORIDE. Experimental conditions as in Table 1. Results (counts/min./100 mgm wet tissue/10⁵ counts/min. glucose) are the mean values of three sets of experimental results.

| Amino-acid formed | 5 mM K ⁺ + 0.01 M malonate | 10 mM K ⁺ + 0.01 M malonate |
|-----------------------------|---------------------------------------|--|
| Glutamic acid | 1390 | 995 |
| Aspartic acid | 359 | 533 |
| Glutamine | 301 | 72 |
| Alanine | 133 | 60 |
| γ -Aminobutyric acid | 532 | 194 |

The most noteworthy effect of the malonate is the decrease in labelling of all the amino acids: a total amino acid count of 9,287 counts/min. is reduced by malonate to 3,334 counts/min. The percentage decrease effected by malonate is greater in the presence of 105 mM potassium ions. The total count of 11,381 counts/min found with the high potassium ion concentration is reduced to 1,904 counts/min when the malonate is added. Thus not only is the potassium stimulation of brain respiration abolished by malonate¹² but also its stimulation of amino acid labelling in the presence of radioactive glucose. The suppression of respiration is reflected by the lowered availability of pyruvate and hence in the diminished production of labelled alanine and of α ketoglutarate and hence in the diminished rates of formation of glutamate, glutamine and γ -aminobutyric acid.

Effects of Sodium Amytal on Amino-acid Formation from Glucose

In accordance with the conclusion by Michaelis and Quastel¹³ that a narcotic, such as chloralhydrate suppresses specifically at low concentrations the activity of a process playing an intermediate part in tissue respiration between a flavoprotein involving diphosphopyridine nucleotide and cytochrome oxidase it has been shown¹⁴ that amytal (5-ethyl 5-isoamyl barbiturate) is a highly effective inhibitor of the oxidation of reduced diphosphopyridine nucleotide and its associated phosphorylations.

An effect, therefore of the addition of a narcotic, such as amytal, to respiring tissue is to bring about an increase in the ratio of reduced diphosphopyridine nucleotide to diphosphopyridine nucleotide in the cell. The change in this ratio or the diminished availability of diphosphopyridine nucleotide for its various linked reactions in cell metabolism has a variety of consequences. One obvious result is an increase in the rate of reduction of pyruvate, derived from aerobic breakdown of glucose in the brain cell to lactate, so that an increased aerobic glycolysis in the presence of the narcotic takes place. This is a well known phenomenon.¹⁵ Other results due both to the changed velocities of the diphosphopyridine nucleotide linked reactions and to the diminished availability of adenosine triphosphate consequent upon the suppression of oxidation of reduced diphosphopyridine nucleotide may be expected to take place.

The effects of the addition of 0.5 mM sodium amytal on amino acids formed from glucose uniformly labelled with carbon 14, in the presence and absence of 105 mM potassium ions are shown in Table 4. At this concentration amytal exerts only a small inhibitory effect on the oxidation of glucose by the unstimulated brain cortex slices but almost a complete suppression of the potassium stimulated respiration of brain cortex in the presence of glucose.¹⁶ The results (Table 4) demonstrate these effects.

Table 4. INFLUENCE OF 0.5 mM SODIUM AMYTAL ON AMINO-ACID FORMATION FROM GLUCOSE UNIFORMLY LABELLED WITH CARBON 14 WITH AND WITHOUT 0.1 M POTASSIUM CHLORIDE. Experimental conditions as in Table 1.

| Amino-acid formed | 5 mM K ⁺ + glucose-U- ¹⁴ C 0.5 mM amytal | 105 mM K ⁺ + glucose-U- ¹⁴ C 0.5 mM amytal |
|-----------------------------|---|---|
| Glutamic acid | 5703 \pm 335 | 6761 \pm 450 |
| Aspartic acid | 1002 \pm 55 | 601 \pm 51 |
| Glutamine | 1095 \pm 80 | 111 \pm 10 |
| Alanine | 1104 \pm 70 | 856 \pm 36 |
| γ -Aminobutyric acid | 1793 \pm 45 | 1470 \pm 123 |

(a) In normal physiological media (5 mM potassium ions) the presence of 0.5 mM amytal produces a marked increase in the rates of formation of labelled γ -aminobutyric acid and alanine, with relatively small changes in the rates of appearance of labelled glutamate, aspartate and glutamine.

(b) In the presence of 105 mM potassium ions and 0.5 mM amytal there is a very large fall in the rate of formation of labelled glutamine from 2,397 counts/min. (Table 1) to 111 counts/min. (Table 4). There is a fall also in the rate of formation of labelled alanine and aspartic acid and also in that of glutamic acid.

The results may be explained in the following manner.

(1) With the unstimulated slice of brain cortex the amytal brings about a diminution of available diphosphopyridine nucleotide, so that less pyruvate is oxidized to acetyl-coenzyme A and less α ketoglutarate is converted to succinate. There is not only, therefore, an increased rate of conversion of pyruvate to lactate but also an increased rate of conversion, by transamination, of labelled pyruvate to alanine and of labelled α ketoglutarate to glutamate. The latter reaction is reflected in an increased rate of formation of labelled γ -aminobutyrate. The rate of formation of glutamine is not increased; it is in fact decreased, presumably because the suppression of oxidation of reduced diphosphopyridine nucleotide leading to a diminished synthesis of adenosine tri-

phosphate, results in a diminished amount of the latter being available for synthesis of glutamine

(2) With the stimulated slices of brain cortex, in which the oxidation of pyruvate by diphosphopyridine nucleotide to acetyl-coenzyme A is greatly enhanced, the effect of the presence of the narcotic is to suppress this oxidation owing to the lowered availability of diphosphopyridine nucleotide. The increase of reduced diphosphopyridine nucleotide leads to an increased rate of formation of lactate (that is, increased aerobic glycolysis), this process taking place partly at the expense of pyruvate that would otherwise be transformed to alanine. A similar suppression of oxidation of α -ketoglutarate leads to enhanced labelling of glutamate. The synthesis, however, of glutamine from glutamate is almost entirely blocked by the narcotic, by its suppression of synthesis of adenosine triphosphate normally coupled with the oxidation of reduced diphosphopyridine nucleotide.

It is evident that the processes controlling glucose - amino-acid inter-relations in both the unstimulated and stimulated slice of brain cortex and in the absence or presence of a narcotic such as amytal may be interpreted satisfactorily on the basis of the conclusions that the stimulation consists of an acceleration of the conversion of pyruvate to acetyl-coenzyme A and that the narcotic brings about a suppression of endogenous oxidation of diphosphopyridine nucleotide by cytochrome oxidase and its associated phosphorylations.

Summary

(1) Glucose and fructose, both uniformly labelled with carbon-14, in the presence of slices of rat brain cortex, are partly converted to radioactive glutamic acid, glutamine, γ -aminobutyric acid, aspartic acid and alanine. The yields, and relative proportions, of these amino-acids found with the uniformly labelled glucose differ considerably from those found with uniformly labelled fructose. An outstanding difference is the large yield of labelled aspartic acid found with fructose as compared with that from glucose.

(2) When brain cortex respiration in the presence of glucose or fructose is stimulated by the addition of 105 mM potassium ions, large changes take place in the yields and relative proportions of radioactive amino-acids. With glucose, the effect is greatly to increase the yield of glutamine and γ -aminobutyric acid. With fructose, the effect is greatly to diminish the yield of labelled glutamate.

(3) It is concluded, from the effects of the addition of 105 mM potassium ions on the formation of carbon-14 dioxide from pyruvate-1-¹⁴C and pyruvate-2-¹⁴C, and on the relative inhibitory effects of malonate on these processes, that the stimulating effect of addition of potassium ions on the respiration of brain cortex is largely directed to an acceleration of a pace-making step, the conversion of pyruvate to acetyl-coenzyme A.

(4) The presence of malonate, which abolishes the potassium ion stimulation of respiration of brain cortex, brings about a greatly diminished labelling of all amino-acids derived from glucose, uniformly labelled with carbon-14, and in the presence of added potassium ions almost completely blocks the formation of alanine, glutamine, and γ -aminobutyric acid.

These results can be satisfactorily explained on the basis of the conclusions that the amino acids are derived from glucose by transamination of the α -ketonic acids derived during the operation of the citric acid cycle and that the potassium ion stimula-

tion of the metabolism of brain cortex is due to its acceleration of the oxidation of pyruvate to acetyl-coenzyme A.

(5) The presence of the narcotic, 0.5 mM sodium amytal, produces, with the unstimulated brain cortex slice, a marked increase in the yield from glucose uniformly labelled with carbon-14, of labelled γ -aminobutyric acid and alanine, with relatively small changes in the yields of labelled glutamate, aspartate and glutamine. With the stimulated brain cortex slice (that is, with 105 mM potassium ions) the narcotic at small concentrations brings about a very large fall in the yield of labelled glutamine, falls in the yields of labelled alanine and aspartic acid and a rise in the yield of labelled glutamic acid. These results may be adequately explained on the basis of the conclusions given above, together with the conclusion that the main effect of the narcotic is to suppress the oxidation of reduced diphosphopyridine nucleotide by cytochrome oxidase and its associated phosphorylations.

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LETTERS TO THE EDITORS

OCEANOGRAPHY

Application of Ultra-Violet Lights to Underwater Research

We believe this to be the first report of the use of ultra violet lights by divers in underwater research. In addition to opening up a new technique of exploration, it is believed that our preliminary findings may be of considerable interest to marine biologists, geologists and archaeologists.

This work was conducted at depths of 3-5 fathoms in the waters of Northwest Harbor, Deer Isle, Maine, during August 1958, using hand carried ultra violet lights of our own development. Self-contained breathing apparatus ('Sonba') was used throughout and all dives were conducted at night.

Two ultra violet lights were used. Each light was completely self contained and consisted essentially of a G.E. tubular ultra violet lamp 6 watts (T-5, BLB self filtering) as an ultra violet light source (about 3500-4000 Å) which was energized by a 6 V battery-driven circuit consisting of an interrupter making and breaking the current to the low voltage side of a transformer (Stancor, A-3879). Sufficiently high voltage was obtained from the transformer secondary to cause a discharge through the ultra violet light tube. Acknowledgment is made to Transspace Laboratory for the use of their laboratory and workshop in the development of these lights.

Five preliminary findings merit presentation. (1) The general prevalence of fluorescence (often extremely beautiful) under ultra violet irradiation of much of the material matter and objects occurring growing and making up the ocean bottom, in the waters explored. (2) The difference in the observed fluorescence of many objects removed from the water and the same objects *in situ*—for example 'coralline algae' which out of water generally fluoresce rose or pink in their natural habitat appear to fluoresce white. (3) The apparent absence of any significant fluorescence of the suspended matter in the naturally turbid Maine waters, and the absence of any dazzling Tyndall beam phenomenon. This made it possible to see objects (which fluoresced) approximately eight times beyond the range at which such objects could be seen through these waters using natural light or during the daylight hours. Normal visibility is about 6 ft in these waters. At night using ultra violet light, fluorescent objects approximately 50 ft away could be detected. This latter suggests because of the natural fluorescence of the human skin (of light skinned persons) and the fluorescence of white clothing particularly clothing washed in modern detergents which contain optical whiteners, that searches in turbid and sediment-filled waters for bodies of the drowned might best be conducted in the dark, at night using ultra violet light. (4) The fluorescence of the bottom, in mud areas under which long submerged pieces of ships' timbers were known to be buried, appeared to be significantly different from areas which were free of timber. This suggests the use of ultra violet light as an aid in locating the

presence of artefacts buried in mud. (5) The fluorescence of naturally fluorescent petroleum intermixed with seabottom mud which suggests the possible value of ultra violet light in submarine prospecting for petroleum and fluorescent minerals.

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June 11

The North Kenya Banks

A BANK off the northern Kenyan coast is acquiring significance. Its presence is unique along the coastline of tropical East Africa and it is of considerable interest as an abstract marine problem of this region and as a likely boost to local fishery resources.

Africa has least shelf area, relative to its size of all the continents and off tropical East Africa the shelf is particularly narrow. The 100 fathom contour off Tanganyika and Kenya usually lies only 2-5 miles offshore the only notable exception being the bank mentioned that is sketchily indicated in Admiralty Charts off Lamu, North Kenya. It is tiny compared to world fishery banks following about 40 miles of coastline and extending offshore to a maximum of about 30 miles. The chart suggests a simple bank but we have found there to be several banks with a very distinctive, steep valley separating the south western half of the bank complex from the shore at the normal position of the edge of the continental shelf. The offshore area has complicated topography 'irregular in configuration with hills and pits often side by side'. For example a lull rising to 58 fathoms lies less than 1 nautical mile from a pit dropping to 92 fathoms. At the blind end of the valley mentioned where the bank system runs into the shallows of Lamu Bay there is a sizeable area of apparently very smooth bottom at 42 fathoms and other regions of smooth bottom are to be found at greater depths although interspersed with undulant or rough areas.

Certain conjectures regarding the history of these banks are worth mention until geological examination (for which we are not equipped) reveals their structure. They are likely to consist of deltaic alluvium for the Lamu area is plainly the ancient delta of a river that was many times greater than the nearby present-day Tano River. The Tano now opens into the sea southerly of Lamu and its water is carried northwards by the coastal current throughout the year but meets, off Lamu, a southward flowing current for part of the year. It is reasonable to infer that precipitation of river sediment occurs off Lamu and this would perpetuate the ancient banks. In addition the folds and planities of the bottom as revealed by our explorations, strongly suggest to me an underpinning

by rock (although this is remarkable in view of the flat adjacent countryside) It is interesting that soundings from old and modern sources suggest shifts of alluvium from one place to another, yet no dispersion of the bank as a whole despite the currents that sweep it

Accounting for the presence of the banks is, perhaps, of abstract importance to their potential fishery value and so is explanation of the actual and unique association of fishes to be found. A rock-cod (*Serranidae*) can be caught in fair numbers but it has never been found by us south of the North Kenya banks. It is almost certainly the same species as one trawled off the south of India. Yet, below the water that comprises the surface coastal current other fishes can be plentifully caught that are common off south-eastern South Africa. Newell's² exposition of the current system of these waters is of great interest regarding the geographical distribution of the species.

By world standards the fishery production off British East Africa is infinitesimal³ due to primitive fishing methods, to the infertile sea water and to scarcity of shelf area. It is a pity that Worthington⁴ omitted emphasis of this last and vital factor in his memorable review of modern African biological resources, for it is a severe handicap to development. Demand for fish is great as shown by the annual importation of fresh fish from Europe and South Africa and of salt fish from Arabia and Somalia. Any increase in productivity would be tremendously important, and fortunately the North Kenya banks have been proved very promising^{5,6}. A few trawling trials have been made off this coast but most came to grief due to insufficient knowledge of suitable areas of clean bottom. Our departmental explorations in *M.V. Manihine* have now charted areas of the North Kenya banks where trawls may be cast with favourable chances and where, moreover, fishes have been caught on handlines. Even a small trawling ground would raise the annual harvest appreciably, for traditional fishing by handlining and trapping is time-consuming. Whether or not trawling proves feasible the rough areas on these banks yield commercially valuable fishes to handlining and may support longlining on the mother-ship and dory system, a development that the hardy local fishermen appear to be suited to.

The assay of commercial possibilities of handlining and trapping in certain rich areas is being done by the Provincial Fisheries Officer (Coast) of the Kenya Fisheries Division. Our Organization is tackling the wider exploration of the banks, principally charting, hydrography and fishing by various methods (but chiefly by handlines and reels loaded with wire) here, there and everywhere to see whether other rich areas are present and to obtain a fuller picture of the fishing potential. (A report is being prepared.) Clearly there are fishing grounds and I am attempting to determine the grounds in relation to benthos by dredging, but there is unfortunately little time available for this and for the lengthy process of identifying specimens and evaluating the benthic ecology. Extensive echometer work is being done to map smooth and rough areas. A bathythermograph is often cast into the deeper places for there is a segregation of fishes into those that frequent the surface current and those in the different body of water beneath. Knowledge of the depth of the thermocline between the two water layers helps to determine what species to fish for, and where to position the boat.

My hope is that other workers would like data or specimens for I would happily co-operate so that our

work on the North Kenya banks may achieve a scope beyond our present resources of time and man-power. With only one of our staff available for this investigation we restrict ourselves to aspects of direct fishery value.

J F C MORGANS

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June 1

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PHYSICAL SCIENCES

An Absolute Scale of Time

PHYSICAL time is customarily measured by counting the number of times a suitably chosen cyclic process (for example an oscillating pendulum) is repeated, and equal intervals are defined as those during which the process is repeated the same number of times. It would, in principle, be possible to choose, instead of a cyclic process, a purely random one and define equal intervals of time as those during which random events are equally likely. Most random processes vary too much with environment (for example, molecular bombardment of a surface varies with temperature) to be selected as standards for measuring time but radioactive decay is believed to be virtually independent of environment. Thus, if radioactive decay is truly random, the number ΔN of nuclei disintegrating in a time-interval $t, t + \Delta t$, out of N like nuclei existing at time t is given by

$$\Delta N = -\lambda N \Delta t \quad (1)$$

where λ is a constant characteristic of the particular nuclei chosen.

Let a clock be constructed to count one every time an arbitrary fixed number of nuclei disintegrate from an assembly of N_0 like nuclei at $t = 0$, which has become N at time t so that

$$N = N_0 e^{-\lambda t} \quad (2)$$

The number disintegrating in the interval $t = 0, t = 1$ is $N_0(1 - e^{-\lambda})$. Let this be chosen as the arbitrary fixed number.

The number that have disintegrated by time t is $N_0(1 - e^{-\lambda t})$ so the time-interval X indicated by the clock (that is its count) will be $N_0(1 - e^{-\lambda t})/N_0(1 - e^{-\lambda})$ and

$$1 - e^{-\lambda t} = X(1 - e^{-\lambda}) \quad (3)$$

As judged by customary time-scales equal intervals by such a clock would appear to be getting longer and longer and the clock would be deemed unsuitable. Let there be a second clock of the same kind but using different nuclei the decay constant of which is μ , then for it we have

$$1 - e^{-\mu t} = Y(1 - e^{-\mu}) \quad (4)$$

where Y is the time indicated by the second clock which is just as unsuitable as the first one.

An additional observable quantity is dY/dX , the rate of one clock as judged by the other and we have

$$\frac{\mu e^{-\mu}}{1 - e^{-\mu}} = \frac{dY}{dX} \frac{\lambda e^{-\lambda}}{1 - e^{-\lambda}} \quad (5)$$

In equations (3), (4), and (5) X , Y and dY/dX are known so that λ , μ and t are calculable and t does not depend at all on the nuclei chosen, so from the two clocks a true or 'absolute' scale of time is derived and also the decay constants of the two sorts of nuclei chosen.

It is not suggested that a useful practical system of this sort could be constructed, the accuracy in practice obtainable in counting disintegrations is far too low by any presently known methods. Even if counting were perfect the fluctuations occurring in these random processes would make the attainment of anything like the precision of a good ordinary clock only attainable if the number of disintegrations counted per second of ordinary time was very large indeed, and there would among other difficulties be either that of ensuring that each clock was pure in the sense of the disintegrations counted all being of like atoms or of a much more complex analysis.

The interesting point remains that from two such clocks a scale of time could, in principle, be derived that is independent of their nature and could be of any desired precision if only the clocks contain enough atoms. The accuracy with which the derived scale matched conventional time might be a test of the truth of the assumption that the decay processes are random.

Perhaps, without stretching the significance of this curious result too far one may suggest it implies that providing the universe is not composed solely of identical particles but contains at least two sorts capable of random disintegration at different rates there is a natural rate of change inherent in the structure of the universe itself independently of any man-made timepieces.

Another point of interest is that, with any set of finite clocks of this kind, the uncertainty in measurement of a time interval increases without limit as the interval tends to infinity.

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Signals from Satellite 1958 52 (Sputnik III)

In a recent communication Munro¹ reported Australian observations of the radio signals from Satellite 1958 52 which led to the conclusion that the pulse modulation was absent when the Satellite was not illuminated by the Sun. This lapse of modulation was first noted early in March.

There has been little opportunity for observers in Great Britain to detect such a lapse because on all near transits since late February the Satellite height has been sufficient for it to be illuminated over practically the whole of its observable track. There was, however, a short period from April 14 to 28 when the early part of the track was in darkness and observations made at the Radio Research Station Slough, during this period showed that the signals were not received as early as expected and did, in fact, not

commence until the predicted time at which the Satellite emerged from eclipse.

Up to the end of February and afterwards, except during the above period in April, signals have been received over the whole of the observable track. The condition of complete illumination on all near tracks continued until mid August.

The Radio Research Substation at Singapore has also reported the absence of signals at night. This lapse was first noted on March 27, and during June when the conditions were appropriate it was observed that the signals ceased abruptly within a minute of the predicted time of the Satellite passing into eclipse.

Although our results confirm Munro's observation of the lapse of modulation the c.w. signal during these lapse periods, which he also observed has not been detected so far either at Slough or Singapore. This may be due to lack of sensitivity in the receiver at Singapore and to the absence of suitable observing conditions at Slough.

This work was carried out as part of the programme of the Radio Research Board, and this communication is published by permission of the Director of Radio Research of the Department of Scientific and Industrial Research.

B. G. PRESSER

Department of Scientific and Industrial Research,
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¹ *Munro G. N. Nature* 183 1549 (1959)

Upper Atmosphere Density Variations Due to Hydromagnetic Heating

This communication describes a mechanism which explains: (1) the irregular orbital accelerations of satellites^{1,2}, and (2) the sudden disappearance of trapped radiation from the *Argus* nuclear explosion coincident with a geomagnetic storm³. These two observations may be explained by the calculated rates of ionospheric heating by hydromagnetic waves⁴. The hydromagnetic waves are generated at a distance of six to ten Earth radii from the centre of the Earth by the instabilities as the solar wind interacts with the geomagnetic field, and by variations in solar wind pressure^{5,6}.

The major features of the satellite orbital decay to be explained are the correlation between the orbital acceleration and the 10 and 20-cm solar radio noise intensity and the increased orbital acceleration during magnetic storms. Since the orbital decay increases during a magnetic storm and not at the time of a solar flare Jacquin⁷ has concluded that it is probably corpuscular radiation from the Sun, that is the solar wind which affects the atmospheric drag. The corpuscular radiation itself cannot penetrate the geomagnetic field closer than about 5 Earth radii from the Earth's centre (except during severe magnetic storms). However, as stated above, the solar wind can generate hydromagnetic waves which will be dissipated as heat in the altitude range 150–200 km (the F₁ region of the ionosphere). The amplitude and frequency of the fluttering at the edge of the geomagnetic field varies with the strength of the solar wind⁸. Therefore the high temperature of the F₁ region, which is at least in part due to hydromagnetic heating⁴ will vary with the strength of the solar

wind Since the density above the *F*-region depends on the temperature of the *F*-region, the hydromagnetic heating provides the mechanism whereby the solar wind can affect satellite drag

The correlation between the 10- and 20-cm solar radio noise intensity and the orbital acceleration is independent of whether perigee is over the dark or sunlit hemisphere Since the hydromagnetic wave velocity varies with height in such a way as to refract the waves completely around the Earth⁸, the hydromagnetic heating gives a natural explanation of why the correlation between the 10- and 20-cm solar radio noise intensity (which is apparently an index of solar wind intensity) and the orbital acceleration is not affected when perigee moves from sunlight into darkness

The ionosphere will also be heated by the hydromagnetic waves which are generated during magnetic storms The magnetic storm fluctuations have periods of the order of minutes which are much longer than the steady state flutter periods of about 1 sec The hydromagnetic heating rate is dependent on frequency in such a way as to make the low frequency disturbance fluctuations much less effective for ionospheric heating than the 1 cps steady-state flutter frequency unless the amplitude of the low frequency fluctuations rises above some critical value Since the magnetic *K* index is a measure of the amplitude of the low frequency fluctuations and is not sensitive to the 1 cps flutter frequency amplitude, no correlation between orbital acceleration and *K* index should be expected unless the *K* index should rise to a rather high value (as it would during a magnetic storm) Thus, ionospheric heating by the large amplitude low frequency hydromagnetic waves generated during a magnetic storm can account for the increased orbital acceleration observed during magnetic storms⁷

The same general arguments may be applied to the sudden disappearance of electrons from the *Argus* nuclear explosion These electrons had been trapped in the geomagnetic field It has been shown⁴ that atmospheric heating will not distend the geomagnetic field even though the upper atmosphere expands (briefly, because (1) the slight increase in ion pressure is much less than the magnetic field pressure stress, and (2) even if the magnetic field were pushed out, it would very quickly diffuse back to its equilibrium position) Therefore, the shell of *Argus* radiation is fixed with respect to the earth and any ionospheric heating will increase the atmospheric density at the altitude of the *Argus* radiation This increase in atmospheric density will, of course, increase the rate of loss of the trapped particles The radiation intensity of the trapped *Argus* electrons was observed³ to decay inversely with time until a magnetic storm occurred Then, the rate of decay of radiation intensity increased markedly and the radiation disappeared in a few hours It has been pointed out that magnetic scattering of the electrons due to breakdown of the conservation of the magnetic moment is unlikely since the cyclotron frequency for electrons is too high and the cyclotron radius is too small for hydromagnetic waves to have any effect on the invariants of motion⁹ That is, the electron cyclotron frequency is much greater than the hydromagnetic wave frequency and the electron cyclotron radius is much less than the hydromagnetic wavelength so that the adiabatic conditions are maintained However, an increase in atmospheric density at high altitudes due to ionospheric heating would shorten

the trapping lifetime of the *Argus* electrons due to scattering by atmospheric gas Thus, the loss of the *Argus* radiation and the increased orbital acceleration during a magnetic storm may be taken to be two independent observations of the same phenomenon ionospheric heating by hydromagnetic waves

Another phenomenon which may be explained by hydromagnetic heating is the increased X-radiation intensity observed at balloon altitudes during a magnetic storm¹⁰ (These observations were made at latitudes far below the auroral zone and were not associated with visible auroras) The ionospheric heating increases the atmospheric density in the lower part of the Van Allen radiation belt and thereby increases the scattering loss of trapped particles The electrons which are scattered out of the Van Allen belt will emit bremsstrahlung upon being stopped in the atmosphere, and thus account for the increased radiation intensity measured at balloon altitudes during the magnetic storm This explanation requires that the intensity of the lower part of the Van Allen radiation belt decrease during a magnetic storm

The conclusion reached is that ionospheric heating by hydromagnetic waves (generated by interactions between the solar wind and the geomagnetic field) can explain (1) the observed variations in the orbital acceleration of satellites, (2) the sudden loss of the trapped *Argus* radiation coincident with a magnetic storm, and (3) the X-ray flux observed at balloon altitudes far below the auroral zone during magnetic storms This flux is presumably associated with changes in particle radiation intensity at the lower edge of the Van Allen radiation belt The hydromagnetic heating of the ionosphere produces the above effects by increasing the scale height of the atmosphere and thereby increasing the atmospheric density at high altitudes

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June 11

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Auroral Frequency Lines

In his recent letter, Dr B. Hultqvist¹ compares lines of equal auroral frequency drawn by E. H. Vestine and by C. W. Gartlein with auroral frequency lines deduced theoretically. He finds that his lines agree better with Gartlein's International Geophysical Year data in that both sets bulge much farther south of the geomagnetic latitude circles over north-east America than do Vestine's lines which were based on a combination of the original Fritz data with those collected in the years 1872-1942

This is interesting, but it is not surprising that the Vestine and Gartlein frequency-lines diverge and it can scarcely be taken as confirmation of the theory

behind Hultqvist's lines. As nearly as can be judged from his Fig. 1, he compares the position of Gartlein's once a year ($1/yr$) frequency with Vestine's $5/yr$ line which lies southward of it, and Gartlein's $70/yr$ line with Vestine's for $50/yr$ lying for the most part well north of it. Thus by itself would not be critical because the frequency lines of any one family should have the same general shape. But as the belt of greatest auroral frequency and associated geomagnetic disturbance expands southwards at times of greatest activity it is important that similar methods should be used for reducing different sets of data to a common basis of activity. It is also necessary that similar adjustments are made for incidence of cloud and daylight. In his redrawing of the Fritz lines, Vestine introduced corrections to his later observations based on the data from the British First and Second Polar Year Station at Fort Rae in the zone of maximum frequency in north west Canada. He also corrected for length of daylight. But there is no evidence that any similar procedure was used for Gartlein's International Geophysical Year data.

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Hultqvist *B. Nature* 183 1478 (1949)

DIFFICULTIES are certainly associated with the preparation of observational auroral frequency lines. In general some of the most important ones are supposed to be those due to too low density of the observational net, individual variations among the observers with regard to observational scheme and definitions, variations of the sensitivity of observational method, etc. Correction for variation of the solar activity over the observational periods for the different observers must be introduced. In addition to these adjustments for cloud and daylight must be made as mentioned by Dr Stagg.

The difficulties seem, however, to be least if only the frequency lines over a limited part of the Earth are to be determined, if the observational material is restricted to a fairly small period in time and especially if the net of observations is dense and all the observers are using the same nomenclature definitions and observational scheme.

This latter advantageous case is that of Gartlein who has had at his disposal the closest and best prepared net of well co-ordinated observers, which so far as I am aware has ever worked over American territory. In contrast Vestine has used a less homogeneous and less defined observational material obtained at fewer points in the United States as basis for his curves.

As Dr Stagg himself mentioned, the family of frequency curves may safely be supposed to have the same general shape over a wide range of absolute frequency values.

For the reasons mentioned it seems reasonable to suppose that the shape of Gartlein's curves are at least as reliable as that of Vestine's over American territory and to draw the conclusion of my earlier communication.

BENGT HULTQVIST

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Polarization and Resolving Time Effects in Photon Correlation

SEVERAL papers¹⁻³ have been published recently reporting an enhancement of the coincidence rate due to photons detected by photomultiplier tubes viewing coherent light beams. Here we wish to report on the effect of varying several of the factors which influence the magnitude of the enhancement, in particular the degree of polarization of the beam and the resolving time of the coincidence apparatus. The variation of the enhancement with spectral line width (0.006 \AA and 0.009 \AA) has been reported previously² to be in agreement with the theoretical predictions.

To obtain simultaneous recording of two resolving times ($2\tau = 8 \times 10^{-9} \text{ sec}$ and $4 \times 10^{-9} \text{ sec}$) as well as to simplify the running of the experiment the cable switching was made automatic and new coincidence circuits were designed similar to those described by Moody⁴. This change from our previous experimental arrangement, which used a Bell-Graham and Petch coincidence circuit⁵ with manual switching in addition gave improved accuracy. Long ($20 \times 10^{-9} \text{ sec}$) and zero relative delay cables were automatically switched over 30 seconds. The light source was an electrodeless mercury 198 discharge tube in a coaxial chamber⁶ excited by 2450 Mc/sec radio frequency power. This lamp was water-cooled, the water temperature being regulated at 45°C and run near the maximum intensity. The 5461 \AA line of mercury was isolated by means of Schott filters. Several types of experiment were performed, alternating the mercury 198 lamp with a high pressure mercury lamp alternating the cases of photomultipliers 'superimposed and displaced sufficiently for the coherence to drop to zero and alternating the cases with a polarizing filter in the beam and without this filter.

The results of the experiments may be expressed in terms of the enhancement of the counting rate for zero delay over that for long delay after the attenuation corrections have been applied. These corrections were obtained by measuring the counting rates with one photomultiplier displaced so that the coherence factor was zero. As a check on the performance of the equipment a high pressure mercury arc producing a broad emission line (about 1.5 \AA wide) was used as the light source several times during the course of the experiment. With the mercury 198 lamp (unpolarized light) the observed enhancement was 0.0087 ± 0.0008 for $8 \times 10^{-9} \text{ sec}$ resolving time. For plane polarized light the predicted enhancement^{1,2} is twice the value for unpolarized light. To compare with this prediction a Polaroid filter was placed between the lamp and the pinhole. Under these conditions (polarized light) an enhancement of 0.0230 ± 0.0042 was obtained 2.75 ± 0.73 as large as that without the Polaroid. For a resolving time of $4 \times 10^{-9} \text{ sec}$ with polarized light an enhancement of 0.0300 ± 0.0047 was obtained, 3.45 ± 0.86 as large as the value for unpolarized light with a resolving time of $8 \times 10^{-9} \text{ sec}$ compared with an expected factor of four.

The experimental variation of enhancement with resolving time, polarization of the beam and spectral line width have been found to be in agreement with theory¹⁻³ within the experimental error. Further experiments are being carried out in order to obtain increased accuracy and to obtain results under different conditions.

We are indebted to the National Research Council of Canada for the financial support of this research programme

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May 26

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Experiments on the Acousto-Electric Effect

PARMENTER¹, and later Gurevich², predicted that a single longitudinal acoustic wave passing along a metal or semiconductor should produce a steady potential difference in the material. Weinreich and White³ and Sasaki and Yoshida⁴ observed the effect in germanium.

We have attempted to observe the acousto electric effect in copper and aluminium. In our most conclusive experiment, vibrations of high energy, at 25 kc/s, produced by an ultrasonic drill were passed along a copper wire, and were absorbed at the other end by a mass of 'Plasticine' to prevent reflection. The particle amplitude of the specimen was observed under the microscope. The vibrations were continuous over the whole length of the wire from the transducer to the absorber, showing that no standing waves were formed.

The acoustic energy in the wire was calculated to be about 9 watts, and its diameter was 0.07 cm, giving an intensity of 2000 watts/cm². According to Parmenter's theory this should produce an acousto-electric e.m.f. of 400 μ V/cm. (For a good conductor, Gurevich calculated an even higher e.m.f. of 0.3 μ V/cm for each 0.1 watt/cm² acoustic intensity.) In actual fact, we observed at most only 1.4 μ V on a specimen of 25 cm length, and also on another of 150 cm length. (The smallest detectable signal was about 0.3 μ V.) As this potential difference required an appreciable time to appear and to disappear, it was probably due to heating effects. Thus the observed effect would be at most only a very small fraction (about 1/7000) of that predicted by the theory.

In an earlier experiment high-energy pulse trains, of 300 kc/s, were produced in a nickel magnetostriction tube and passed along an aluminium specimen. No effect was observed.

The tests were carried out at room temperature.

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May 29

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Intensity of the (111) Reflexion for Diamond

RECENTLY¹ the intensity of the (111) reflection of diamond was measured. A value was found which deviated from that given formerly² but which agreed with the value based on McWeeny's³ calculations of the atomic scattering factor for carbon.

F-values given in the recent publication¹ were calculated from the experimental data using the absorption coefficient for CuK α -radiation $\mu/\rho = 4.52$ as given in Compton and Allison, p. 802, Table 1 (1942) and also in D'Ans-Lax, "Taschenbuch für Chemiker und Physiker", p. 83 (1949). But, since also the higher value of 5.50 is cited (for example, "Internationale Tabellen zur Bestimmung von Kristallstrukturen", 1935), and because the absorption coefficient also was found to vary from crystal to crystal,² a determination of μ/ρ was carried out on the sample used for the above-mentioned measurements. It was found that $\mu/\rho = 5.56 \pm 0.14$.

With this absorption coefficient the mean value of f_{111} determined by the reflection-method becomes 2.39, and the weighted mean of all experimental values, that is, including the data obtained by the transmission method (which are independent of μ), is 2.35 in agreement with the former determination². It must be concluded, therefore, that while for higher $\sin \theta/\lambda$ values the agreement of measurements and McWeeny's calculations is generally good, an appreciable discrepancy is present at $\sin \theta/\lambda = 0.141$, that is, for f_{111} at diamond.*

It can be shown that this is due to the fact that the accumulation of binding electrons between two carbon atoms in diamond which gives rise to the appearance of 222, also strengthens the intensity of 111. It does not influence 220, however, and the experimental value of f_{220} agrees, indeed, accurately with McWeeny's calculation. On the other hand, f_{311} is expected to be weaker and this is also in agreement with the experimental observation². At higher orders these effects fade out. The details and an extended discussion will be given elsewhere.

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Fibre Surface Replication by Rolling

A TECHNIQUE for replicating fibres by rolling has been developed in these laboratories. It is only applicable to fibres which approximate to a cylindrical shape, such as nylon, 'Terylene' and wool, but with these it can give replicas with sufficient resolution for the full magnification available in light microscopy. It is not known yet to what extent the replicas are suitable, either directly or in second stage form for electron microscopy.

A glass microscope slide is dipped in 'Necol' cement (diluted with acetone to more than three times its volume) and allowed to dry, protected from dust. When it is sufficiently dry to be non-tacky, three lengths of fibre, each about 3 mm long, are placed on

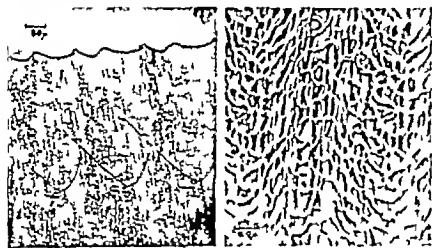
the 'Necol' film in a triangular array, the fibres parallel to the short side of the slide. Another glass slide is laid on top, then, while slowly pulling the top slide along so as to roll the fibres, a weight between 200 and 500 gm is carefully applied above the fibres to press them on to the 'Necol' film.

'Necol' cement which is principally based on nitro cellulose has been used so far as the replica medium. Other possible media are also being tried. We produce the steady motion of the top slide (10 microns/sec) by coupling it to a considerably geared down 'Drayton' motor.

The photographs illustrate the use of the technique on nylon and wool. Fig 1 shows a replica of a scratched length of an undrawn nylon filament clearly demonstrating the repeated replication of the fibre surface. This technique provides a means of checking on one replica by the occurrence of identical detail at intervals across the replica that the features reproduced are produced by the replication and are therefore presumably true fibre surface detail.

The distribution of surface detail over the whole fibre circumference is also immediately available on one replica and a better understanding of the significance of any particular feature is obtained.

Fig 2 is at a higher magnification, showing one

Fig 2 ($\times 200$)Fig 1 ($\times 50$)

complete revolution of a wool fibre. Both photographs are taken in phase contrast. Fig 1 with a numerical aperture of 0.28 and Fig 2, 0.65.

I am indebted to Miss J. I. Tidmarsh for the photographs, Mr J. F. Williams for valuable collaboration in developing the technique and to British Nylon Spinners Limited for permission to publish this communication.

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CHEMISTRY

Rotational Friction Coefficients of Models of Tobacco Mosaic Virus and the Size of the Virus Particle

Much valuable information about the shape of macromolecules in solution can be derived from hydrodynamic studies. Two recent measurements of the rotational friction coefficient of tobacco mosaic virus, by the electro-optical effect¹ and by flow

birefringence², have, however, led to values of the length that were more than 10 per cent greater than the length observed in the electron microscope³. This serious discrepancy which is well outside the presumed experimental errors, could be explained by changes in the dimensions of the virus particle on drying, or by failure of the available hydrodynamic formulae adequately to describe the actual behaviour of the rod shaped particle.

It has been generally believed that the hydrodynamic behaviour of this highly asymmetric cylindrical particle (axial ratio 20:1) is practically the same as that of a prolate ellipsoid of the same length and axial ratio, for which an exact formula is available. This belief has been strengthened by an approximate calculation of Burgers⁴, which gave a result for the cylinder that was almost the same as the ellipsoid. The rotational friction coefficient, C , is the torque needed to make an object rotate about a given axis at unit angular velocity in a viscous fluid that has stationary boundaries at infinity. For a prolate ellipsoid of semi axes a and b , Perrin obtained⁵ (for a/b large)

$$C = 8\pi\eta a^3/3 [-0.50 + \ln(2a/b)] \quad (1)$$

For a cylindrical rod Burgers⁴ obtained the same formula except that the negative constant in the denominator was 0.80 instead of 0.50. For an object with a/b equal to 20 the values of C calculated from the two formulae differ by only 11 per cent.

Since the Burgers's formula is admittedly approximate, it was decided to test the validity of the hydrodynamic equations directly by studying models of tobacco mosaic virus were carefully inclined from brass. An ellipsoid and a rod were made having an axial ratio of 20:1 and a length of 10.16 cm. Another rod of similar dimensions was made having hemispherical ends. Another cylinder had the same axial ratio but was half as long (5.08 cm). Experiments were also made with a polymethyl methacrylate sphere having a diameter of 5.38 cm.

Experimental determinations of torque were made by suspending the models in the centre of an oil bath from fine calibrated tungsten torsion wires. Silicone oil was used for most of the experiments but confirming experiments were also made in a mineral oil of comparable viscosity. The cylindrical oil bath was mounted on a turntable and rotated about its axis at speeds from 0.3 to 1.3 r.p.m. Torque was invariably found to be proportional to speed. Reynolds's numbers were estimated to be far below the turbulent range.

For the experimental values of C to be meaningful the walls of the vessel must not interfere. A rough estimate of the effect of the walls on the torque N can be obtained from an equation given by Lamb⁶ for a spherical container

$$N = N_\infty (1 + N_\infty/6\eta\omega I) \quad (2)$$

where N_∞ is the torque in a vessel of infinite radius, V is the volume of the container, and ω is the angular velocity. One can argue from dimensional considerations that a very similar equation should also be valid for cylindrical containers. For the vessel used the error is estimated in this way as less than 1 per cent compared to a reliability in the measurement of ± 2 per cent.

The experimental frictional coefficients are summarized in Table 1. The value for the sphere agrees with theory quite closely, which confirms the validity of the experimental procedure. The value for the ellipsoid is too large by an amount outside experi-

mental error. This is believed to be due to errors in the machining of the shape, since the volume of this model was measured and found to be about 4 per cent greater than expected. The rod with hemispherical ends has a frictional coefficient somewhat lower than the rod with square ends, demonstrating the importance of the geometry at or near the end of the rod. The data for the smaller rod are much less precise due to the reduction of sensitivity in the measurement, but they can be taken as a satisfactory confirmation of the a^3 relationship. The most noteworthy point, however, is the difference between the rod and the ellipsoid. The data given show very definitely that the rotational friction coefficients for rods having the axial ratio of tobacco mosaic virus are much higher than earlier calculations indicated. Apparently tobacco mosaic virus cannot be adequately represented by an ellipsoidal model, since the friction coefficient of the rod is 56 per cent greater than that of the equivalent ellipsoid. Burgers's approximation is also inadequate for the virus since it predicts only an 11 per cent difference.

Table 1 FRICTIONAL COEFFICIENTS (DYN/CM/SEC/RAD) IN SILICONE OIL AT 25°C $\eta = 54.4$ CP

| Shape | Experimental C | Calculated C | Ratio |
|--------------------------------|------------------|----------------|-------|
| Sphere | 284 | 266 1* | 0.932 |
| Ellipsoid | 193 | 187 6† | 1.06 |
| Large rod (square ends) | 292 | 208 5‡ | 1.40 |
| Large rod (hemispherical ends) | 273 | — | — |
| Small rod | 38.7 | 20 1‡ | 1.48 |

* Formula of Stokes

† Formula of Perrin (ref. 5)

‡ Formula of Burgers (ref. 4)

S. Broersma (private communication) has recently made improved calculations for the rotational diffusion constants for cylindrical particles. His results indicate a value for C within 10 per cent of our experimental value.

A revised length for the tobacco mosaic virus particle can now be calculated, assuming that C varies as ηa^3 at constant axial ratio. The relevant data are the value of 292 for C for the rod of length 10.16 cm in an oil of viscosity 54.4 cp, and the value of 1.24×10^{-16} previously found¹ for C for tobacco mosaic virus in water at 0.894 cp. The length of the virus particle comes out to be 3000 ± 50 Å, in excellent agreement with the value of 2980 ± 10 Å found for the dry particle under the electron microscope.² The flow birefringence measurements of Boedtker and Simmons³ now also agree. In these calculations we have tacitly assumed an axial ratio of 20, corresponding to a diameter of 150 Å, which is, in fact, the diameter of the virus as determined by X-ray scattering.⁷

It can be concluded that the dimensions of the tobacco mosaic virus particle in solution are not significantly different from those in the dry state. This precludes the notion that tobacco mosaic virus carries with it a large, rigid, ice-like hydration shell as has been suggested for some proteins and nucleic acids.⁸

We are indebted to Prof. Broersma for showing us his work in advance of publication.

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A Modified Rotating-Sector Method of Measuring Kinetic Chain Lifetimes

In order to evaluate the individual velocity coefficients for the propagation and termination reactions involved in polymerization and other chain processes, it is necessary to measure the lifetime of the kinetic chain. This is usually done by means of the rotating-sector method¹, or one of the non-stationary state methods²⁻⁶. The main disadvantage of the former method is that the complete determination of a kinetic chain lifetime cannot normally be made with a single filling of a dilatometer, unless the reaction is taken beyond the initial stage which may lead to gel effects and other complications. A number of dilatometers are therefore usually employed in a single determination of a lifetime, and errors often occur due to difficulty in reproducing the exact conditions, especially when the monomer involved is difficult to purify. The non-stationary state methods, on the other hand, yield a value for the lifetime in <30 sec, but unfortunately they often are inaccurate when lifetimes of <0.5 sec occur, since instrument lags or personal response times become particularly important for the very short lifetimes. The actual rate measurements, however, are quite accurate in this range of lifetimes, and can be measured in about 10 sec, that is, when 0.01 per cent reaction has occurred. By combining the two methods it is possible to cope with lifetimes of ± 0.5 sec, and to carry out a complete determination of a lifetime of the kinetic chain before 1 per cent reaction has occurred. The method is not valid for lifetimes ≥ 0.5 sec, since when flashtimes of several seconds are used the measurement of the rate by non-stationary state methods becomes inaccurate.

The procedure employed was to measure the reaction rates for a series of different sector speeds as in the normal rotating-sector method¹, but the rates were obtained from the expansion/time plots as in the dilatometric non-stationary state method⁶ instead of the usual contraction/time curves. By so doing, it was possible to obtain a rate determination in approximately 10 sec compared with about 20 min by the contraction method. This clearly reduces the

extent of conversion involved in a given number of rate measurements by a factor of more than 100

This combined method has been used in evaluating the ratio of the velocity coefficients of propagation to termination (k_p/k_t) at 25°C for the polymerizations of acrylonitrile in dimethyl formamide solution (30/70 v/v) initiated with 3.8×10^{-3} moles/l *azobisisobutyronitrile*, and of vinyl chloride initiated by 8×10^{-3} moles/l bromotrichloromethane. The values obtained were 3.4×10^{-4} and 7.1×10^{-7} respectively. Values of the ratio of the sectored to unsectored rate for a number of different flash times obtained in vinyl chloride polymerization are given together with the theoretical plot in Fig. 1. It will be seen that the experimental points lie mainly on the theoretical curve and that the agreement is better than is often obtained in the normal sector method

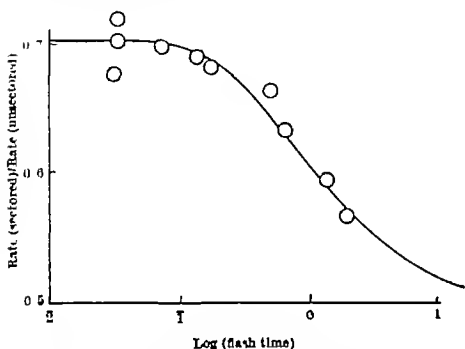


Fig. 1. Ratio of sectored to unsectored rates against log (flash time) for the polymerization of vinyl chloride at 25°C. \circ Experimental points — theoretical curve

We express our thanks to Prof P. D. Ritchie for his interest in the work, to the Department of Scientific and Industrial Research for maintenance awards to two of us (S. A. M. and R. A. M. T.) and to the Distillers Co. for a gift of vinyl chloride

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Thermal Decarboxylation of Some Keto-Acid Hydrazones

The 2,4-dinitrophenylhydrazones of keto acids are frequently used to identify these metabolic intermediates. The clear statement by Clift and Cook¹ regarding the ready thermal decarboxylation of the 2,4-dinitrophenylhydrazones of oxaloacetic and acetoacetic acids has sometimes been overlooked, particu-

larly in the use of melting points as a means of identification. Some of our observations bear on the problem.

Oxaloacetic acid 2,4-dinitrophenylhydrazone (I) synthesized by the usual procedure, when inserted into a bath at about 190°C or above, melted with vigorous bubbling and resolidified immediately, with a final melting point of 214°C. The substance after resolidification (II) was re-analysed by paper chromatography (*n*-butanol/ethanol/0.5 M ammonium hydroxide 7:1:2 in the dark) and was recrystallized. After paper chromatography the spot was eluted and examined spectrophotometrically. Authentic samples of *trans* (III) and *cis* (IIIa) pyruvic acid-dinitrophenylhydrazones were prepared by the method of Katsuki et al.² As shown in Table I, (I) was decarboxylated to

Table I. PROPERTIES OF 2,4-DINITROPHENYLHYDRAZONES

| Substance | R_F | Melting point (deg. C. corr.) | λ_{max} (nm) |
|-----------|-----------|-------------------------------|----------------------|
| I | 0.05-0.11 | 214 (final) | 450 |
| II | 0.55* | 217 | 446 |
| III | 0.55 | 217† | 446 |
| IIIa | 0.56 | ? | 416, 530 |
| IV | 0.57 | 123 (final) | 437, 524 |
| V | 0.55 | 123 | 430, 524 |
| VI | 0.55 | 123‡ | 430, 524 |

* With large sample a weak spot of *cis* pyruvic acid-dinitrophenylhydrazone was also found.

† Mixed melting point of II and III 217°C. of V and VI 123°C.

‡ Melting point not sharp because of thermal isomerization to *trans* form.

pyruvic acid dinitrophenylhydrazone (chiefly *trans*) under these conditions. When (I) was heated slowly from a lower temperature, for example 100°C, double melting was not observed and only the melting point of 214°C was obtained. Under these conditions too chromatography showed that most of the hydrazone was converted to (II) during the longer heating.

When acetoacetic acid 2,4-dinitrophenylhydrazone (IV) was placed in the bath at about 115°C or above it melted, bubbled and resolidified, the final melting point was 123°C. The resolidified material after recrystallization (V) also melted at 123°C. Thus, (V) is acetone 2,4-dinitrophenylhydrazone as shown by comparison with an authentic sample (VI). This conversion also took place when the heating was done slowly from a lower temperature but only a single melting at 123°C was observed.

The melting point of the 2,4-dinitrophenylhydrazones is not a reliable criterion for confirmation or identification of oxaloacetic or acetoacetic acids. Resolidification during melting point determination was observed by Snell³ with a ketosuccinic acid—dinitrophenylhydrazone but no explanation was suggested.

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Synthesis of Boron Phosphide and Nitride

A NOVEL technique has been found for the synthesis of boron nitride and phosphide involving thermal decomposition of halide addition compounds. Further work is intended on the reactions involved but the information thus far obtained is felt to warrant a brief, preliminary report for the benefit of other workers in this field.

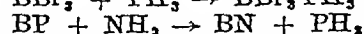
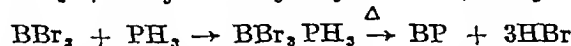
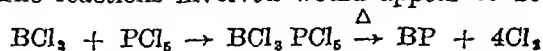
The addition compound BCl_2PCl_2 was prepared by refluxing phosphorus pentachloride in triethanolamine and passing boron trichloride into the reaction mass. The white product obtained was filtered off, washed with ether and dried *in vacuo* at room temperature. Samples were then sealed into Carius's tubes and heated under their own pressure development to about 300°C . Thermal dissociation occurred with the production of chlorine, some sublimation of the addition compound and deposition of a material on the tube walls. The colour of the deposit varied through the length of the tube and from experiment to experiment, from white through brown to black. On breaking the tube after cooling, chlorine gas escaped, residual addition compound was then decomposed and washed out with water and the film deposit also floated out on to water. The film was very resistant to hydrolysis and thermal decomposition, and could be heated in air to temperatures in excess of $1,000^\circ\text{C}$ without decomposition or apparent loss of integrity. X-ray and chemical analysis showed the material to be essentially cubic boron phosphide.

Further samples of the film were reheated at 800°C in a flowing atmosphere of 5 per cent ammonia in nitrogen when even the darkest film became white in colour and phosphine was evolved. X-ray analysis of the product showed it to be cubic boron nitride.

Addition compound was prepared from phosphine and boron tribromide or trichloride. When submitted to direct heating *in vacuo*, thermal dissociation immediately occurred, yielding again a film deposit of boron phosphide, but in better yield than before. Analysis of several specimens prepared under apparently similar conditions showed the product to vary between BP and B_2P_3 . A mixture of boron phosphide samples produced by the second reaction was submitted to reaction with dilute ammonia gas and again yielded boron nitride of cubic structure.

Thermal decomposition of BCl_2PCl_2 or BBr_2PCl_2 has not yet been examined, but it is felt that similar results would obtain in these systems.

The reactions involved would appear to be



Addition compounds of boron and phosphorus halides have been known for several years, but the process of their thermal decomposition does not appear to have been investigated before. It would seem possible that this mode of metalloid reaction might also be applicable to other similar systems.

Fuller experimental details shortly will be submitted for publication elsewhere.

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3,4, ω -Trihydroxyacetophenone 3-methyl Ether in Adrenal Extracts

IN the course of the isolation of aldosterone from adrenal gland extracts ('Eucortone', Allen and Hanbury), the English authors detected a compound with properties similar to aldosterone in certain paper and column partition systems. This compound had ultra-violet absorption peaks at about 230 m μ and 280 m μ and gave a positive reaction with the $\text{FeCl}_3\text{-K}_3\text{Fe}(\text{CN})_6$ reagent. It therefore seemed probable that it was phenolic¹. It also gave a blue fluorescence on irradiation with ultra-violet (compound X)² and reduced blue tetrazolium at about the same rate as steroids having an α -ketol side chain. The compound ran as though slightly more polar than aldosterone in the Bush B_5 paper system³ and could be completely separated from the steroid by column chromatography using the same solvent system².

Preliminary work⁴ on a very small scale led to the conclusion that aldosterone did not absorb maximally at 240 m μ . It now seems likely that this was due to the presence of the phenol as a contaminant. The combined peaks of the phenol and aldosterone at 230, 240 and 280 m μ tend to give a flat absorption curve obscuring the single peak of the steroid. On separation of the phenol from aldosterone on the column, the steroid had maximum absorption² at about 240 m μ .

A fairly pure sample of the phenol, which was not crystalline, was sent to the Swiss authors who later, during large-scale isolation work on aldosterone using freshly frozen adrenal glands as source of material, isolated the compound in crystalline form and determined its structure as 3,4, ω -trihydroxyacetophenone 3-methyl ether. This has been confirmed by synthesis. The later work will be reported in detail elsewhere.⁵

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Incorporation of DL-[2-¹⁴C] Mevalonic Acid Lactone into Polyisoprene

THE incorporation of DL-3-hydroxy-3-methyl-[2-¹⁴C] pentano-5-lactone (DL-[2-¹⁴C] mevalonic acid lactone) (MVA) into cholesterol in rat-liver homogenates was first demonstrated by Tavormina, Gibbs and Huff¹. Subsequent work showing that this lactone is incorporated into squalene² and β -carotene³ supported the view that mevalonic acid, or a derivative containing the same branched carbon atom structure, is directly involved in the biosynthesis of a wide range of polyisoprenoid compounds. Park and Bonner⁴ showed that when MVA is incubated

with freshly tapped *Hevea* latex it is incorporated into polyisoprene, although the reported efficiency of conversion was only about 2 per cent. Gascoigne and Jones¹ however were unable to observe the incorporation, *in vitro*, of MVA into rubber with the aid of fresh latex. We now wish to report an investigation which fully confirms the conclusions of Park and Bonner.

In our preliminary experiments, in which MVA was incubated with diluted fresh *Hevea* latex, no appreciable activity was detectable in the rubber. However, when undiluted fresh latex was used as described below, the MVA was converted into polyisoprene with an efficiency considerably higher than has been reported hitherto. It was also established that the polyisoprene formed was of high molecular weight.

Two aliquots of freshly tapped undiluted latex from 7 year-old seedlings of *Hevea brasiliensis* were incubated with MVA under the conditions shown in Table 1. Each reaction mixture was then coagulated with methanol and a weighed portion of the coagulum was placed in compartment X of the extraction apparatus (Fig. 1). This was constructed so as to

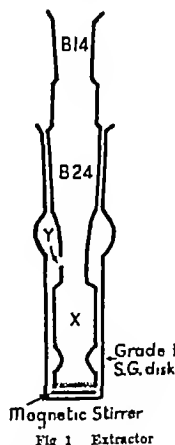


Fig. 1 Extractor

reduce manipulative losses in the subsequent treatment of the rubber. The coagulum was dispersed over the walls of the central portion of X by slow rotation of the vessel after the addition of oxygen-free chloroform, care being taken to prevent the rubber from coming into contact with the sintered glass disk. After removal of the chloroform *in vacuo* the dry rubber film was weighed *in situ* and extracted with acetone for 24 hr to remove unreacted MVA and other non-rubber components. The soluble fraction of the rubber was dissolved in chloroform-ethanol (97:3 w/w), intermittent operation of the magnetic stirrer causing the level of solvent in the outer tube to rise to Y and then fall. This ensured efficient extraction of the film, insoluble material being retained above the sintered glass disk.

To remove any compounds of low molecular weight, the rubber solution was dialyzed against three changes of the chloroform/ethanol solvent in alkali-pre-treated cellophane tubing which was

readily permeable to β -carotene but practically impermeable to polymers with molecular weights of about 100,000. Subsequent experiments also showed that mixtures of β -carotene and natural rubber could be separated quantitatively using the same membrane. The rubber was then ozonized in ethanol/chloroform (1:3 v/v) the ozonide being decomposed with a mixture of hydrogen peroxide and formic acid², and the product converted to the 2,4-dinitrophenylhydrazone. The latter was purified via the sodium salt. After two recrystallizations from aqueous acetic acid this material had a melting point of 199–200° C (uncorrected) and gave a single spot of the same R_f value as authentic levulinic acid dinitrophenylhydrazone (LADNP) when chromatographed on paper with *n*-butanol/ethanol/ammonia as the solvent⁴. Isotope dilution of the recrystallized levulinic acid dinitrophenylhydrazone, using an authentic sample of inactive material and recrystallization of the mixture from ethanol/pyridine also indicated a high degree of purity for the final active levulinic acid dinitrophenylhydrazone. All radiochemical assays of the various rubber fractions and the derived levulinic acid dinitrophenylhydrazone's (Table 1) were carried out using a standard gas-counting technique, with a counter having an efficiency of 45 per cent.

Table 1 INCORPORATION OF MVA INTO POLYISOPRENE

| | Experiment 1 | | Experiment 2 | |
|---|---|--|---|--|
| Weight of latex (mgm.) | 613 | | 707 | |
| Weight of MVA (mgm.) | 0.55 (2.47%) | | 0.67 (3.03%) | |
| Time of incubation (min.) | 30 | | 300 | |
| Temperature of incubation (°C.) | 20 | | 23 | |
| Weight of dried coagulum (mgm.) | 205 | | 312 | |
| | Weight of fraction as per cent of coagulum weight | Activity c.p.m./mmole active carbon dioxide* | Weight of fraction as per cent of coagulum weight | Activity c.p.m./mmole active carbon dioxide* |
| Dried coagulum | 100 | — | 100 | 17,400 |
| Extracted coagulum | 93 | — | 93 | — |
| Chloroform in solution | 10 | — | 14 | 17,000 |
| Chloroform soluble rubber (before dialysis) | 83 | 1,360 | 84 | 14,125 |
| Chloroform soluble rubber (after dialysis) | — | 1,450 | — | 15,600 |
| LADNP purified via sodium salt | 6 | — | 63 | 14,800 |
| LADNP twice recrystallized | — | — | — | 14,630 |
| LADNP after isotope dilution | — | — | — | 14,600 |

* Corrected for any inactive carbon atoms introduced.

The results of experiment 2 show that the soluble rubber (84 per cent w/w of the coagulum) was converted to levulinic acid dinitrophenylhydrazone in 75 per cent yield. The fact that a highly purified sample of the latter had at least 93 per cent of the specific activity of the dialyzed rubber shows that the active constituent had been degraded to levulinic acid in a similar yield. There is little doubt that only polyisoprene could give levulinic acid with such efficiency. The increase in [¹⁴C]-activity of the rubber after dialysis indicates the removal of some

active material of low molecular weight. Spectroscopic analysis shows that carotenoid material was removed by the acetone extraction, and none was present in the chloroform-soluble rubber (limit of detection less than 10 μ gm per gm of rubber). The increase in [14 C]-activity with time of incubation is further strong evidence that enzymic conversion of MVA occurred rather than physical adsorption of impurities on the rubber. Taking the corrected value of 14,600 c.p.m./mole of active carbon dioxide for the purified α -lactone acid dimethylphenylhydrazide from experiment 2, and assuming all the carbon in the dialysed rubber was polyisoprenoid, calculation shows that 9.3 per cent of the mevalonic acid lactone was transformed into chloroform soluble polyisoprene of high molecular weight.

We wish to thank Prof M. Stacey and Dr E. G. Cockbain for their interest and encouragement.

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BIOCHEMISTRY

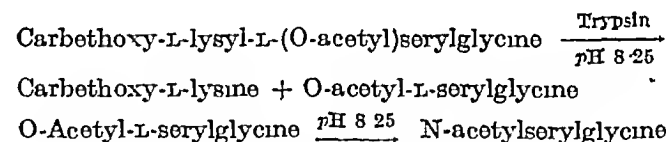
O-Phosphorylated and Unphosphorylated Peptide-Substrates suitable for Trypsin Action

A PREVIOUS communication reported the synthesis and action of trypsin on α -carbethoxy-L-lysyl-L-seryl-glycine and its O-phosphorylated analogue¹. The striking resistance of the latter to the action of trypsin throws additional light on the unusual resistance of various phosphopeptides obtained from casein. It was, however, felt to be of interest to further investigate the inhibitory role of the O-phosphoric acid residue of serine along different lines.

First it was felt necessary to exclude the possibility that a lysylserine sequence is not attacked by trypsin unless the hydroxyl group of serine is free. Therefore, α -carbethoxy-L-lysyl-L-(O-acetyl)seryl-glycine was synthesized as follows. α -Carbethoxy-L-lysyl-L-seryl-glycine benzyl ester¹ was treated with 100 per cent excess of acetic anhydride in dry pyridine to produce α -carbethoxy-L-(ϵ -carbobenzoxy)-L-lysyl-L-(O-acetyl)seryl-glycine benzyl ester (I), melting point

163–164° C, $[\alpha]_D^{20}$ –17.6° (c, 1.7 in acetic acid), almost in quantitative yield. Analysis calculated for $C_{25}H_{40}N_4O_{10}$, C 59.22, H 6.4, N 8.9, found, C 59.60, H 6.61, N 9.04. Hydrogenolysis of I afforded α -carbethoxy-L-lysyl-L-seryl-glycine (II) with an $[\alpha]_D^{20}$ value of –22.5° as a 1 per cent solution in water. Compound II was incubated with trypsin in 0.2 M tris(hydroxymethyl)aminomethane hydrochloride buffer pH 8.25 at 25° C. Ascending paper chromatography in butanol/acetic acid/water (4:1:5) revealed complete splitting of the lysylserine bond in the above tripeptide derivative after 30 min. When the course of the hydrolysis was followed by colorimetric ninhydrin analysis², surprisingly enough, a decrease in the colour yield was observed after 3 min (Fig. 1). This could be well explained on the assumption that the amino-group of the O-acetyl-L-seryl-glycine, resulted from the cleavage of II, was gradually masked by an O→N acetyl shift. To confirm this hypothesis, O-acetyl-L-seryl-glycine was synthesized by acetylation of carbobenzoxy-L-seryl-glycine benzyl ester³ in a manner similar to that described for the synthesis of I. Hydrogenolysis of carbobenzoxy-L-(O-acetyl)seryl-glycine benzyl ester, melting point 113–116° C, afforded O-acetyl-L-seryl-glycine (III) with an $[\alpha]_D^{20}$ value of +5° as a 1 per cent solution in water. Paper chromatography in butanol/acetic acid/water (4:1:5) revealed one ninhydrin-positive spot.

Samples of III were tested under the experimental conditions used for the enzymic digestion of II. A similar decrease in the colour yield, either in the presence or the absence of trypsin was also detected (Fig. 2). This again is in agreement with the assumed O→N migration of the acetyl group and strongly supports the following series of reactions:



Guttmann and Boissonnas⁴ have also mentioned an O→N acetyl shift in the case of O-acetyl-L-seryl-L-tyrosine over pH 7.

As the next step it was of interest to study the effect of an uncharged phosphoric acid derivative attached to the hydroxyl group of α -carbethoxy-L-lysyl-L-seryl-glycine.

Though there are several analogues that come to mind, the one having a diisopropylphosphoryl residue at this position held special interest to us. For its preparation α -carbethoxy-(ϵ -carbobenzoxy)-L-lysyl-L-seryl-glycine benzyl ester¹ was treated with 100 per cent excess of diisopropylfluorophosphate in dry pyridine to give α -carbethoxy-(ϵ -carbobenzoxy)-L-lysyl-L-(diisopropylphosphoryl)seryl-glycine benzyl ester, (IV), melting point 175–176° C. Analysis calculated for $C_{35}H_{51}N_4O_{13}$, N 6.91, found, N 6.80. Hydrogenolysis of IV produced α -carbethoxy-L-lysyl-L-(diisopropylphosphoryl)seryl-glycine (V) with an $[\alpha]_D^{20}$ value of –23° as a 1 per cent solution in water.

When V was subjected to the action of trypsin for 30 min and the incubation mixture was then checked by paper chromatography, the lysylserine bond was found to be almost completely hydrolysed. In this connexion it was ascertained that the substrate V suffered no loss of its diisopropylphosphoryl residue by β -elimination⁵ under the experimental conditions described here.

The course of the enzymic hydrolysis of V by trypsin was also followed by colorimetric ninhydrin analysis², the result of which is indicated by Fig 1

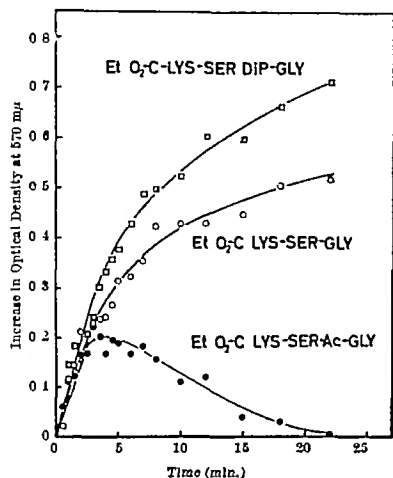


Fig. 1. Hydrolysis of various *o*-carboxy L-lysyl L-serine derivatives (0.01 M) with trypsin (0.017 mg/ml crystallized twice 50 per cent MgSO₄, Lot 3388 Mann) in 0.2 M Tris buffer pH 8.25 at 25°C. □ *o*-Carboxy L-lysyl (0-difluorophosphoryl)-L-serine; ○ *o*-carboxy L-lysyl L-serine; ● *o*-carboxy L-lysyl-(*o*-acetyl)-L-serine

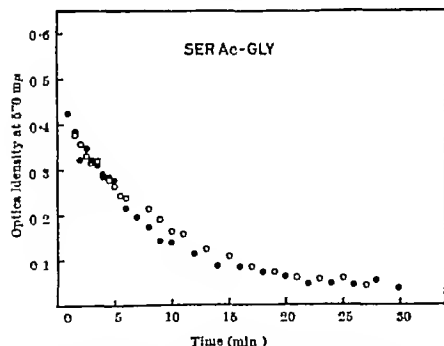


Fig. 2. 0.01 M solution of *o*-acetyl L-serine in 0.2 M Tris buffer, pH 8.25 at 25°C. ○ Trypsin added (0.022 mg/ml crystallized twice 50 per cent MgSO₄, Lot 3388 Mann); ●, no trypsin added

Thus it appears that a substituted and uncharged phosphoric acid residue at the vicinity of the trypsin sensitive peptide bond does not even retard the hydrolysis of this particular bond by means of steric effect. However, a phosphoric acid residue at this position, probably due to its negative charge³ renders the susceptible peptide bond resistant to tryptic action

Work is in progress on the inhibitory spectrum of the *O* phosphoric acid residue of serine

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Unidentified Growth Factors

It is well known that spent wash (the liquor remaining in the whisky still after distilling the spirit) contains factors which increase the growth of chicks. This growth promotion appears to be unrelated to mineral components, and although complementary to the effect of penicillin in chick feed², it may similarly result from changes in the gut flora³.

In an attempt to test this theory, chicks were fed with a control diet supplemented with procaine penicillin or with malt distillers dried solubles (made from spent wash). Comparison of the duodenal contents of chicks fed with either type of supplemented diet, or with the control diet, revealed a shift for both types of supplement in the balance of bacterial flora in favour of a lactobacillus type. Suppression of sensitive micro-organisms seems to be a likely explanation for the shift caused by the penicillin supplemented diet, on the other hand direct stimulation of lactobacilli by malt distillers dried solubles is a more likely explanation on the other diet.

The dominant type of lactobacillus culture was isolated from the duodenum of chicks fed with distillers dried solubles, and used in a rough microbiological assay for comparing sources of growth factors. It was confirmed that malt distillers dried solubles acted *in vitro* as a microbiological growth factor. Other feed additions such as molasses distillers dried solubles, dried yeast and dried whey acted similarly by enhancing the growth of the lactobacillus (although in varying degree), and when these additives were given to chicks, stimulation of the chick growth occurred (following communication) correlating with the microbiological test.

Further estimation of the number of lactobacillus types in the duodenal flora (by Sharpe's method⁴) showed that the increase attributable to the supplements was considerable (about 100 fold; a difference which is significant at the 1 per cent probability level) in birds receiving distillers dried solubles or molasses distillers dried solubles. Chicks and lactobacilli gave growth responses for both additives which were

roughly comparable. Further work is in progress, and it is hoped to publish a more detailed account elsewhere.

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Table 1

| Diet | Mean weight increases (gm.) | | | | |
|--|-----------------------------|--------|--------|--------|--------------------|
| | Week 1 | Week 2 | Week 3 | Week 4 | Week 4 Adjusted |
| 1 Control | 41.8 | 115.6 | 229.4 | 372.8 | 383.5 |
| 2 Control + 5% fish meal | 47.2 | 125.3 | 256.0† | 395.2† | 392.5 |
| 3 Control + 2½% dried whey | 51.6 | 136.0† | 262.2† | 414.8* | 418.8† |
| 4 Control + 2½% dried yeast | 50.8 | 135.8† | 266.8† | 421.8* | 425.4† |
| 5 Control + 2½% molasses distillers dried solubles (ethyl concentrate) | 53.7† | 137.6† | 271.4† | 423.2* | 420.9† |
| 6 Control + 2½% E.C. + 5% fish meal | 48.0 | 134.2† | 260.6† | 421.3* | 421.4† |
| 7 Control + 2½% E.C. + 2½% dried whey | 51.4 | 135.2† | 265.4† | 430.8* | 424.0† |
| 8 Control + 2½% E.C. + 2½% dried yeast | 55.0 | 145.1† | 272.8† | 433.6* | 426.0† |
| Standard error of mean weight increases | 4.2 | 6.5 | 8.6 | 8.2 | |

* Differences from control significant at 0.1 per cent probability level

† Differences from control significant at 1 per cent probability level

‡ Differences from control significant at 5 per cent probability level

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Unidentified Chick Growth Factors

The previous communication refers to a tentative microbiological assay method for certain unidentified chick growth factors, based on their growth stimulating effect on a strain of *Lactobacillus* isolated from chicks receiving distillers dried solubles in their diet. This method derives from the hypothesis that the growth factors act by modification of the microbial flora of the chick's gut.

Among materials submitted to the tentative microbial assay were fish meal, dried unextracted brewers yeast, dried whey and molasses distillers dried solubles. The latter material is obtained by vacuum evaporation and subsequent spray drying of the liquid remaining in the still following the distillation of ethyl alcohol produced by the yeast fermentation of molasses. Of these four materials only the first (fish meal) failed to elicit a marked response from the *Lactobacilli*.

Using the purified diet which has been detailed elsewhere¹, we endeavoured to confirm these findings with chicks. Eight diets, as shown, were used in an effort to demonstrate whether or not such growth factors as may be present in the various additives were the same. The chicks were housed in two electrically heated, thermostatically controlled brooders with one replicate of each diet in each brooder. Each replicate consisted of 25 Rhode Island/Light Sussex cockerels and the birds went into the units as day olds. The results obtained are given in Table 1.

There were no significant differences between diets 2, 3, 4 and the corresponding double additive diets 6, 7, 8 except that, at 4 weeks only, the mean weight increase on diet 6 was significantly higher (at the 5 per cent level) than diet 2.

Examination of the feed intake figures showed considerable differences and when the above results were adjusted to a common feed intake by the use of regression coefficients the growth response to fish meal disappeared whilst the other responses remained, albeit at a lower level. These results will be discussed

in more detail elsewhere but it appears that under our conditions fish meal acts only as a source of known nutrients (provided already in the control diet) and as an appetite-stimulating factor. On the other hand, responses are obtained to dried yeast, dried whey and molasses distillers dried solubles which are evidently due to an unidentified growth factor common to them all. It has also been established by other work including chick growth trials and the direct examination of gut flora that malt distillers solubles and molasses distillers solubles are directly equivalent in terms of unidentified growth factor activity. All these conclusions are consistent with the findings of the tentative microbial assay discussed in the communication already referred to, to which this letter is complementary.

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Heterogeneity of Human Foetal Hæmoglobin: Incidence of Foetal Variants in Singapore

THREE variants of foetal hæmoglobin have so far been described primarily on the basis of electrophoretic mobility. These are known as 'Fessas and Papaspyrou' type¹, 'Bart's' type², and 'Alexandra' type³. The 'Fessas and Papaspyrou' type appears to be relatively common and reports of its incidence have so far appeared from Singapore⁴ and Indonesia⁵. 'Bart's' hæmoglobin has been identified in specimens from Texas (Dr R. Schneider) and Thailand (Dr S. Tuchinda) (Drs J. A. M. Ager and H. Lehmann, personal communication) and in one sample from Singapore.

During the period March 1958–March 1959, 2517 blood samples were obtained from the umbilical cord, at birth, of babies delivered at the Kandang Kerbau Maternity Hospital, Singapore and the British Military Hospital, Singapore and submitted to filter paper electrophoresis using a horizontal arrangement with the filter paper (Whatman 3 MM) sandwiched between glass plates treated with silicone grease.* The blood samples were collected in potassium oxalate bottles and prepared by washing twice in 0.9 per cent aqueous solution of sodium chloride, laked with a volume of water, shaken manually with half a volume of toluene and centrifuged (2500 r.p.m.) till a clear haemoglobin solution was obtained.

It soon became clear that small amounts of fast-moving and slow moving pigments (appearing as a faint yellow-coloured front and trail) were present in most samples in addition to the dark red band which contained the haemoglobins *A* + *F*. These minor fractions could be demonstrated well on staining with a protein stain (bromophenol blue) or with a benzidine reagent (pseudoperoxidase reaction) as described by Liang.⁷ The incidence of visually detectable fast and slow fractions in unstained electrophoretograms is shown in Table 1. The amount of

detected in either of the parents when these were available for study. On starch block electrophoresis the mobilities were very similar to those noted on paper.

The presence or absence of the slow or fast fractions did not appear to be related to the sex or body weight of the infant from which the blood had been obtained or to the content of alkali resistant haemoglobin (measured as described by Chernoff⁸). In a study of more than 100 children between the ages of a few days and six months who were being investigated for anaemia with or without jaundice in the Paediatric Unit of the General Hospital, Singapore, during the same period, in only one instance was a fraction (approximately 15 per cent of the total) identical in mobility with the Fessas and Papaspyrou type noted (FC 372, Figs 1 and 2). The child was treated in

Table 1 INCIDENCE OF ABNORMAL HAEMOGLOBINS IN CORD BLOOD SAMPLES IN SINGAPORE.

| Ethnic group | Number studied | Fessas and Papaspyrou type | Bart's type | Alexandra type |
|-------------------|----------------|----------------------------|-------------|----------------|
| Chinese | 1062 | 63 | 2 | 8 |
| Malay | 102 | 2 | — | 2 |
| European | 142 | 1 | — | 1 |
| Indian | 225 | 2 | — | — |
| Eurasian | 10 | — | — | 1 |
| Nepalese (Gurkha) | 10 | — | — | — |
| Total | 2517 | 68 | 2 | 12 |

fast- or slow moving pigments in these samples varied between 8 and 20 per cent of the total haemoglobin when determined by a dye-elution method, while in the two samples listed under Bart's type, the fast fractions accounted for 24–25 per cent of the total haemoglobin. In the majority of cases when insufficient amounts of fast or slow pigment were present to be detected by inspection of the wet or dried untreated electrophoretograms with the naked eye, staining with bromophenol blue or benzidine produced evidence of the presence of small amounts of these fractions. The electrophoretic mobilities of these fractions appearing on staining were very similar to those of the fast- or slow moving fractions listed in Table 1 under Fessas and Papaspyrou type and Alexandra type. At pH 8.6, on paper electrophoresis, using veronal buffer, the fast fractions had the mobility described by Fessas and Papaspyrou¹ being slower than haemoglobin *H* and a shade slower than haemoglobin *J*, while the slow fractions migrated just ahead of *E* or *A₂* and just slower than *S* or *D*. At pH 6.5, the fast fraction had a definitely anodal mobility though much less than that of haemoglobin *H*. No abnormal haemoglobins were

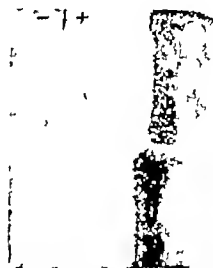


Fig. 1. FC 372 compared against haemoglobins *A* and *J* pH 8.6, veronal buffer. Note mobility of fast fraction, slower than that of *J*.



Fig. 2. FC 372 compared against a sample containing Bart's haemoglobin pH 8.6, veronal buffer. Note mobility of fast fraction, distinctly slower than Bart's.

hospital for severe anaemia and jaundice which developed 12 days after birth, but since his erythrocytes were found to be deficient in the enzyme glucose 6-phosphate dehydrogenase, which is known to be related to drug induced haemolytic anaemia, the anaemia can not safely be considered to be a consequence of the presence of the fast haemoglobin.⁹ It thus seems that small amounts of fast and slow moving haemoglobin fractions are present in the cord blood of the majority of new born babies and that in certain individuals for



Fig 3 Direct comparison of FC 890 against Bart's haemoglobin pH 8.6, veronal buffer

no apparent reason, the amount of these fractions may increase so as to account for up to about 20 per cent of the total haemoglobin. This picture is closely similar to that widely accepted for haemoglobin A. Normal adult haemoglobin is a heterogeneous mixture consisting of at least three variants (A_1 , the major component, A_2 and A_3 , the minor components), of which the minor components can be demonstrated on filter paper electrophoresis by staining with a protein dye⁹.

In two samples, obtained from Chinese male newly borns, a faster fraction was noted on paper electrophoresis at pH 8.6. This separated well from the main component (mixture of A and F), and had a mobility faster than that of haemoglobin J but slower than that of H. It was possible to send one of these samples (FC 890) to Drs Ager and Lehmann in London for further study. On paper electrophoresis at pH 8.6 the mobility was found to be that described above. On ion-exchange resin chromatography, the fast component moved faster than H which is the position described for 'Bart's'. Actual comparisons against 'Bart's' haemoglobin revealed the identity of the two specimens. The ultra-violet absorption spectrum of the fast component in FC 890 revealed the tryptophan fine-structure band of haemoglobin F.

A further indication that the 'Fessas and Papaspyrou' type of haemoglobin is a normal minor component of human foetal haemoglobin is obtained from the work of Fessas and Mastrolakos¹⁰. Using a starch-gel electrophoresis technique these workers have found, in all samples of cord blood studied, a well-defined zone which gives a positive pseudoperoxidase reaction, which amounts to 0.5–1.0 per cent of the total haemoglobin and which has an electrophoretic behaviour which corresponds very closely to that of the 'Fessas and Papaspyrou' type. Both this variant and the 'Alexandra' (slow-moving) haemoglobin may thus represent abnormal amounts of fractions which are normally present only in small amounts. The 'Bart's' haemoglobin may represent a truly abnormal variant of foetal haemoglobin. In electrophoretic behaviour at pH 8.6 it differs noticeably from the 'Fessas and Papaspyrou' type, in being definitely faster and having the mobility, at pH 8.6, described for haemoglobin N². It occurs at a much lower incidence, only two cases having been detected in this study and when present amounts to some 24–25 per cent of the total haemoglobin.

I am grateful to Dr H. Lehmann of St Bartholomew's Hospital, London and to Dr J. A. M. Ager of St Thomas's Hospital, London for continued interest

in this work and for help in identifying the sample FC 890 as 'Bart's' haemoglobin. Mr Stephen Pang rendered valuable technical assistance during this work.

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Biosynthesis of Chondroitin Sulphates

LITTLE information is available regarding the biosynthesis of acid mucopolysaccharides. Knowledge of biosynthetic pathways to the chondroitin sulphates in particular is practically confined to the fact that glucose is utilized for both the hexosamine and uronic acid moieties¹ and that 3'-phosphoadenosine 5'-phosphosulphate (PAPS) is involved in sulphate transfer². Uridine intermediates are thought to take part by analogy to the synthesis of chitin, cellulose, and hyaluronic acid³.

This communication describes the effect of the addition of various mucopolysaccharides on the biosynthesis of chondroitin sulphate (CSA) in an isolated enzyme system.

One of the mucopolysaccharides isolated from cornea by Meyer and co-workers⁴ was the sulphate-free chondroitin, the C₄ hexosamine epimer of hyaluronic acid. They suggested that chondroitin was probably the precursor of chondroitin sulphate, the polymer being first formed and then sulphated. In a particle-free enzyme system derived from chick embryo condyles, chondroitin did not act as an acceptor of sulphur-35 labelled sulphate however⁵. This system is able to synthesise chondroitin sulphate when incubated with adenosine triphosphate and magnesium chloride².

When a partially purified sample of umbilical cord hyaluronic acid was tested in this enzyme system, strong stimulation of chondroitin sulphate synthesis resulted. Hyaluronic acid itself does not occur as a sulphate ester so that one possible interpretation of this result was that sulphation occurred at C₄ of the glucosamine moiety with inversion at this position to yield the galactosamine sulphate, namely, CSA-A. Chemical fractionation of a saline umbilical cord extract however yielded hyaluronic acid (containing protein) and a mucoprotein rich in sulphate (SMP). Stimulation of chondroitin sulphate synthesis was associated with this sulphated fraction—the hyaluronic acid fraction was without effect. The SMP had an electrophoretic mobility about half that of pure chondroitin sulphate on paper and was strongly metachromatic. When the paper was cut up into

sections, eluted and the eluates tested for stimulating power, activity was found to correspond with the metachromatic zone. After treatment of the paper electrophoretogram with chlorine followed by starch/potassium iodide, a band was evident which was superimposable with the metachromatic band obtained by staining with toluidine blue. Both reagents showed a slight zone at the origin. Free protein is then probably absent, the mucoprotein migrating as a stable covalent compound.

When SMP was digested with proteolytic enzymes a free mucopolysaccharide was obtained which was identified as CSA C ($[\alpha]_D^{20}$ Ratios hexosamine/uronic acid/nitrogen/sulphur/acetyl 1.0/1.1/0.97/0.81/1.2. The hexosamine was identified as galactosamine) (CSA C has previously been shown to occur in umbilical cords). Stimulating activity of the SMP and the CSA C were of the same order on a weight basis. CSA C isolated by enzymatic digestion of the cord residues also stimulated to the same degree (ratios hexosamine/uronic acid/nitrogen/sulphur 1.0/0.91/1.04/0.91). In addition stimulation resulted when active sulphate 3 phosphodenosine 5 phospho sulphate labelled with sulphur 35, was used as a tracer in place of sulphur 35 labelled sulphate. Activity varies with the particular enzyme extract used, the maximum degree of stimulation so far found has been 3.5 times the control.

CSA A isolated from bovine trachea by alcohol fractionation ($[\alpha]_D^{20}$ ratios hexosamine/uronic acid/nitrogen/sulphur 1.0/1.07/1.04/0.95) and further identified by its infra red spectrum, was found to have a low degree of stimulation compared to CSA C. The reality of this was born out by the fact that the more soluble alcohol fraction obtained from the preparation of the trachea chondroitin sulphate mixture, was strongly stimulating. This fraction contains the CSA C present in the cartilage and was confirmed to be a mixture of CSA A and CSA C by its infra red spectrum. Since the trachea chondroitin sulphate had been isolated by extraction with hot alkali as compared to the mild saline extraction used on the cords, CSA C was treated with alkali under the conditions used for obtaining CSA A. No loss in activity resulted.

Chondromucoprotein isolated from cartilage by the method of Malawista and Schubert⁸ was found to inhibit slightly the formation of chondroitin sulphate.

Re-extraction and reprecipitation of the counted samples led to a loss in radioactivity. This loss was about 60 per cent in the case of the controls and 40-50 per cent in the presence of added chondroitin sulphate. A broadening response above the control becomes apparent after reprecipitation. The loss of radioactivity is thought to be due to a higher solubility of radioactive chondroitin sulphate composed of shorter chain molecules as compared to the chondroitin sulphate used as a carrier. Results are summarized in Table 1.

The infra red spectrum of the mucoprotein isolated from 20-day old chick embryo condyles by high speed homogenization showed it to be predominantly CSA A with perhaps small amounts of CSA C present. Material derived from 15 day old chick embryo condyles gave a very similar spectrum the bands corresponding to CSA C being slightly more intense.

It is evident that no primer or template mechanism is involved in the biosynthesis of chondroitin sulphate. Because the enzyme system as prepared necessarily

contains relatively large amounts of mucoprotein, this probably accounts for the difference in stimulating power of CSA A and CSA C. The system being already rich in CSA A in the form of the mucoprotein. Addition of CSA C then results in a greater response than addition of CSA A if we presume that enzyme systems are present which synthesize both types of chondroitin sulphate.

TABLE 1. EFFECT OF ADDED SUBSTANCES AT EQUAL CONCENTRATION OF THE RADIO ACTIVITY OF CHONDROITIN SULPHATE FORMED BY INCUBATING A PARTICLE FREE EXTRACT OF 15-DAY-OLD CHICK EMBRYO CONDYLES WITH ALKALINE TRIPHOSPHATE AND MAGNESIUM CHLORIDE AS DESCRIBED PREVIOUSLY.¹ THE CHONDROITIN SULPHATE FORMED WAS ISOLATED BY ADDITION OF CARRIER AND PRECIPITATION WITH CETYLAL.

| Tracer | Substance Added | Radio activity of CSA relative to control as 1.0 | |
|-----------------|--|--|-----------------|
| | | Initial Precipitate | Reprecipitation |
| $Na_2^{35}SO_4$ | CSA-C Sodium salt | 1.7 | 2.9 |
| $Na_2^{35}SO_4$ | SMP Sodium salt | 1.5 | 2.3 |
| $Na_2^{35}SO_4$ | Chondromucoprotein | 0.8 | 1.0 |
| $Na_2^{35}SO_4$ | Muco-protein of chick condyles (20 days old) | 0.8 | 1.0 |
| $Na_2^{35}SO_4$ | CSA A Sodium salt | 1.3 | --- |
| $Na_2^{35}SO_4$ | CSA A Sodium salt | 1.1 | --- |
| $Na_2^{35}SO_4$ | CSA-C Sodium salt | 1.8 | --- |
| $Na_2^{35}SO_4$ | CSA C Sodium salt | 1.9 | --- |
| $Na_2^{35}SO_4$ | CSA A Calcium salt | 1.1 | 1.5 |
| $Na_2^{35}SO_4$ | CSA A + C Calcium salt | 1.5 | 2.3 |
| | 60% alcohol fraction from trachea | | |

If priming rather than template action is the mechanism involved, it must function by the alternative addition of acetyl galactosamine sulphate and glucuronic acid residues or by the addition of the preformed disaccharide or similar unit. Some evidence for the existence of a uridine derivative containing both hexosamine and uronic acid has been presented by Dorfman *et al.*⁹ When uridine diphosphoglucuronic acid was incubated with the chick condyle enzyme a suppression of chondroitin sulphate synthesis was the result.

The reason for this suppression is not clear, at the present time. Uridine diphosphoglucuronic acid has however been demonstrated to be utilized for the synthesis of hyaluronic acid by streptococci.¹⁰

A full report of this work, together with results obtained on the influence of chain length on stimulating power, will be published elsewhere.

I am indebted to Dr R. I. Cox, Dept of Veterinary Physiology, University of Sydney, for the infra red spectra.

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Significance of Lactose in the Diet in Aminoaciduria caused by Maleic Acid

IN studies with rachitic rats Harrison and Harrison¹ established aminoaciduria as one of the signs of maleic acid intoxication. Angielski *et al.*² produced, by intraperitoneal administration of maleic acid, aminoaciduria in rats receiving a diet containing 50 per cent skim milk. We have studied the effect of dietary lactose on the production of aminoaciduria by maleic acid. Three groups of rats received the three diets described in Table 1.

Table 1 COMPOSITION OF DIETS (gm./kgm.)

| Component | Diet | | |
|------------------------|------|--------------|-----------------|
| | Milk | With lactose | Without lactose |
| | I | II | III |
| Dried skim milk | 480 | — | — |
| Caseln | — | 170 | 170 |
| Wheat starch | 270 | 270 | 480 |
| Sucrose | 130 | 130 | 230 |
| Lactose | — | 310 | — |
| Rape-seed oil | 88 | 88 | 88 |
| Wesson's* salt mixture | 32 | 32 | 32 |

To 1 kgm. of diet were added: 331 mgm. of a vitamin mixture⁴; 1,000 mgm. choline hydrochloride; 5 mgm. menaphthone; 150 mgm. vitamin E, 25,000 I.U. vitamin A, 2,500 I.U. vitamin D.

The rats were kept in metabolic cages allowing quantitative collection of urine uncontaminated by faeces or diet. They received unlimited food and water. Neutralized maleic acid was given intraperitoneally as a molar solution, in one dose of 400 mgm./kgm. body-weight. α -amino nitrogen was estimated in urine by the method of Yemm and Cocking⁵. The rats received their respective diets for 7–14 days before injection of maleic acid. The results are given in Table 2.

Table 2 ADULT RATS, MALES AND FEMALES WEIGHING 120–370 GM. MEAN VALUES PER RAT FOR 24 HOURS FOR GROUPS OF 5 RATS. FIGURES IN PARENTHESES SHOW THE RANGE.

| | α -Amino nitrogen (mgm.) | | |
|---|---------------------------------|---------------------|-------------------|
| | Diet I | Diet II | Diet III |
| Before administration of maleic acid (mean over 4 days) | 3.3 (1.65–5.7) | 6.2 (4.0–8.1) | 4.6 (2.5–7.5) |
| After administration of maleic acid | | | |
| Day 1 | 7.5 (5.0–9.3) | 22.5 (14.8–31.6) | 4.1 (3.4–5.8) |
| Day 2 | 10.9 (5.4–15.3) | 18.0 (15.0–22.0) | 1.7 (1.1–2.2) |
| Day 3 | 20.5 (11.5–27.5) | 37.0 (16.0–57.0) | 3.2 (1.1–7.7) |
| Day 4 | 9.5 (6.5–12.2) | 25.5 (17.3–30.5) | 7.1 (3.1–12.0) |
| Day 5 | 4.6 (2.6–9.5) | 11.8 (7.0–15.9) | 6.8 (4.0–9.4) |

400 mgm. maleic acid per kgm. body weight produced no aminoaciduria in rats on a diet devoid of lactose. Rats receiving lactose, whether from milk or as such, responded by marked aminoaciduria to the same dose of maleic acid. Maximum excretion of α -amino nitrogen was generally observed on the second or third day after administration, the values reached being five to ten times those before maleic acid was injected. After a week the excretion returned to normal again.

Maleic acid is the causative agent of the aminoaciduria but lactose seems to be necessary for its appearance.

A full report of these findings will be published in *Acta Biochimica Polonica*.

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Extraction of an Actomyosin-like Protein from Human Thrombocytes

CONTINUING the work of Luscher¹, we have studied the metabolism of blood platelets in relation to clot retraction, as the latter seems to be one of the most important thrombocytic functions. Luscher² and Bounameaux³ have pointed out that in the presence of a buffered medium containing divalent cations (Mg^{++} or Ca^{++}), glucose is a factor which improves retraction. On the other hand the existence of mitochondria has been observed with electron microscopic techniques and it has been known for years that blood platelets are able to consume oxygen.

In our experiments⁴ we noticed a constant relationship between an active glycolytic system and maximal retraction capacity. This relationship does not exist for oxygen consumption. Using isolated and washed thrombocytes we were able to confirm the results of Born⁵ obtained with platelet-rich plasma. This author observed that the adenosine triphosphate level, which is very high in thrombocytes, shows a rapid fall during clotting. Also, fresh thrombocytes exhibiting maximal retraction have a high adenosine triphosphate content (about $5 \times 10^{-2} \mu$ moles/ 10^9 platelets for isolated and washed cells), whereas platelets, even if preserved at $0^\circ C$, hydrolyse their adenosine triphosphate and at the same time lose their ability to retract.

Lüscher⁶ has suggested that viscous metamorphosis is linked to the appearance of a viscous and retractile protein of complex composition, which was obtained from platelets and named 'protein S'.

In view of these facts and the results obtained by Hoffmann-Berling⁷ on undifferentiated cells, from which he isolated a contractile protein, we tried to extract a contractile protein from thrombocytes, in a way analogous to the extraction of actomyosin from muscle.

Thrombocytes from normal human blood were isolated by means of centrifugal fractionation, they were washed twice in 0.9 per cent sodium chloride containing 1% of the disodium salt of ethylenediamine tetra-acetic acid, they were washed once more with a Weber-Edsall solution (potassium chloride, 0.6 M, sodium carbonate, 0.01 M, and sodium bicarbonate 0.04 M) and after discarding the supernatant they

PHYSIOLOGY

Response of Cholinergically Innervated
Sweat Glands to Adrenaline and
Noradrenaline

were resuspended in the same medium. For a single experiment 40 ml of a suspension containing about 3.5×10^7 platelets per μ l with less than one leucocyte per 100 000 platelets, were used. This suspension was homogenized in a small refrigerated blender turning at 17,000 r.p.m. for 15 minutes. The homogenate was left overnight in the refrigerator and centrifuged for one hour at 60,000 g in order to eliminate undestroyed platelets (about 5 per cent of the initial count), cell fragments and insoluble proteins. All operations were carried out at a temperature between 0 and 4° C. The pH of the extract (13 ml) was about 7.4 and the protein content about 6.5 per cent (Kjeldahl). The extract contained some fibrinogen (clottable with thrombin) but consisted mainly of a protein which had the characteristics of actomyosin: it was soluble in a

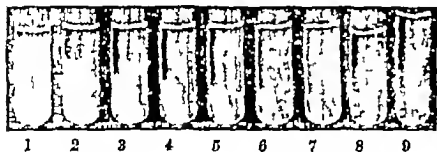


Fig. 1. Contraction and precipitation of the actomyosin-like protein from human thrombocytes. 1-7 pictures of the same test tube taken 0-5, 1-0, 1-5, 2-0, 3-0, 5-0 and 20-0 minutes after the addition of adenosine triphosphate. The sample contains 0-25 ml. of the extract (6-4 g./ml. protein dissolved in Weber-Eisall solution), adenosine triphosphate $4 \times 10^{-3} M$, magnesium sulphate $3 \times 10^{-3} M$ water to 1-5 ml. 8 same composition without adenosine triphosphate. 9 protein solution and water only.

medium of ionic strength 0.8 and precipitated if the ionic strength was lowered by dilution with water to 0.1. If Mg^{++} and adenosine triphosphate were added to the protein at this lower ionic strength a superprecipitation or a contraction took place. After discarding the supernatants, the precipitates of the protein were readily soluble if resuspended in 0.6 M potassium chloride. The viscosity measured after the addition of adenosine triphosphate to the actomyosin-like protein in 0.6 M potassium chloride showed a significant fall as compared to the value obtained with out adenosine triphosphate. The viscosity rises again after the adenosine triphosphate has been consumed.

In conclusion a contractile protein has been extracted from normal human thrombocytes. This protein shows characteristics of muscle actomyosin and is most probably responsible for clot retraction. The conditions under which it functions during viscous metamorphosis and clot retraction are under study.

We wish to thank Dr. H. Portzehl for critical discussion and Miss M. Schneider for valuable technical assistance.

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THAT the innervation of the sweat glands in the cat's foot pad is cholinergic has been recognized and generally accepted since the classical demonstration in 1934 by Dale and Feldberg¹. However, sweat droplets have been seen to appear on the foot pad following intradermal or systemic injection of adrenaline or noradrenaline, most recently by Nakamura and Hatanaka². The sweating is said to be minimal and not regularly reproducible³. In summarizing the situation, Rothman⁴ takes the view that the appearance of sweat droplets in response to adrenaline injection represents expulsion due to myoepithelial contraction, rather than secretory activity. On the other hand a dual innervation, adrenergic and cholinergic, has been postulated by Kuno⁵.

In the course of the present experiments a few droplets of sweat have been seen to appear following intravenous injection of adrenaline, but only if the ducts were filled by prior stimulation of the sudomotor nerve supply⁶. Interpretation is equivocal: there is no way of deciding from this sort of experiment whether adrenaline causes expulsion through contraction or whether it has a mild secretory action, enough to produce visible sweat if the ducts are full but not if they are empty or partly empty through reabsorption. In any event visual inspection is not a very satisfactory method for it yields information only as to sweat emergence (rather than sweat formation) which must undoubtedly be responsible for the variable results and conflicting reports in the literature.

Impedance change across the cat's foot pad is a good, although logarithmic, measure of the course of the sweat duct filling and emptying, which is to say of sweat formation and reabsorption⁷. During stimulation of the sudomotor nerves impedance falls from a high to a low value at a rate determined by the frequency of stimulation, as can be seen by comparing A and E of Fig. 1. At the close of stimulation the impedance level slowly returns to initial resting level as reabsorption progresses. After a maximal bout of activity up to 90 min are required for complete reabsorption and full recovery to resting impedance level. Injected acetylcholine produces similar changes and the effects both of nerve stimulation and injected acetylcholine are blocked by atropine, as would be expected.

Adrenaline and noradrenaline cause impedance changes similar to that resulting from acetylcholine injection. Fig. 1 illustrates an experiment in which the action of noradrenaline was examined. The cat was in nontubal anaesthesia. Stimulation was applied to the centrally covered plantar nerves which contain the sudomotor supply to the foot pads. Recording was done by means of zinc-zinc sulphate electrodes (one on the central foot pad, the other subcutaneously placed near by) an impedance bridge, the generator supplying a 20-cycle sine wave, an amplifier and cathode ray oscilloscope. Drugs were injected intravenously through the antebrachial vein.

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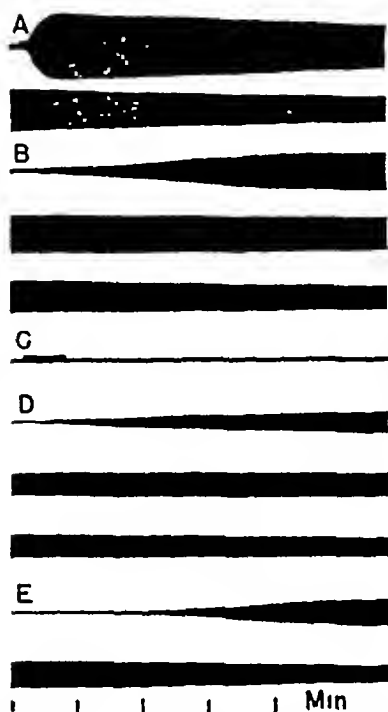


Fig 1 Oscillographic recordings of impedance changes across the foot-pad of the cat. For each record A-E the impedance bridge was balanced initially with the sweat glands in the resting state. Width of the line indicates the degree of bridge imbalance caused by a lowering of impedance across the foot-pad. The successive lines of each lettered recording are continuous each with the next.

Record A illustrates the impedance changes due to a 10-sec electrical stimulation at a frequency of 10 per sec. There is, in the first line, a rapid decrease in impedance and a slow return toward normal which is continued in the second line. The entire recovery course in this and subsequent recordings is not illustrated. Record B presents a typical record of change following intravenous injection of noradrenaline, 40 μ gm per kilo. Lowering of impedance progresses more slowly than in A and the beginning of return toward normal is delayed indicating that the noradrenaline continues to act for some time.

Between the making of records B and C atropine, 0.5 mgm per kilo, was injected. Record C, containing the result of a 38 sec stimulation at 10 per sec, shows the effect of nerve stimulation to be completely blocked. In normal circumstances the response to the 38-sec stimulation would be enormously greater than that seen in record A. Record D, obtained immediately after record C, shows the response to a further injection of noradrenaline, 40 μ gm per kilo. Although the response is smaller than that in record B there is as yet no sure indication that atropine antagonizes the noradrenaline action⁸. Certainly, however, it is not blocked by atropine.

Record E, from another experiment, illustrates the manner in which impedance change occurs when stimulation frequency is lowered, in this case to 12 per min. Duration of this stimulation was 5 min. It is evident that response to electrical stimulation could be made to duplicate that to adrenaline or noradrenaline by careful selection of stimulus duration and frequency.

Since atropine completely blocks the effect of nerve stimulation it is unlikely that some sweat glands are adrenergically rather than cholinergically innervated. At the present time the most likely interpretation is

that all the sweat glands are cholinergically innervated, but that in addition their secreting cells are responsive to adrenaline and noradrenaline.

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Coating of Red Blood Cells with Antigenic Substances

COATING of red blood cells with antigenic substances is used for titration of antibodies because the blood cells are a stable and uniform vehicle for the antigen¹⁻³. In our experiments red blood cells of sheep were first treated with tannic acid (1:20,000 in saline, pH 7.2) to stabilize them. If the solution is stronger, spontaneous agglutination takes place. The protein (bovine γ -globulin) was coated on the cell at a pH 6.4. The cells were lysed in distilled water. The cell walls were then shadowed with gold-palladium, and studied in a Siemens Elmiskop I. Fig 1 shows an untreated

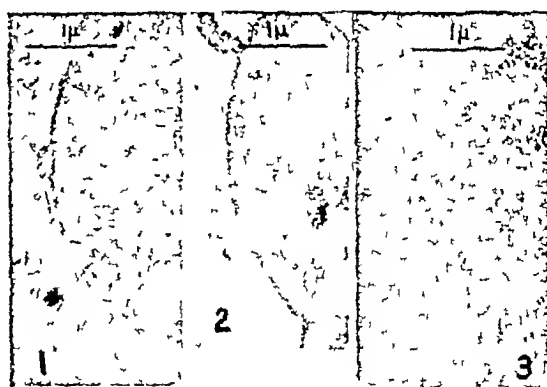


Fig 1 Cell wall, untreated ($\times 10,700$)

Fig 2 Cell wall, treated with tannic acid ($\times 10,700$)

Fig 3 Cell wall, treated with tannic acid and coated with protein ($\times 10,700$)

cell wall. The surface is fairly smooth. After treatment with tannic acid the surface becomes rougher (Fig 2). Coating with protein produces a mottled appearance, and the outlines of the shadow of the edge of the cell wall are somewhat diffuse (Fig 3). It is difficult to explain these morphological changes in terms of physical and chemical processes, especially as the arrangement of the molecules on the cell surface is not fully understood. Tannic acid acts presumably as a fixative like formalin and the micrographs show that a change has taken place on a sub-microscopic scale. It is possible that the protein adheres more readily

to the rough surface. The roughening of the surface may also explain why a stronger solution of tannic acid produces agglutination of the cells. Judging by the electron micrographs it appears that the protein covers the cell wall in shapeless masses, which produce the mottled appearance.

I wish to express my gratitude to Mr. D. Dresser, Department of Zoology, University of Edinburgh, for preparing the red blood cells and also to the Melville Trust for Cancer Research who equipped the electron microscope laboratory in which the experiments were carried out.

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Effect of Adrenalectomy on the Hormone Content of the Thymus in the Rat

A LARGE number of publications have dealt with the influence of the adrenal cortex on the morphology of the thymus. Adrenalectomy has been found to result in an enlargement of the thymus^{1,2}. The administration of various preparations of adrenal cortex (in large amounts) resulted in atrophy of the thymus. This was confirmed with purified cortico-adrenal extract³, cortisone⁴, dehydrocorticosterone⁴ and deoxycorticosterone⁴. The same effect could be obtained with adrenocorticotrophic hormone⁵. Since the active fraction of the thymus can be obtained in a purified form⁶ and since a minute quantity of this fraction can be bioassayed⁷, we thought it of interest to investigate the effects of adrenalectomy on the thymus by these techniques.

50 male rats of 120–160 gm were used. They were divided in groups of 5 animals and operated as follows:

(1) Bilateral adrenalectomy, three groups:

(a) Control,

(b) 200 µgm of deoxycorticosterone acetate subcutaneously daily,

(c) 200 µgm of cortisone acetate daily.

(2) Thymectomy, one group.

(3) Thymectomy, following 5 days later by adrenalectomy. The animals were autopsied 6 days after the adrenalectomy, that is 11 days after the thymectomy.

(4) Sham thymectomy and adrenalectomy. The thymus and the adrenals were removed and replaced.

Table 1. HORMONAL ACTIVITY OF THYMUS, LYMPH NODES AND SPLEEN IN THE RAT

| Group | Activity (units per gm. of fresh organ) | | |
|------------------------------------|---|------------|------------|
| | Thymus | Lymph node | Spleen |
| Normal males | 62.5 ± 5.6 | 20.0 ± 4.0 | 17.0 ± 4.0 |
| Thymectomized | — | < 6 | < 4 |
| Adrenalectomized | 33.0 | < 10 | < 6 |
| Adrenalectomized and thymectomized | — | < 4 | < 4 |
| Adrenalectomized + DOC | 79.0 | 14.0 | 10.8 |
| Adrenalectomized + cortisone | 30.4 | < 4 | < 3 |
| Sham operated | 57.4 | 22.0 | 14.8 |

without interruption of their vascular connections.
(5) The remaining 20 animals were autopsied as controls.

In every group, at autopsy, the thymus (except, of course, groups 2 and 3) the spleen and the lymph nodes (jugular and mesenteric) were pooled and extracted by the method of Bezonoff and Comas⁸. These extracts were bioassayed by the method of Comas⁷. The activity found was expressed in guinea pig units per gram of fresh organ weight.

The 20 normal animals were divided in 4 groups of 5 animals each. Thus we obtained 4 normal extracts for control.

As can be seen from Table 1, an active extract could be obtained from the normal thymus and a less-active one from lymph nodes and spleen. Yet thymectomy resulted in an important decrease in the activity of lymph nodes and spleen. Thus it can be asserted that the hormone found in these organs came from the thymus. This could also be concluded from previous experiments on guinea pigs⁹.

Adrenalectomy resulted in a decrease of the activity of the thymus to less than half the normal level. In both lymph nodes and spleen, the activity decreased too, yet it cannot be said whether this decrease was parallel, since the activity fell below measurable limits.

These effects of adrenalectomy could be prevented almost completely by repeated injections of deoxy corticosterone in normal amounts. Cortisone has no comparable influence.

The difference between the influence of deoxy corticosterone and cortisone is still more obvious if results are recalculated with a weight correction. Indeed the relative weight of the thymus in our animals was (parts per thousand):

2.5 ± 0.3 in normal rats

3.3 ± 0.5 in adrenalectomized rats

5.4 ± 0.6 in adrenalectomized rats treated with deoxy corticosterone

3.2 ± 0.4 in adrenalectomized rats treated with cortisone

Thus, for the total activity of the thymus in every group, we have

In normals 23 units per 100 gm. living weight

In adrenalectomized

15 units per 100 gm. living weight

In adrenalectomized deoxycorticosterone treated

35 units per 100 gm. living weight

In adrenalectomized cortisone treated

14 units per 100 gm. living weight

It can be concluded that the hormonal activity of the thymus is conditioned by the adrenal cortex to a large extent. This influence of the adrenal cortex upon the thymus is supported by the deoxy corticosterone fraction. In other words, it seems to be connected with the mineralocorticoid and prothymogenic effects of the adrenal cortex.

I am grateful for the technical assistance of A. Moser.

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Quantitative Changes in γ -Aminobutyric Acid Induced by Low Temperature in Rice Plants

AMONG the free amino-acids occurring in higher plants increasing attention is being paid to γ -aminobutyric acid, although it has not been identified as a constituent of proteins. The significance of this compound in the nitrogen metabolism of plants is clearly indicated by the work of Steward and collaborators^{1, 2}, and also by our recent studies on rice varieties exhibiting various degrees of resistance against the 'browning disease' of rice ('*brusone*,' '*aki-ochi*')

Our experimental material consisted of the brusone-resistant *Precoce Allorio* and brusone-susceptible *Dunghan Shali* rice varieties. The experiments were carried out in the field on limeless soils. The shoots of rice plants were removed shortly after flowering, the exudate yielded by guttation was collected and analysed for free amino-acids by paper chromatography³ in a solvent system containing butanol, acetic acid, and water in the proportions 2:1:1. γ -Aminobutyric acid was not detected in the exudate of *Dunghan Shali* (susceptible variety) for some days after a period at a low temperature (12–14°C) and of unfavourable light relation. A similar decrease in γ -aminobutyric acid did not occur in *Precoce Allorio* which is regarded as a variety resistant to brusone. The content of γ -aminobutyric acid of both varieties was similar and constant in rice plants kept at normal temperatures (20–22°C). The experiments were repeated several times with the same results (Fig. 1).

When, due to bad weather, the temperature of the inundation water and of the soil drops, the incidence of disease is higher. Therefore, low temperature is regarded as one of the main factors increasing the susceptibility of rice plant to brusone⁴. It seems possible that the detection of resistant varieties by

means of some chemical characteristics will yield a reasonable tool which might substitute the long and empirical work of plant breeders.

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BIOLOGY

Plastron Respiration in the Eggs of *Drosophila* and other flies

It has long been known that the conspicuous projections near the anterior end of the eggs of *Scopeuma*, *Drosophila*, and other flies are concerned in respiration, and the projections have been called respiratory horns. The site of entry of oxygen into the horn has not previously been determined, but where not explicitly stated it has been implied that oxygen enters through holes in the distal end of the horn. Reaumur¹ regarded the respiratory horns of *Scopeuma* as floats that served to prevent the submergence of the eggs and so their asphyxiation. A similar function has been postulated for the respiratory horns of *Drosophila* by Wigglesworth and Beament². However, the eggs of *Scopeuma stercorarium* L. and *Drosophila melanogaster* Meig., as well as those of many other species with similar respiratory horns, are heavier than water even when the chorion and plastron are air-filled and besides are normally stuck to the substrate: they do not float if submerged, when under natural conditions they might be washed away from the larval food supply. Portions of cow pats containing eggs of *Scopeuma* and *Hebecnema umbratica* Meig. were repeatedly submerged in water, but the eggs were never detached. Of course these eggs and those of *Drosophila* and other species can be suspended from the surface film if they are freed from their attachment to the substrate and a line of contact with the water and air is established. Under these conditions their centres and buoyancy and gravity are such that the tips of the respiratory horns often project above the surface film.

The term plastron has been restricted to describe a gas film of constant volume and an extensive water-air interface. Such films are held in position by a system of hydrofuge structures and are capable of resisting water under pressure. In well-aerated water a plastron enables the insect to remain immersed indefinitely, when it obtains the oxygen it requires from the ambient water. What was known of plastron respiration in insects was summarized by Thorpe³ in 1950. Since then the plastron method of respiration has been found in a variety of insect pupae^{4, 5} and now in the eggs of *Sepsis violacea* Meig., *Drosophila melanogaster* Meig. and other species of the genus, *Musca autumnalis* Deg., *Hebecnema umbratica* Meig., *Scopeuma stercorarium* L., and other flies.

A detailed account of the structure of the respiratory horns of the eggs of *Drosophila*, *Scopeuma* and other flies will be published elsewhere. In all the

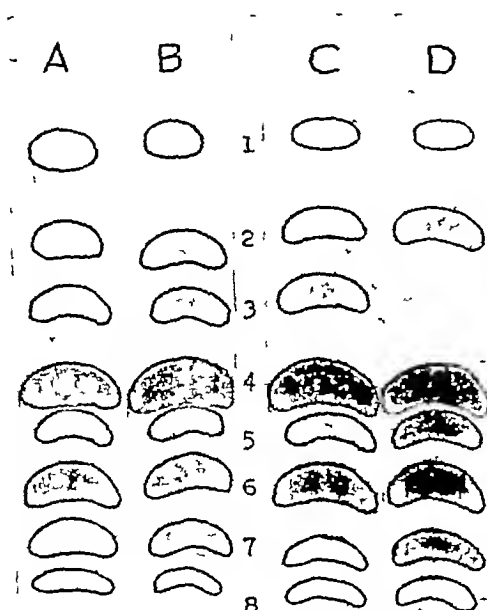


Fig. 1. A, *Precoce Allorio* (control), B, *Precoce Allorio* (low temperature), C, *Dunghan Shali* (control), D, *Dunghan Shali* (low temperature).

1, leucine, 2, valine, 3, γ -aminobutyric acid, 4, alanine, 5, glutamic acid, 6, aspartic acid + serine + glutamine, 7, histidine + arginine, 8, cyst(e)ine.

surface of most of the respiratory horn consists of an open hydrofuge meshwork that provides a large water air interface, as shown in Figs 2 and 3. At the base of the respiratory horn the air in the plastron meshwork is continuous with the air film contained between the vertical columns connecting the inner and outer laminae of the chorion (Fig. 4). Wigglesworth and Beament² claim that in *Drosophila* the air is contained in the vertical columns and not in the spaces between them. This claim is based upon the appearance of eggs injected with cobalt sulphide. When dipterous eggs are heavily injected with sulphide, the sulphide fills the spaces between the columns, but when they are lightly injected the sulphide adheres to the surface of the columns so that at first sight the columns themselves appear to be impregnated with the sulphide. The vertical columns of the chorion do not contain air in any of the dipterous eggs examined by me (Syrphidae, Sphecidae, Sepsidae, Drosophilidae, Muscidae, Cordulidae).

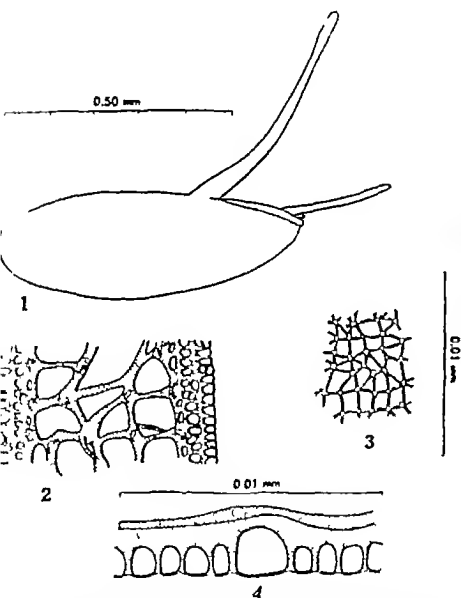


Fig. 1. Egg of *Drosophila gibberosa*, a species with two pairs of respiratory horns. Fig. 2. Part of a longitudinal section of the larger respiratory horn of *Drosophila gibberosa*. Fig. 3. Surface network of part of apical half of respiratory horn of *Drosophila gibberosa*.

Fig. 4. Section through chorion of *Drosophila melanogaster*.

Besides having a sufficient surface area, if a plastron is to be an efficient respiratory adaptation it must resist both wetting at pressures to which it is normally subject in nature and loss of water proofing from surface active materials. It was found that the plastron of many species of flies (*Sepsis*, *Drosophila*, *Musca*, *Hebecnema*, *Scopema*) resists in water a hydrostatic pressure of 3 feet for more than 24 hours, and the plastron of some species of *Drosophila* resists an excess pressure of 1 atmosphere for over 30

minutes. The plastron of none of the three species is wetted even when the contact angle is reduced by surface active materials to 50°–55°, which corresponds to a reduction of the surface tension of water to about 25 dyne/cm.

Insects with a plastron are restricted to well aerated waters such as rapidly flowing streams since a plastron is also a means of extracting oxygen from the tissues if the oxygen pressure of the environment falls below that of the tissues. The plastron method of respiration therefore seems unlikely to be found in an environment such as relatively fresh cow dung, where reducing conditions probably sometimes occur. However, the respiratory horns bearing the plastron project above the crust of the cow pat and provide a direct route for the entry of oxygen into the layer of air held beneath the relatively impermeable chorion. The significance of the plastron immediately becomes apparent when cow pats are observed in the rain: when it rains a rapidly moving and well aerated layer of water flows over the cow pat and over the respiratory horns. The incubation period of the eggs of *Scopema* and *Hebecnema* is only two to three days and thus in a rainy period much of the incubation period may be passed beneath a layer of water.

The respiratory horns of dipterous eggs are adapted both for the extraction of oxygen dissolved in the water and for atmospheric respiration. In water they provide a relatively enormous surface area for diffusion, and their structure is such that they do not collapse under the hydrostatic pressures to which they are normally subject. When the egg is not covered with water, the respiratory horns do not involve water loss over an enormous surface area because the connection between the plastron and the layer of air in the chorion is relatively restricted. The respiratory horns of dipterous eggs are thus structures that enable the immobile eggs to meet the contradictory demands presented to them by environments that are alternately dry and flooded.

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¹ Réaumur M. de "Méthodes pour servir à l'histoire des Insectes" 4 (1738).

² Wigglesworth, V. D., and Beament J. W. L. *Quart. J. micr. Sci.*, 91 129 (1940).

³ Thorpe W. H., *Biol. Rev.* 25 344 (1950).

⁴ Hinton H. E. *Proc. Roy. Soc. B* 147 90 (1957).

⁵ Hinton H. E. *Proc. Tenth Int. Congr. Ent.*, 1 643 (1955).

A Seasonal Sex Difference in the Infestation of Rabbits with the Nematode *Trichostrongylus retortaeformis* (Zeder, 1800)

LARGER numbers of nematodes in male than in female hosts have been recorded for *Ascaridia galli* in chickens¹ and for *Aspiculuris tetraptera* in mice², with *Syngamus trachea* in partridges, on the other hand, infestations are more severe in females than in males.³ The present results, relating to *Trichostrongylus retortaeformis* in European wild rabbits, *Oryctolagus cuniculus* (L.), are of interest in indicating a seasonal change in host resistance: males being more resistant in summer and females in winter.

The abundance of *T. retortaeformis* was studied in 1072 rabbits collected during one year at Gwavas Forest some 30 miles south west of Napier in the North Island of New Zealand; supplementary samples (Table I) were obtained from Gwavas and elsewhere in

Table 1

| | Locality and date sample collected | No of Rabbits | | Mean No worms in. | |
|---------------------------|------------------------------------|---------------|---------|-------------------|----------------|
| | | males | females | male rabbits | female rabbits |
| Winter (June-Aug) samples | Gwavas, June 1956 | 20 | 19 | 124 | 57 |
| | Gwavas, July 1956 | 18 | 10 | 62 | 51 |
| | Gwavas, Aug 1956 | 52 | 50 | 72 | 52 |
| | Gwavas, July 1958 | 74 | 45 | 59 | 42 |
| | *Waikoloi, Aug 1958 | 44 | 51 | 374 | 63 |
| Summer (Nov-Jan) samples | Gwavas, Dec 1955 | 16 | 6 | 24 | 73 |
| | Gwavas, Jan 1959 | 21 | 31 | 37 | 54 |
| | *Duntroon, Nov 1953 | 10 | 15 | 70 | 210 |
| | †Rose Is, Nov 1954 | 40 | 59 | 185 | 382 |
| | †Enderby Is, Nov 1954 | 38 | 51 | 65 | 283 |
| | Kourarau, Jan 1959 | 18 | 17 | 80 | 194 |
| | Taupo Jan 1959 | 14 | 12 | 30 | 128 |
| | *Lake Tekapo, Dec 1958 | 19 | 18 | 15 | 31 |

* South Island localities

† Auckland Island Group, some 250 miles south of Stewart Island.

subsequent years. Worm abundance was assessed by a dilution-sampling technique⁴, the values obtained and shown in Fig 1 and Table 1 represent one tenth the number of worms present.

Fig 1 illustrates monthly variations in the mean number of worms in full-grown (> 900 gm paunched weight) male and female rabbits collected at Gwavas during 1950-51. During March-September, levels of infestation were higher in males than in females, but this relationship was reversed during October-February, a period that covers the middle and end of the rabbits' breeding season. The differences between the sexes were statistically significant at the 5 per cent level in June, July and in early August, when males had the higher infestations, and in December and in January, when females were the more heavily infested. The supplementary samples from Gwavas and elsewhere in other years (Table 1) conform to the general pattern found at Gwavas in 1950-51, males having the higher infestations in winter and females in summer. The seasonal changes illustrated in Fig 1 are therefore both regular and widespread.

Rabbits of both sexes frequently graze over the same ground, so it is unlikely that females ingest substantially more worm larvae than do males in

summer or that males ingest more than females in winter. The differing levels of worm infestation are therefore interpreted as due to differences in host resistance rather than as due to differences in the host's opportunity to acquire infestation.

In districts where *T. retortaeformis* is abundant, the presence of adult rabbits with no worms other than infective larvae indicates recent self-cure⁵. At Gwavas in 1950-51, the proportion of uninfested male rabbits was much higher from October to December (17 per cent) than in the preceding or following 3-month periods (0 and 4 per cent respectively), and this implies that self-cure was important in causing the rapid decline in the level of infestation in male rabbits in October (Fig 1). Only 2 of 52 female rabbits showed self-cure during the period October-December. It is concluded therefore that the March-September trend towards high levels of infestation was terminated in October by the onset of self-cure in male rabbits and that some factor prevented self-cure in females. The October sample contained only 13 female rabbits and the apparent low level of infestation is probably fortuitous, since, unlike the males, the females were heavily infested again in the following months.

In young females (900-1100 gm paunched weight), infestations were higher in pregnant than in non-pregnant animals, the difference being significant at the 1 per cent level. Sex of host had little effect on the abundance of *T. retortaeformis* in sexually immature rabbits (< 900 gm paunched weight). It seems therefore that the high levels of infestation in female rabbits in summer is associated with pregnancy. A comparable situation occurs in sheep where a rise in nematode egg counts is associated with pregnancy and lactation⁶.

It is difficult to explain why male rabbits are more heavily infested than females in winter. The establishment of *Cysticercus crassicolis*⁷ and the growth of *Hymenolepis diminuta*⁸ in rats were favoured by male sex hormones, and something similar may occur with *T. retortaeformis* in rabbits, the effect being masked in summer by the lowered resistance of pregnant and lactating females.

The differing levels of worm infestation shown in Table 1 are due to two main factors: sex of host (involving differences in host resistance only) and locality of collection (involving differences in host resistance and in the availability of worm larvae, the latter resulting from variations in climate, vegetation and host density). It is interesting that the sex-linked differences in levels of infestation are as great as the locality-linked ones even though the localities differed widely in climate, vegetation and density of rabbits. This emphasizes the importance of density of rabbits in determining levels of nematode infestation in wild animals. The present results indicate the necessity of recording sex of host in parasitological studies involving wild or laboratory animals.

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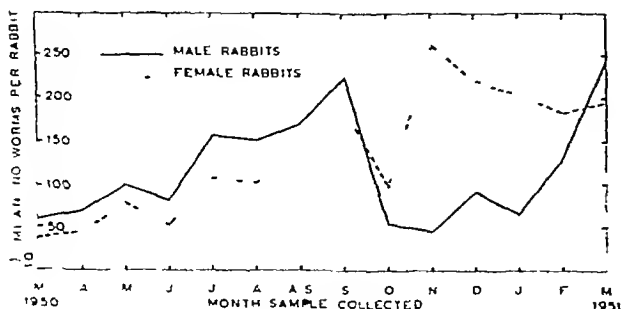


Fig 1 Mean numbers of worms per host in 717 full-grown male and female rabbits collected at Gwavas between March 1950 and March 1951. Samples were obtained at four weekly intervals, not calendar months. The average number of rabbits per sample was 31 for males and 20 for females, each sample contained more than 10 animals of each sex, except that only 9 males were obtained in October and 5 in November.

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 Campbell, D. H., *Science*, 89, 415 (1939)
 Addis, C. J., *J Parasit*, 32, 574 (1946)

Sodium Regulation in the Blood of Parr and Smolt Stages of the Atlantic Salmon

THE seaward migration of the salmon (*Salmo salar*) which coincides with the parr smolt transformation involves the solution of important osmotic and mineral regulation problems by the fish. The lack of tolerance for salt water at the parr stage has been noted previously.¹ However neither the capacities for mineral regulation of this stage nor their probable shift in the smolt have been subjected to an analysis made more desirable by the fact that, like the endocrinological changes which occur at the same time² they may be causally connected with migration itself.³

Working at Laholm in the South of Sweden we were able to investigate the regulation capacities for sodium of the young salmon in the parr stage as well as those of one and two year-old smolts reared under the same conditions in running water of the Lagan stream. Moreover an opportunity arose which allowed us to conduct simultaneously similar experiments on individuals migrating downstream captured in the nearby Ätran stream in water having the same temperature (0.3°C). The blood plasma of the animals in 10 λ quantities was subjected to micro sodium analysis by means of flame spectrophotometry.

When abruptly transferred from fresh water to full sea water (at the same temperature) none of the two year-old parrs survived for more than 26 hours. The living individuals analysed showed, as time went on, a rapidly rising sodium concentration in their blood. None of the individuals in the smolt stage whether one or two year-old died when submitted to the same abrupt change in salinity. The sodium concentration in their blood remained nearly constant in the days following the transfer. The smolts trapped on their downstream migration still showed parr characteristics to a certain degree. Two out of ten died within 18 hours when abruptly transferred to sea water. A further three showed great distress. The sodium level in the blood of the surviving individuals increased strongly, the normal level being however restored 4-5 days later. Obviously they were in a transitory condition which also includes the sodium regulation of their blood. Similar results were obtained in other experiments.

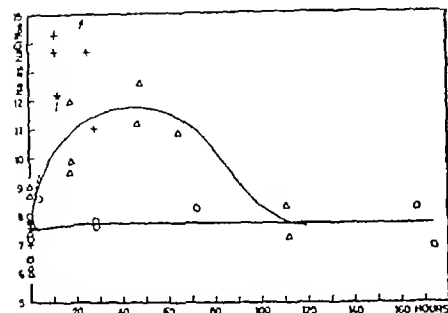


Fig. 1. Variations of the sodium concentration of the blood after abrupt transfer from fresh water (0.3°C) to full sea water (0.3°C). +, two-year-old parr; O, two-year-old smolt; Δ , wild smolt caught on downstream migration.

It has been observed in Hölle during the parr smolt transformation that a large percentage of the smolts die when kept back in fresh water. The osmotic capacities of the smolts in fresh water seem to be impaired at the time when the parr smolt transformation occurs. Wide individual variation in the sodium level of wild smolts in fresh water is obvious from Fig. 1. Details of this and previous work will be published elsewhere.

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Release by Flight Exercise of a Chemotropic Response from Photopositive Domination in a Scolytid Beetle

ONE of the remarkable features of bark beetles and ambrosia beetles is their power of discovery and selection of host tree material. From a mass of varied material in a forest they select and bore into specific parts of specific trees usually only when those trees are under stress of age, environment injury or encroaching death. Certain of the ambrosia beetles show a strong preference for logs that have 'ripened' for a period of some weeks or months after being felled. The species *Trypodendron* (*Trypodendron*) *lineatum* Oliver (Scolytidae), is one of these.

The present communication is a preliminary report on an aspect of behaviour in *T. lineatum* that appears to be a key to elucidating the host finding process in this insect and perhaps other Scolytids.

Trypodendron, on issuing from its overwintering quarters in the litter of the forest floor, takes to flight and arrives in large numbers at partly 'ripened' logs of coniferous species. It appears to accomplish this result without expending time and effort on unsuitable material. Theoretical considerations of the known physiology of trees and behaviour of insects, suggested that odour must be examined as a possible clue that these beetles use in host discovery and selection. Studies were undertaken to determine whether they show any kinetic or directional response to airborne odours from attractive wood. Many failures under illuminated conditions to detect decisive or even statistical differences of activity in beetles exposed to wood odour led to the conclusion that the failure lay not in the environmental conditions nor in the method of observation, but in the photic orientation responses that dominated behaviour at a particular time. This conclusion led to the search for a natural

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subsequent years. Worm abundance was assessed by a dilution-sampling technique⁴, the values obtained and shown in Fig 1 and Table 1 represent one tenth the number of worms present.

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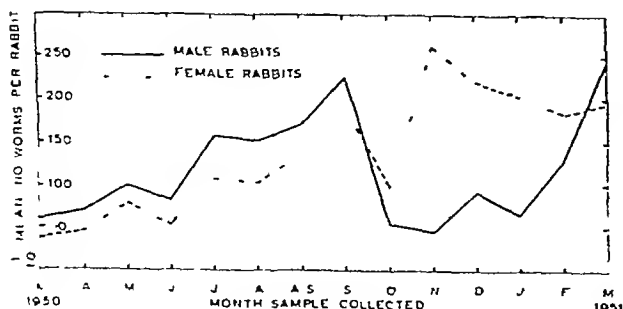


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but in tonic smooth muscles the diameter is very variable (150–1000 Å in *Mytilus*, 150–500 Å in *Gryphaea*). This range of diameters is seen in the cross section of any fibre and may simply be due to variations between filaments. An alternative explanation is that the filaments are discontinuous along the fibre each filament has the shape of an elongated spindle, and (these being smooth muscles) the filaments are not transversely aligned.

There are large numbers of thin filaments (Fig. 1) and bridges link them to the thick ones (Figs. 2, 3). The axial spacing of the bridges is about the same (100–200 Å) as in similarly prepared sections of striated and *Loligo* muscles (see electron micrographs in refs. 1 and 2). Again as in striated muscles the bridges may belong to the thick filaments, for in preparations of the oyster muscle from which all the thin filaments have been extracted (by a fixative containing too little salt) bridges can be seen on the thick filaments.

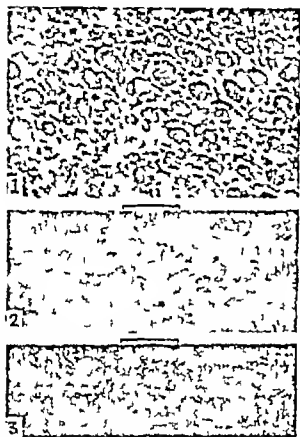


Fig. 1. *Gryphaea* transverse section. Fig. 2. *Gryphaea* longitudinal section. Fig. 3. *Mytilus* longitudinal section (Scale: 1000 Å).

Evidence that the thick filaments in the *Mytilus* muscle do not shorten when the muscle shortens comes from measurements which were made of their diameters in equivalent fibres in pairs of muscles which had been fixed at different lengths. Although the short muscles were as little as one third the length of their partners, they showed no differences in filament diameters or in the relative numbers of filaments in each size category. (It should be noted that the filaments are thick enough to be measured sufficiently accurately.) These thick filaments therefore do not shorten and they must be discontinuous along the fibre. There is ample evidence that they remain straight and parallel to the fibre axis. Secondly, it was argued that if the thick filaments were continuous from one end of the fibre to the other, and contracted then transverse sections through stretched and shortened fibres should show considerable and predictable differences in the numbers of filaments per unit area: thus a fibre with an initial cross sectional area of a would, after shortening

by 60 per cent show the same number of filaments distributed over an area of $2.5a$ if the fibre remained at constant volume. Making such a comparison we find that there is in fact no consistent difference in the numbers of filaments per unit area in long and short muscles, and never a difference on the scale predicted. All these results support the view that the thick filaments are discontinuous and do not contract, but instead change their positions as they slide. Whether or not this is also true of the thin filaments is still an open question. But we have observed in transverse sections through extended fibres of the oyster muscle that the thin filaments are absent around the thickest of the thick filaments but present around the others: in shorter fibres all the thick filaments are surrounded by thin ones. This could mean that the thin filaments are discontinuous and, in an extended muscle do not reach as far as the middle (thickest) part of the thick filaments: a state of affairs which would be comparable to that in the H zone of a striated muscle.

By analogy with the contractile mechanism in striated muscles it could be assumed that in these tonic smooth muscles of lamellibranch molluscs the tension developed during the active state is due to the formation of linkages between thick and thin filaments. The next problem will be to explain in structural terms the observation that in such smooth muscles the decay of tension can be two orders of magnitude slower than that of the active state: their capacity for prolonged tonic contraction may well be due to this extremely slow decay of tension.

The muscles were held taut at a defined length and extracted with water glycerol, then equilibrated with 0.1 M potassium chloride at pH 6.8 and fixed at 0°C for 1 hr in a 1 per cent osmium tetroxide solution buffered at pH 7.0 or 7.4 and containing 0.4 M sodium chloride (approximately isosmotic with sea water). After additional staining with phosphotungstic acid (in 100 per cent ethanol) the fibres were embedded in Araldite and sectioned. Similar results were obtained when living muscles were prepared by the same method: but the removal of material soluble in water glycerol greatly clarified the appearance of the contractile apparatus.

We understand from Dr. Andrew G. Szent-Györgyi that a paper describing the presence of two kinds of filaments in tonic smooth muscles of lamellibranch molluscs has been submitted for publication in the *Journal of Ultrastructure Research* by Philpott, Kahlbrock and Szent-Györgyi.

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ENTOMOLOGY

Relationship between Larval and Pupal Periods of some Lepidopterous Insects

EXPERIMENTS have been carried out in the United Kingdom and the United Arab Republic (Egypt) to show the effect of population density on the silver Y moth, *Plusia gamma* L and the cotton leaf worm, *Prodenia litura* (Fab) respectively. In these experiments two parallel cultures of solitary and crowded conditions were maintained for each species.

When discussing the results obtained, an interesting phenomenon attracted our attention. That is, a negative relationship exists between the larval and pupal periods of each species irrespective of sex and culture. In other words, the longer the larval period, the shorter the pupal period and *vice versa*. This phenomenon occurred in both solitary and crowded cultures as shown in Fig 1. Results also showed that the larval period was longer in the solitary culture than in the crowded culture, while the opposite occurred in the

differences between solitary and crowded conditions for larval and pupal periods were significant.

It has been found that crowding accelerated pupation by the shortening of larval period of some Lepidoptera¹ and this was probably due to competition in the crowded culture. Accordingly, it may be suggested that the longer pupal period in the crowded condition and the shorter period in the solitary treatment might be a result of the negative relationship between the larval and pupal period. However, explanation of the nature of this negative relationship implies the need for further physiological investigations of both larvae and pupae of each culture.

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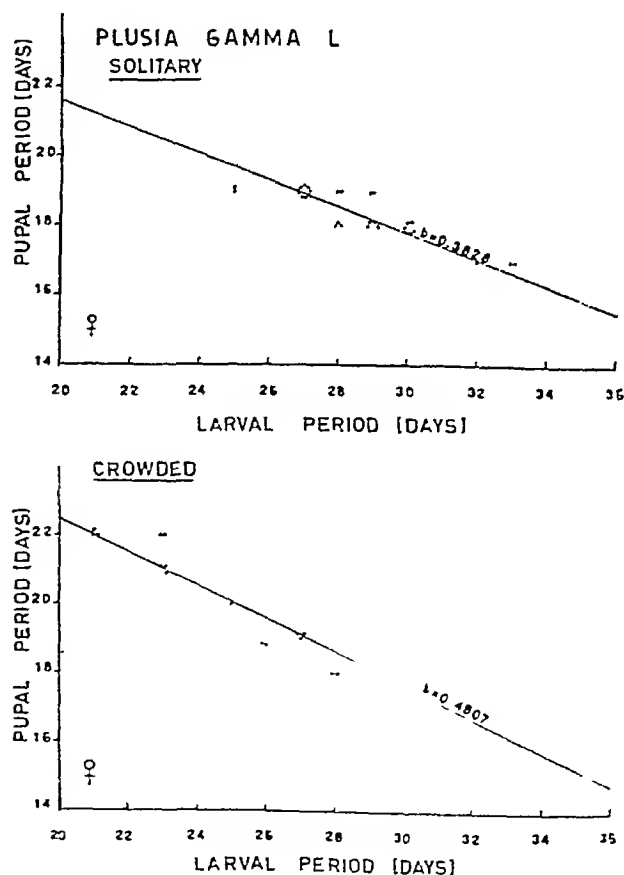
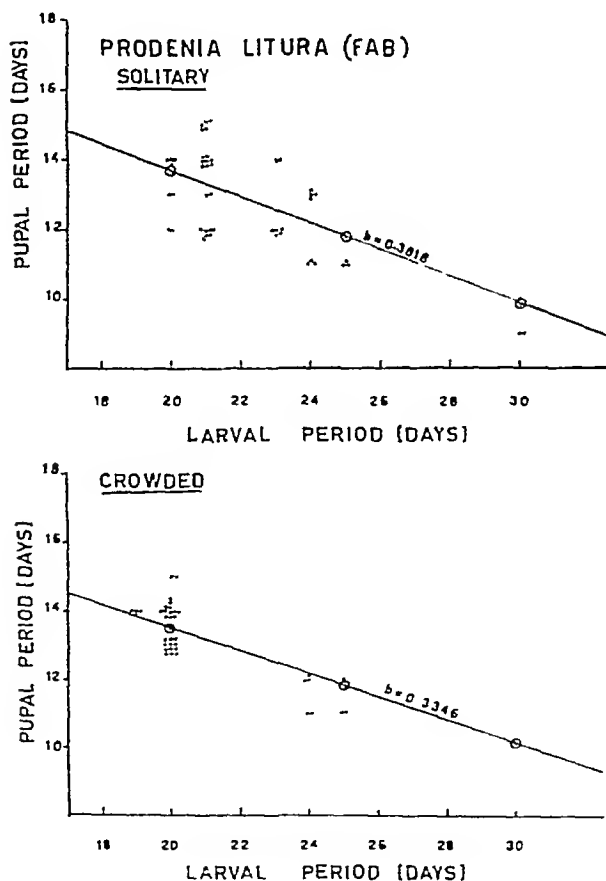


Fig 1

pupal period as the solitary ones had the shorter period (Table 1). Statistical analysis showed that the

Table 1

| Species | Larval period (days) | | Pupal period (days) | |
|------------------------------|----------------------|---------|---------------------|---------|
| | Solitary | Crowded | Solitary | Crowded |
| <i>Plusia gamma</i> (female) | 28.3 | 26.2 | 18.3 | 19.5 |
| (male) | 29.0 | 27.2 | 18.8 | 19.5 |
| <i>Prodenia litura</i> | 23.3 | 22.4 | 12.7 | 13.1 |

Possible Role of Glycerol in the Winter-Hardiness of Insects

DURING investigations into the carbohydrases of insects¹ in the winter of 1957-58 it was found that the macerated tissue of the dormant larvae of the wood-boring insect of the species *Melandrya striata*, found in felled wood of *Saxx amygdaloides* Anderss, contained a considerable proportion of glycerol as revealed by paper chromatography. This preliminary obser-

vation indicated that glycerol might be acting as an anti freeze² a view supported by the observation that the larvae and the adult insects of *M. striato* did not contain glycerol during summer

The dormant black carpenter ants (*Camponotus pennsylvanicus pennsylvanicus* var.) and their eggs found in Minnesota have now been shown to contain, in winter time, about 10 per cent of glycerol based on the weight of the dormant ants, the water content of the dormant ants was 55 per cent. Chromatographic analysis also indicated that the ants contained glucose and an unidentified oligosaccharide, whereas the eggs contained no such compounds. The same species of ants in an active state obtained in November, 1958, from Maryland contained glucose and fructose but no glycerol. That the glycerol is probably playing a major part in the winter hardiness of this species of carpenter ants is indicated by the observation that when the Minnesota ants were brought out of their state of dormancy by slowly allowing them to attain room temperature (20-25°C), they became active and, after about three days, glycerol could no longer be detected in their macerated tissue. When the ants were returned to the dormant state, by cooling them slowly and keeping them for about 6 days at 0-5°C, glycerol was again found to be present in their tissue. We have taken the Minnesota ants out of, and returned them to, a state of dormancy 3 times by alternate warming and cooling. During induced dormancy the ants always contained glycerol and each time they resumed an active state the glycerol disappeared.

The glycerol was isolated from the Minnesota ants and from their eggs by extracting the macerated tissue with methanol. After purification by sheet paper chromatography, using pyridine/ethyl acetate/water (2:5:7) as the solvent, the glycerol readily formed a tri p nitrobenzoate, m p and mixed m p 196° (after recrystallization from acetone).

The active ants from Maryland seemed to show some resistance to induced dormancy by cooling since they showed slight movement even at 0 to 5°C whereas the Minnesota ants, treated in the same manner, were motionless. Nevertheless after keeping the Maryland ants at 0-5°C for 30 days they contained glycerol.

The dormant larvae of the European corn borer (*Pyrausta nubilalis*) have also been found to contain glycerol.

Although glycerol may well play a major part in the winter hardiness of insects it is evidently not the only agent which enables insects to survive the effects of freezing temperatures for we have found that the larvae of the wood boring insect *Porandria brumnea*, and those of *Osmoderma crenicollis*, do not contain glycerol.

It is of some interest to note that the finding of glycerol in insects offers a biological analogy for the technique of preserving bone marrow and semen in glycerol at low temperatures.

We are grateful to Mrs. Hewitt Fletcher, Sandy Springs, Maryland for a supply of notho carpenter ants. We also thank Dr. E. F. Cook, Dr. A. C. Hodson and Dr. F. G. Holdaway, Department of Entomology, University of Minnesota, for their assistance and interest in this work, and the U.S. Department of Agriculture for their support.

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Mode of Egg Laying in Tingidae (Hemiptera)

According to Imms¹ tingid bugs insert their eggs into plant tissue. Patel and Kulkarny², who studied the hibernation of the brinjal tingid, *Urentius echinus* Dist., and Sharga³ and Samuel⁴ who studied the egg laying habit of *Monanthio globulifera* Wlk., merely state that the eggs are inserted into the leaf tissue, none of these workers describes the actual way in which the eggs are thrust into the plant tissue and what precedes the deposition of eggs. The purpose of the present communication is to describe an apparently unknown series of actions on the part of the female tingid, culminating in the deposition of an egg, which is invariably preceded by extensive probing and actual marking by the rostrum.

The tingids included in the present study are *Galeatus* sp. on *Borlaria cristata* *Urentius echinus* Dist. on brinjal and *Monanthio globulifera* Wlk. on *Coleus* sp.

The three species insert their eggs into the tissue of tender portions of their host plants. The ovipositor is well developed dagger shaped and pointed at the tip. While ovipositing, the female bug in all these species follows a very uniform procedure, the exact significance of which is not clearly understood. Before depositing an egg, the female moves about on the surface of the leaf or tender twig all the time probing by means of the tip of her rostrum, and occasionally even inserting the stylets into the plant tissue and drawing them out. Finally, perhaps on finding a suitable site for egg laying the whole length of the stylets is driven deep inside the plant tissue.

With her stylets still inside the plant tissue the female moves her body forward by changing the inclination of the legs, which were formerly inclined backwards and now lean forwards carrying the body with them. Then the stylets are withdrawn from the plant tissue, apparently with some difficulty. The ovipositor, as a whole is slowly drawn out from underneath the abdomen so that it almost assumes a position perpendicular to the abdomen. The tip of the ovipositor begins probing, obviously in search of the puncture made by the stylets, in order to insert an egg, and unless the bug locates this puncture with the tip of the ovipositor she does not lay an egg, and moves on to find another suitable place. The ovipositor is inserted through the same puncture and the entire length is driven into the plant tissue. Next a series of alternate distentions and contractions of the abdomen and a sort of pumping action culminate in the deposition of an egg and immediate withdrawal of the ovipositor from the plant tissue. During the process of egg laying the abdominal tip is very near the surface of the plant and the body is inclined at 30° to the plant surface.

The opercular end of the egg is just visible at the surface of the plant. The entire process from probing with the rostrum to the withdrawal of the ovipositor takes 3-4 minutes.

The significance of the rostrum in oviposition in these tingids is not clearly understood.

Further work on the egg laying habit in different forms of the group and the significance of this process is being pursued.

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PATHOLOGY

Aneuploid Deoxyribonucleic Acid Content of Human Carcinomas

THE basic question of whether primary human malignant tumours consist of euploid or aneuploid cells has so far remained unanswered. It has been possible to determine the chromosome complement and deoxyribonucleic acid content only of human carcinomas with cells exfoliated in ascitic fluid^{1,2}, human carcinomas transplanted in rats and hamsters³ and carcinomas grown in tissue culture^{4,5}. This lack of information can be attributed to several technical difficulties. Chromosome counts on solid human tumours cannot be generally obtained since a pre-treatment with colchicine is impossible. The deoxyribonucleic acid measurement by the one-wave-length method has so far been limited to interphase nuclei⁶ in which the occurrence of deoxyribonucleic acid synthesis prevents any conclusions in regard to euploidy or aneuploidy.

This difficulty in interpreting the deoxyribonucleic acid data can be eliminated by selecting metaphases, anaphases or early telophases for the deoxyribonucleic acid determinations. The deoxyribonucleic acid content of these mitotic stages can be considered to yield the basic amount, since synthesis is completed before the cells enter mitosis. By choosing metaphases and telophases the deoxyribonucleic acid content of dividing cells is revealed. This eliminates the criticism that the observed abnormal values are limited to dying cells of necrotic areas, which do not contribute to the growth of the tumour.

The two-wave-length method of Patau has been applied for the deoxyribonucleic acid determination⁷. Each nucleus was measured twice. The average values are given in Fig. 1. Lymphocytes or polymorphs present in the same section as the tumour cells were used to obtain the deoxyribonucleic acid value of a diploid cell. The accuracy of the method applied becomes evident by comparing the ratio between lymphocytes and normal epithelium in metaphase and telophase, and between such metaphases and telophases. The ratios expected theoretically are 1.2, 1.1 and 2.1, respectively. The values actually obtained are in close agreement with the theoretical ones, namely 1.202, 1.099 and 2.1.

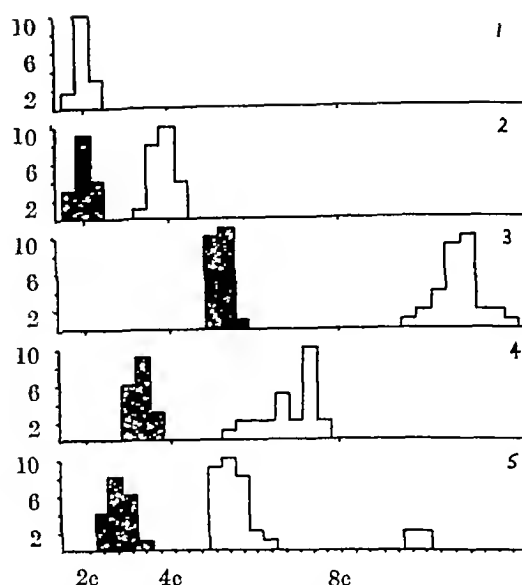


Fig. 1 The deoxyribonucleic acid content of telophase nuclei (solid) and of metaphase plates (outlined) of normal epithelium and adenocarcinomas of breast, bronchus and large intestine. The diploid amount of deoxyribonucleic acid is given by the interphase nuclei of lymphocytes. 1, Lymphocytes; 2, epithelium; 3, breast carcinoma; 4, bronchogenic carcinoma; 5, intestinal carcinoma.

The distribution of deoxyribonucleic acid in the cell population of lymphocytes, of normal intestinal epithelium and of carcinomas of bronchus, breast and large intestine is shown in Fig. 1. All three carcinomas consist of cells with aneuploid amounts of deoxyribonucleic acid. The deoxyribonucleic acid content of the breast carcinoma cells accumulate around a hexaploid value and the carcinoma of the intestine around a hyperdiploid modal value, whereas the deoxyribonucleic acid values of the bronchogenic carcinoma cells are scattered over a wider aneuploid range. The deoxyribonucleic acid content of the early telophases exhibits in both the carcinomas of the breast and bronchus a narrower range as compared with the values of the metaphase plates. This indicates that several of the aneuploid cells are unable to finish the mitotic cycle, a conclusion which is supported by the results obtained on human ovarian tumours⁸.

Cells with aneuploid deoxyribonucleic acid contents have so far been found in 25 carcinomas of the large intestine⁹, in 4 carcinomas of the stomach⁹, in 5 carcinomas of bronchus and 5 carcinomas of the breast. The aneuploid modal value and the spread of the deoxyribonucleic acid values around this value varies from tumour to tumour. No correlation between a particular aneuploid deoxyribonucleic acid amount and histological grade of malignancy has been observed. The only difference found so far was between benign polyps and adenocarcinomas of the intestine, the former having a normal diploid and the latter having an aneuploid deoxyribonucleic acid content⁹.

The results obtained on different carcinomas of man demonstrate that primary malignant epithelial tumours regularly consist of cells with an aneuploid deoxyribonucleic acid content. The aneuploidy of the viable dividing cells is clearly demonstrated by the presence of aneuploid deoxyribonucleic acid contents in metaphases as well as in anaphases or early telophases. It can be concluded therefore that primary carcinomas of man are aneuploid and that the results

obtained on ascites fluids^{1, 2} or on grafted tumours³ are comparable to the conditions present in the tumour of origin

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Effect of Bacillus Calmette-Guérin Infection on Transplanted Tumours in the Mouse

DURING the growth of certain transplanted tumours considerable hyperactivity of the reticulo endothelial system is observed.¹ Similar alterations are also found in the first stage of experimental infections suggesting that the host response to foreign tissue and some infectious agents is closely related. Agents such as endotoxins, zymosan, products of the tubercle bacillus, and Bacillus Calmette Guérin infection which enhance the activity of the reticulo endothelial system² and the capacity for antibody production³ also increase natural resistance to infection.⁴ In light of these observations, we have attempted to alter the growth and lethality of various experimental tumours by agents known to possess the common property of stimulating the phagocytic capacity of the reticulo endothelial system. One such agent, zymosan, has been demonstrated to increase significantly the regression rate of the mouse tumour sarcoma 180 (S 180) under certain conditions.⁴ The present report deals with the course of three transplantable tumours, S 180 carcinoma 755 (Ca 755), and Ehrlich ascites in mice infected with Bacillus Calmette Guérin.

Young, female Ha/ICR Swiss mice and C57 hybrid mice (bred by Dr J. J. Bittner, University of Minnesota) weighing approximately 18–20 gm., were injected intravenously with one mgm. Bacillus Calmette Guérin wet weight. The Bacillus Calmette Guérin (Phipps strain) was grown in either Santon's (supplied through the courtesy of Mr H. J. Henderson Phipps Inst., Phila Pa) or the Dubos liquid medium. Neither morbidity nor mortality attributable to Bacillus Calmette Guérin infection alone was observed. Infected animals appeared active and perfectly healthy. At selected intervals following Bacillus Calmette Guérin inoculation infected animals and appropriate controls were challenged with either solid tumour (S 180, Ca 755) implanted subcutaneously or by intraperitoneal injection of Ehrlich ascites cells.

Growth of S 180 in normal Ha/ICR Swiss mice is characterized by death of 85–90 per cent of hosts in two to five weeks, the remainder of the mice undergo spontaneous regression of their tumours. The effect of Bacillus Calmette Guérin infection on the mortality associated with growth of this tumour is presented in Table 1. In mice implanted with S 180 one day

Table 1. MORTALITY FOLLOWING S 180 IMPLANTATION

| Controls | Days between B.C.G. infection and tumour inoculation | | | | | |
|----------|--|------|------|------|-----|-----|
| | 1 | 7 | 14 | 19 | 25 | 67 |
| 68/70† | 13/15 | 3/12 | 0/12 | 0/30 | 0/5 | 0/0 |

† mortality/number per group

following infection the regression rate was normal whereas mice inoculated with the tumour seven days, or longer, after Bacillus Calmette Guérin infection showed definite protection. Of the groups at seven and nineteen days post infection, 70–75 per cent of tumours regressed. Mice inoculated with S 180 fourteen, twenty five, and sixty seven days following Bacillus Calmette Guérin infection were completely resistant to tumour growth. The tumours in Bacillus Calmette Guérin infected animals developed normally for the first seven to ten days and then began decreasing in size after the second week. The process of regression in animals infected with Bacillus Calmette Guérin was essentially similar to that observed in the few control mice which rejected their tumours. In a group of C57 hybrid mice implanted with S 180 fourteen days following Bacillus Calmette Guérin infection only one out of eight animals regressed. The implanted tumour, none of the tumours in the control animals regressed. The finding that C57 hybrid mice responded poorly to S 180 inoculation at a time when Swiss mice were completely protected correlates well with our unpublished observation that the C57 hybrid does not attain as high a degree of reticulo endothelial stimulation as Swiss mice following Bacillus Calmette Guérin infection.

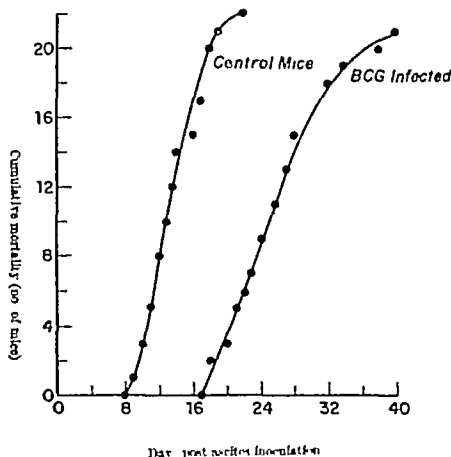


Fig 1 demonstrates the altered course of the Ehrlich ascites tumour in *Bacillus Calmette-Guérin* infected Swiss mice. The average survival time in uninfected controls was 14 days. In animals inoculated with *Bacillus Calmette-Guérin* eleven or thirteen days previously, it was 27 days. Ascites formation in infected animals was not inhibited, in fact, during the course of the enhanced survival time, these animals frequently developed hugely distended abdomens. Despite the presence of appreciable quantities of ascitic fluid, the infected animals remained healthy and active for a longer period than their corresponding controls.

Table 2 *Ca 755* IMPLANTED 17 DAYS FOLLOWING *Bacillus Calmette-Guérin* INFECTION IN C57 HYBRIDS

| | Average tumour diameter (cm) | | Per cent mortality B C G /Controls |
|---------|------------------------------|-------------------|------------------------------------|
| | 13 Controls | 10 B C G Infected | |
| 25 days | 2.04 | 0.82 | 0/0 |
| 33 days | 2.68 | 1.21 | 0/23 |
| 48 days | 3.56 | 2.39 | 0/92 |

B C G—*Bacillus Calmette Guérin*

Table 2 summarizes the results of experiments concerned with the growth of *Ca 755* in both normal and *Bacillus Calmette-Guérin* infected C57 hybrid mice. In addition to the slower growth of this tumour, the *Bacillus Calmette-Guérin* infected mice lived significantly longer and frequently showed advanced-to-complete regressive changes in their tumours prior to death. This retardation in *Ca 755* growth and increased survival time has also been observed in mice of a C57 inbred line following *Bacillus Calmette-Guérin* infection.

The beneficial effect of *Bacillus Calmette-Guérin* infection on the outcome of S-180 growth appears most likely to be an expression of a more vigorous or accelerated homograft reaction. Most important, perhaps, is the finding that the mice are still resistant to the growth of S-180 sixty-seven days following infection. The significant degree of protection to *Ca 755* in terms of tumour retardation and prolonged survival time also points to a more competent immune response in the infected host. The increased survival time in infected animals with Ehrlich ascites may reflect an enhanced, though insufficient, antibody response to the inoculated cells; however the results obtained may also be ascribed to a more efficient reaction to endogenous infection which frequently appears to be a contributing factor in the death of tumour bearers.

The studies reported herein have been exclusively concerned with transplanted tumours. Present experiments are in progress to extend these observations to the behaviour of first and second transplant generations of spontaneous tumours in *Bacillus Calmette-Guérin* infected isologous hosts. If some resistance based on an immunological response exists to the development and progression of spontaneous neoplasms, the *Bacillus Calmette-Guérin* infected host with its greatly enhanced capacity to respond to antigenic stimulation deserves special attention in studies concerning tumour immunity.

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MICROBIOLOGY

Lowered Bactericidal Efficiency of Hydrogen Peroxide on Milk from Cows treated with Penicillin

DURING the course of experiments on the introduction of hydrogen peroxide as a routine means of raw milk preservation, the following anomaly was observed.

In a certain number of trials, the usual rate of bactericidal efficiency, which normally fluctuated between 80 and 94 per cent of chemically pure 30 per cent hydrogen peroxide used at a concentration of 0.2 per cent was considerably lowered, at times by 30–70 per cent. In certain extreme cases, after one hour of hydrogen peroxide treatment, an actual rise in the initial number of milk microflora population occurred. At the same time many raw milk samples with a high catalase content were examined, where the percentage of destruction by hydrogen peroxide was lowered to 75 per cent of normal compared. It was therefore concluded that the anomalous results were caused by an unknown substance, present in raw milk.

The period of the investigation coincided with the summer of mass antibiotic treatment of the cattle, so we investigated the possibility that antibiotics in the milk were the cause of the interference phenomenon. Large number of milk samples containing penicillin were treated with hydrogen peroxide. The results were consistent with the supposition that the interfering substance was penicillin, which had been secreted into the milk during and after the treatment of the cows. Total counts of milk by the pour plate method were made on Difco tryptone glucose yeast agar, and the observed results revealed significant differences in the percentage of destruction, as compared with those of normal raw milk.

Mixtures of 0.1, 0.5, 1.0, 5.0, 10, 20, 100 µl/ml penicillin (crystalline sodium G) with 0.2 per cent of 30 per cent hydrogen peroxide in distilled water, and raw milk did not decompose hydrogen peroxide directly,

as it could be quantitatively recovered when titrated iodometrically with 0.1 N sodium thiosulphate

It was reasonable to assume that this was not a simple case of chemical interference between the two drugs but a more complex interaction connected with the bacterial cell itself

When added artificially to normal raw milk, the different concentrations of penicillin G in certain cases reproduced the interference while in certain other trials the results were not satisfactory

The experiments were carried out with different kinds of raw milk, ranging in total initial count from 10^3 to 10^8 bacteria/ml and with penicillin concentrations 1.0 0.75, 0.50, 0.25 0.10 0.05 r.u./ml. When the milk microflora had been in contact for two hours with the penicillin and the milk was then treated with 0.2 per cent of 30 per cent hydrogen peroxide the interference was directly proportional to the concentration of penicillin

The unsuccessful results suggest that the phenomenon depends chiefly, not on the quantity, but on the quality of the very unhomogeneous milk microflora. Therefore the behaviour of the various isolated groups of milk microflora, such as lactic organisms, coliforms, psychrophilic organisms, thermotolerant and the thermophilic organisms is now being investigated. Results obtained so far indicate that the thermotolerant organisms may be responsible. The phenomenon described above was also reproducible when the microorganisms were grown and treated in nutrient broth. Further metabolic studies are in progress

A detailed description of this work will be published elsewhere

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Sex Chromatin ('Chromosome') in the Purkinje Nerve Cells of some Mammals

The greater percentage of sex chromatin in the nuclei of somatic cells has been used for determining the genetic tissues of most mammals, excepting the Rodentia and Lagomorpha, the nuclei of which harbour chromatin masses which were wrongly interpreted as sex chromatin. Nevertheless the studies of Luers¹ on the blood cells of Lagomorpha, and of Castro *et al.*² on the ameloblasts of Rodentia showed the possibility of determining the sex in these animals

Most authors state that the detection of the genetic sex is based upon the finding of a single sex chromatin of chromosome³, which is supposed to be present in 70-80 per cent of female nuclei, and 5-30 per cent of male

Nevertheless, we hope to demonstrate that the Purkinje cells provide evidence against the general applicability of such a viewpoint. For, in some animals we encountered a greater percentage of two chromosomes in the female and a single one in the male

Cerebellum tissue from 5 pairs of each of the following species was studied: dog, cat, rabbit and human

Fragments were fixed (12-24 hr.) in 10 per cent formalin buffered to pH 6.9. Frozen sections 20 μ thick were treated by the Foulgen technique and mounted in balsam after diaphanization with creosote. Only intact nuclei in the centre of the section were selected for counting

As can be seen from Table 1 in so far as the dog and cat are concerned we fully agree with other authors. In fact, we found many nuclei with a single chromosome in the female and only a small percentage in the male (in the female, 70 per cent for the dog and 76 per cent for the cat; in the male, 28 per cent for the dog and 30 per cent for the cat)

On the other hand, with regard to humans and the rabbit, as we have already remarked in a previous paper⁴ a higher percentage with two chromosomes in the nuclei was discovered in the female, whereas many nuclei from the male had a single chromosome

Thus, using by the method of Barr and Bertram⁵, is valid only within certain limits. In the case of the Purkinje cells, which we varied between the different groups of mammals selected for study, the diagnosis of sex is possible in both humans and rabbits, when the nuclei containing one or two chromosomes are considered

For the dog and cat, we can apply the principles of Barr and Bertram⁵ that the finding of a higher percentage of cells with a single chromosome points to the female sex. For practical purposes a large number of cells containing one chromosome indicate a female, whereas those with no chromosome indicate a male

Similarly in the case of the humans and rabbits, sections which show a high percentage of cells with a single chromosome indicate a male and those with a greater number of nuclei with two chromosomes indicate a female

It is our impression that these changes in the number and behaviour of the chromosomes can be ascribed either to fusion of the heterochromatins of the sex chromosomes⁶, or to a non specific fusion of heterochromatins of homologous parts of other chromosomes⁴

According to our work in progress, such chromatin masses may confirm what Pavan and Breuer⁷, in *Rhynchocystis angelae* called 'genie secretion', which in mammals would be a manifestation of the so-called 'metabolic chromatin'

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Table 1 NUMBER OF CHROMOSOMES IN VARIOUS CELLS (PERCENTAGES EXCEPT COLUMN 1)

| No. of Chromosomes | Man | | Rabbit | | Dog | | Cat | |
|--------------------|-----|----|--------|----|-----|----|-----|----|
| | ♂ | ♀ | ♂ | ♀ | ♂ | ♀ | ♂ | ♀ |
| 0 | 15 | 0 | 15 | 6 | 63 | 14 | 63 | 1 |
| 1 | 83 | 36 | 70 | 64 | 34 | 70 | 36 | 76 |
| 2 | 2 | 62 | 10 | 12 | 8 | 13 | 1 | 7 |
| 3 | — | 3 | 5 | 14 | 1 | 2 | — | — |
| 4 | — | — | — | 4 | — | 1 | — | — |

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⁵ Barr M. L. and Bertram E. H., *Nature* 163 676 (1949)

⁶ Pavan O. and Breuer M. L., *Symposium on Cell Secretion Fac. Med. Univ. Minas Gerais* (1953)

GENETICS

Effect of Different Wild-Type Isoalleles on Crossing-over in *Drosophila melanogaster*

EARLY experiments¹ had shown that wild-type stocks of *Drosophila melanogaster* carry different wild-type alleles at the sex-linked, white-eye (*w*) locus. A more recent² detailed genetic analysis demonstrated that the *w*⁺ loci of the Canton-*S* (*C*) and Oregon-*R* (*O*) wild-type stocks differ in the right-hand two of the four recombinationally separate *w*⁺ loci. Thus *C* and *O* may be described by the notation *CC* and *OO*, where each letter represents two of the four loci. Derived wild-types carrying the right and left halves of the two stocks, that is *CO* and *OC*, have been successfully synthesized.¹

Experiments were designed as follows to determine whether the wild-type isoalleles could differentially influence the frequency of crossing-over in their vicinity. Three marker genes, yellow body (*y*), white-cherry eye (*w*^h) and split bristles (*spl*) were selected and crossing-over studied among the progeny of females heterozygous for the three marker genes and either an intact or derived wild-type *X* chromosome. Since the cross-over frequencies for the two intervals are rather low, the standard distances for each being 1.5, the females were also made heterozygous for the autosomal inversions *Cy* and *Ubx*¹³⁰, thereby maximizing the cross-over frequencies. Such a procedure, it was thought, might magnify any differences in crossing-over between the two wild-types should they exist. Paired, parallel experiments were carried out in order to minimize environmental effects on crossing over. For example, crosses were made so that females heterozygous for *CC* and *OO* developed concurrently on the same lot of culture media. Virgin females of each genotype were collected during the same eight-hour interval and three females were collectively mated to *y w spl sn*³ males in half-pint bottles. Three such matings were made with each heterozygote. After three days females were transferred to fresh media for an additional three-day egg-laying period followed by a third three-day period. Culture media from the same lot was used for each egg-laying period, and flies were raised in a room whose temperature fluctuated between 22 and 24° C.

Table 1 CROSSING OVER IN FEMALES OF GENOTYPE *y wch spl/wt Cy/±, Ubx*¹³⁰/±

| Source of <i>w</i> ⁺ chromosome | Cross-over frequency and per centage for interval | |
|--|---|-----------------|
| | <i>y wch</i> | <i>wch spl</i> |
| <i>CC</i> | 285/8526 (3.58) | 114/8525 (1.74) |
| <i>OO</i> | 240/5210 (4.60) | 125/5210 (2.39) |
| <i>OC</i> | 104/2705 (3.84) | 48/2705 (1.77) |
| <i>CO</i> | 180/4037 (4.40) | 82/4037 (2.03) |
| <i>CrCr</i> | 332/4375 (7.59) | 90/4375 (2.06) |
| <i>FF</i> | 451/5787 (7.79) | 187/5787 (3.07) |
| <i>FCr</i> | 232/6458 (3.59) | 92/6458 (1.42) |
| <i>CrF</i> | 232/4458 (5.17) | 92/4458 (2.05) |

In Table 1 results of the crossing-over experiments have been compiled. The frequencies listed represent summations of all the progeny scored for each cross. It will be noted that the cross-over frequencies for each interval are greater among females heterozygous for *OO* than for *CC*. That this difference is apparently a

function of the right segment of the *w*⁺ region is borne out by comparable crosses where the derived wild-type chromosomes *CO* and *OC* were employed. These results, included in Table 1, show that for each interval the cross-over frequency was greater among females heterozygous for *CO* than for those heterozygous for *OC*. A comparison between the total cross over frequencies for all females whose right *w*⁺ segment was *O* with that of females whose right *w*⁺ segment was *C* established this difference to be statistically significant ($\chi^2 = 9.04$, 1 d.f., $P < 0.01$).

That the aforementioned differences in cross-over frequencies are not spurious is supported by a completely independent set of crosses. Crossing-over experiments were repeated employing intact and derived wild-type *X* chromosomes coming from two wild-type stocks of independent origin, Formosa (*F*) and Crimea (*Cr*). Genetic analysis of these stocks³ established that *F* and *Cr* carry different wild-type isoalleles in the right segments of their *w*⁺ loci. Insofar as can be determined at present these wild-type isoalleles of *F* and *C* are identical as are those of *Cr* and *O*. Parallel experiments were carried out. In one crossing-over in females heterozygous for *FF* or *CrCr* wild-type *X* chromosomes was compared, in the second females were heterozygous for *CrF* or *FCr*. Inversions were included as noted above.

The results of these experiments, listed in Table 1, parallel precisely those obtained with *O* and *C*. Thus for each interval the cross over frequency was greater in females whose right-half *w*⁺ loci carried the *F* isoalleles as compared with those carrying the *Cr* isoalleles. Compared statistically the difference between the total cross-over frequency for all females whose right segment was *Cr* and those whose right segment was *F* is highly significant ($\chi^2 = 34.8$, 1 d.f., $P < 0.001$). These data demonstrate that the presence of a particular wild type isoallele can influence significantly the cross over frequency in its immediate vicinity.

That the differences in cross-over frequency are a primary function of the distinctive wild-type isoalleles is supported by a number of facts. A significant maternal effect seems unlikely since identical females were used throughout in obtaining heterozygotes. Specific autosomal influences are of doubtful importance, especially since the autosomes were randomized while synthesizing the derived wild-types. Interaction effects are, however, not excluded. Precisely how the different isoalleles effect cross-over differences is not clear. One possibility is that they have different pairing affinities for the mutated allele to which they were tested.

These observations serve to explain, in part, the recombination differences between the Oregon and Samarkand wild-types of *D. melanogaster* reported by Lawrence.⁴ They also point to the fact that wild type isoalleles may have important evolutionary significance by providing a base from which genotype producing high or low crossing-over frequencies can be selected.

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¹ Timofeeff-Ressovsky, N. W., *Biol. Zh.*, **52**, 508 (1932). Muller, H. J., *J. Genet.*, **30**, 407 (1935).

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³ Green, M. M., (unpublished).

⁴ Lawrence, M. J., *Nature*, **162**, 889 (1958).

THE DISCIPLINE OF THE SCIENTIFIC METHOD

THE address, "The Message of Science", which Prof P Weiss delivered at the Universal and International Exposition at Brussels on June 25 1958 and which has now been issued as an Occasional Paper of the Rockefeller Institute, develops three main points. Man's hope lies in the advance of civilization, of which science is a part, and to understand the role of science requires insight into its nature, power and limitations. First Prof Weiss argues, man will continue to reap rich fruit from scientific progress. Secondly, understanding the process of science gives man a firmer grounding in reality against his floundering and fumbling in abstractions and thirdly the task of science is to serve man by mastering Nature and not to become man's master. In serving man, science, Prof Weiss urges, must close ranks with other servants of humanity—the creative arts, philosophy, religion—all striving for a new integrated humanism.

In this view, science which has helped to dethrone man from his self appropriated station as the centre of the universe, can help him now to grow into his rightful stature. Prof Weiss's address is thus essentially a contribution to the discussion on the place of the universities in the scientific revolution which Sir Eric Ashby opened in "Technology and the Academics" and which Sir Charles Snow has developed further in his Rede Lecture, "The Two Cultures and the Scientific Revolution".* Prof Weiss does not disparage the material benefits which science can provide, but he lays his stress on the contribution which science can offer to man's intellectual and moral advance. It would be a distortion to suggest that he is advocating science for its own sake but, like Sir Edward Appleton in his presidential address in 1953 to the British Association, he maintains that science itself is one of the great human values.

The power of science Dr Weiss points out, comes from the strict mental discipline and critical detachment that it imparts to those who live and practise by its code, and if living by this code can help men to lead more satisfying lives, so as more fully to enjoy and share promised release from want and drudgery, if science will not just extend man's span of life but also give the content of that span more purpose, if science can convince man that many of the evils and errors and convulsions of the present age arise from his ignorance and neglect of the very code of science then science will have given him another noble gift, namely, a basis for responsible and judicious self-direction as a design for living. This presupposes that man is free to choose his course for better or for

worse, and in this choice, the scientific approach can help him to avoid predictably disastrous turns and missteps. Science is not to blame for man's misdirecting scientific knowledge to evil ends.

If the scientific spirit can teach man reason, the message of science must, however, first be accepted by man and it is Sir Charles Snow's contention that one of the two cultures he predicates as existing does not and will not accept that message. First, however the characteristics which Dr Weiss describes as marking the scientific spirit as superior to the mere application of logic, the Golden Rule or just plain common sense should be noted. It is the categorical demand for validation and verification of each premise each contention and each conclusion by the most rigorous and critical tests of evidence. Every rule and law have to be tested and enforced, and nowhere else is the penalty for error or infringement so prompt and telling.

This discipline of the scientific method broadly applied, could go far toward clearing the underbrush of superstition and prejudice that hampers civilization in its march, but it has its limitations. Since according to the code of science, no positive assertions are final and all propositions approximations and indeed provisional, science is seen to advance more by denying what is wrong than by asserting what is right—by reducing and eventually eradicating errors rather than by bounding straight toward some preconceived final truth. From any point along the frontier of knowledge which mankind faces the imagination and curiosity of individuals may start tracks that radiate in all directions into the unknown. Through trial and error the right path is gradually singled out from the multitude of blind alleys by the fact that it has met, instead of missing other new or familiar lines starting from other points, merging with them in mutual reinforcement. Success lies in the confluence of thoughts from many diverse directions, and this gives science its coherence and consistency with a stable inter-convertible currency of terms and units, modes of operation and standards of proof or disproof, all gained by gradually removing the inconsistencies and incongruities within the system, by the systematic reduction of margins for error.

Dr Weiss points out that this is the method of organic evolution, but on the infinitely faster scale of thought processes, which require much less time to establish their soundness; and from this comes man's unprecedented chance for rapid progress—from the incessant wading out of error. Moreover, for science as a whole, truth is that strip of possibilities left over after all demonstrable untruths have been eliminated, there will remain a fairly

* "The Two Cultures and the Scientific Revolution," by Sir Charles Snow (The Rede Lecture 1959) Pp iv + 322. (Cambridge: At the University Press 1959) 5s 6d net.

broad band of uncertainty, including the indeterminate, the unknown, the indeterminable and the unknowable. The limits of science are frankly acknowledged, and Dr Weiss has no place for either the shallow optimism that Sir Charles Snow marked as contributing to the divergence of the two cultures he describes, or for the uncritical claim that science is a cure for all the ills of mankind and that it can prescribe ultimate goals to guide man's conduct. On the contrary, the humility and courage required to live with partial answers and the disturbance of complacency should assist science—and the scientist—to live with the other claimants to a share in human destiny. The scientific spirit, by stimulating man afresh to search and strive again rather than to conform, to face problems and not to accept past solutions, and to exercise ingenuity instead of abdicating to authority, could rekindle flames which mechanization threatens to extinguish.

Dr Weiss's view of the relations of science with the creative arts, with philosophy, with at least the kernel of religions (not of creeds) and with the lessons taught by history, all of which are companions with science in shaping the fate of mankind, presupposes, however, a bridge rather than the gulf which leads Sir Charles Snow to speak of the two cultures—it invokes comprehension rather than incomprehension on both sides. If the attitude which he depicts should prevent the scientist from contributing to misunderstanding or stirring up resentment, there must none the less be understanding and not prejudice on the other side. It will not suffice for science to be objective, to recognize soberly its own limits, and to claim no greater share of man's allegiance than it can ask on scientific grounds. It can scarcely act as educator unless there is sympathy and receptiveness on the other side. That must precede the abatement of suspicion and resentment, the removal of barriers due to prejudice and the disappearance of any fears of aggressive expansionism of science.

This exposition of the message of science ends with an appeal that men of science should close the ranks with those in other walks of life against the dehumanization of our culture, and that they should look and work for a broad humanism in which science is accepted, not grudgingly but with understanding, by all men in all walks of life, not for its fruits alone but for the ideal of rational thought which it can carry to its highest culmination. At the same time, men of science must ever be on their guard against the danger of specialist isolation to the neglect of other human values, and finally Dr Weiss pleads that science should re-acclaim diversity as the source of progress, including the diversity of human minds in their responsible expression. Simultaneously, he pleads that those humanists who are not scientists should not regard themselves as the prime custodians of civilization, shunning science as if it were inhuman.

The conception of the message of science and the place of the scientist in our civilization which Dr Weiss expounds in this address is dignified and noble as well as restrained, it could well elicit the response he seeks from the non-scientists if it can reach them.

But while Dr. Weiss recognizes as clearly as Sir Charles Snow the gap between the two cultures and the imperative need for co-operation between scientist and non-scientist, he does not indicate how the gap is to be bridged. It is true that, if his counsel is followed, scientists could do a good deal to remove the prejudices and suspicions which have enlarged the gap—or at least to remove the substance of those prejudices and suspicions, but something more is required to restore unity to the intellectual life of Western society, or even to provide a meeting place for the two cultures. The lack of comprehension of science and technology on the part of the non-scientist which leads Sir Charles Snow to describe the literary intellectuals as natural Luddites must be removed also, and this as he sees clearly is a problem of education. Until intellectuals and the nation generally come to understand the scientific revolution and its implications, Britain cannot hope to cope with the problems offered and either avert the dangers or exploit their possibilities.

Sir Charles Snow faces this question in the last part of his lecture. He believes that we need as many outstanding scientists as the country can produce. They present no problem, but their number is limited, and they need a much larger number of professional scientists for the supporting research and high-class design and development, here the problem is not so much that of quality as numbers. These in turn require a large number of supporting technologists and technicians for the secondary technical jobs, some of whom will take major responsibility, particularly in the human jobs. Here our problem is both the numbers required, which will throw an immense strain on the universities, university colleges, colleges of technology and technical colleges of Britain, and the distribution of ability in order that proper and efficient use may be made of their services. Lastly, there must be not merely politicians and administrators, but also an entire community knowing enough science to have a sense of what the scientists are doing.

Sir Charles offers no prescription as to how all this is to be achieved. He simply presents the challenge to the educational system of the country, with the reminder that our real assets in the world to-day are our wits—our capacity for co-operation and our inventive and creative ability. The survival of Britain as a world power requires that we should fully understand the scientific revolution, educate ourselves to the limit and give the lead to the world. We cannot do this without breaking the existing pattern of education, but unless we do so and educate ourselves adequately, we must experience in our own life-time a steep decline in our standards of living. To close the gap between the two cultures is a necessity in the most abstract intellectual sense, as well as in the most practical, in order that we may be able to achieve even the political techniques which will enable us to bring our human capabilities into action. Once again we are summoned to look at education in the broadest sense, and Dr Weiss's message is an invaluable contribution to such a task.

LATIN IN UNIVERSITY ENTRANCE REQUIREMENTS

THE controversy about compulsory Latin for entrance to Oxford and Cambridge flares up sporadically, like the plague, but it does look as though the recent outbreak may be the last. True, Oxford has reversed its decision to make German and Russian alternatives to Latin, but when the committee at present looking into the qualifications for university entrance reports, it seems likely that some means will be recommended whereby Latin can be avoided.

It is difficult to see what benefit the average boy (or girl) who wants to specialize in science can derive from Latin at Ordinary level in the General Certificate of Education. He will not be able to read the simplest texts with any ease, even if he wanted to and the feeling among many scientists that Latin is a waste of time makes it very unlikely that he will. His attitude to Latin which is often crammed in a few months and as quickly forgotten, is one of resigned hostility.

Without Latin the specialists will become even more specialized: is a favourite argument of the anti-abolitionists, yet very few people wish to abolish it unconditionally. At Oxford the suggestion was that Russian and German should be alternatives and a scientist with French and German is no more a specialist than one with French and Latin. Besides, there is far more chance that a modern language will be kept up, since even the least materialistically minded can see its usefulness. More and more people go abroad every year especially school children and university students, and later on the professional scientist will want to read papers in foreign languages. Few are published in Latin.

Three main arguments are advanced by those who wish to see Latin retained besides the one mentioned above.

First, they say that it is the key to the understanding of Western culture. Quite apart from the fact that Latin at Ordinary level is not even a key to the understanding of Latin in order to understand Western culture one has to know a good deal about it, and as is so frequently pointed out most scientists do not—though many are more knowledgeable than is often allowed. Latin is no doubt, an immense asset to the scholar with a wide knowledge of the literature, philosophy, art and history of Europe and America but to the scientist it is rather like studying the quantum theory without knowing what radiation and algebra are, or to take a non-scientific simile to study the sources of Shakespeare's plays without having read "Hamlet". With an educational system which imposes specialization at the age of fifteen we cannot afford the time for intellectual luxuries. It is the stuff of Western culture that should be studied not Latin grammar.

Secondly Latin is said to be a unique training for the mind. This argument is difficult to refute since it is so vague and is so seldom elaborated. It is significant that it is usually advanced by people

whose mental training was largely based on Latin. Furthermore, mathematicians can make a similar claim for mathematics with equal justice. Part of the uniqueness of Latin is said to lie in its being a highly inflected and so a very precise, language but so are German and Russian.

Thirdly, Latin is said to improve one's English. Maybe it does, but it is an extraordinarily round about way of doing so, and one for which the scientist simply does not have the time.

In fact, Latin tends to defeat the very objects it is meant to attain. It becomes associated with other non-scientific subjects and produces an anti-cultural reflex—Latin is a waste of time therefore French history and English are a waste of time. It also takes up valuable hours in school which might be devoted to arts subjects likely to interest the potential scientist. It is not suggested that the time spent on Latin should be given over to more science. A debate held recently in the University of London on the motion "That the Education of our Future Rulers should be primarily in the Sciences rather than the Humanities" where scarcely a speaker from an audience containing many scientists supported the motion, shows how much basic agreement there is that education ought not to become too specialized. In view of this, it is a pity that such an issue should have been made out of the relatively unimportant Latin question.

It is high time that some effort was made towards improving the general as opposed to the specialized standards for university entrance. If the Latin dispute does nothing else, it focuses attention on this need. Scientists entering for State scholarships already have to take a general paper in English, but it is a special paper for scientists and so in a sense it condones the existence of Sir Charles Snow's two cultures, instead of tending to reunite them. If only the universities would demand from everyone three subjects at Advanced level, one a science and one an arts subject, there would be no need to quibble about trivialities like Ordinary level Latin. Quite apart from the wider knowledge this would bring scientists and arts men would be working together right up to the time they left school, and this is surely essential if they are not to separate into two groups. It has been suggested that as a consequence there would be a slight lowering of standards in the entrance scholarships, and that the colleges would not accept this. If so, it would be a great pity, but it would be a very small price to pay. Besides it is illogical to complain about specialization and to object to measures which combat it.

Anyone who wants to see compulsory Latin retained for scientists should sit back and ask himself two questions. What am I trying to achieve? What is the best way of going about it? It is very peculiar reasoning that produces Latin at Ordinary level as an essential part of the final answer. The worthy cause of a wider education is being discredited.

THE LIFE OF FREDERICK SODDY

Pioneer Research on the Atom

The Life Story of Frederick Soddy By Muriel Howorth Pp 362+16 plates (London New World Publications, 1958) 75s

THIS is an uneven and uneasy book. The scientist who reads it is likely to be exasperated by its not infrequent confusions and repetitions—and the general reader will almost certainly find its detailed chronology difficult if not impossible to disentangle, although the framework of the story is simple enough. It is the life-story of Frederick Soddy, pieced together from his casual remarks, from reluctant replies to leading questions, from more sustained and possibly more spontaneous reminiscence, and from the residue of his papers, by his literary executrix and friend of his later years. It is a work of obvious devotion, forcefully and at times movingly written, but it achieves no real synthesis.

Readers of this journal will remember Paneth's tribute to Soddy (*Nature*, 180, 1085, 1957) within the compass of a short article, that was generous, just and discerning, written by an expert in his own field who had known him when he was still active in it. Paneth wrote "The duty to clarify his picture is specially incumbent on us, as it is the tragedy of his life that members of the younger generation may know him only as the person who adopted the term 'isotope', and, perhaps, as the author of provocative statements in economics and other fields far remote from science. The number of those who knew Soddy in his creative period is dwindling. He was gifted in many, perhaps too many, ways. He was such a good writer of English prose that it was all too easy for him to give his polemical essays the sting he wished."

Frederick Soddy died on September 22, 1956, in his eightieth year. His last contribution to the literature of radioactivity was a letter to *Nature* published on September 3, 1932. His present biographer met him first in January 1953. She had then recently read "The Interpretation of Radium" (1909) and had been so impressed by its philosophy that she had sought out its author. At their first meeting she suggested to Soddy that they should "together write the record of his scientific investigations." Within a few days she had his agreement. Within two months the preface, at least, to "Atomic Transmutation: the Greatest Discovery ever Made" had been written. This was to be Volume 1 of the *Memoirs*. Volume 2 was unfinished at Soddy's death. Then Major and Mrs. Howorth came into possession, through Soddy's will, of "all his original papers, letters, and records." In that way the book now under review had its beginning, its conception replacing that of the half-finished *Memoirs*. "Having these [original papers] as my guide", Mrs. Howorth confides in her new preface, "I can now write, with less presumption and more confidence, the story of this remarkable man who was destined to play so great a part in the discovery of one of Nature's phenomena, unique in its potentialities and formidable in its power."

It appears to me necessary to give this brief history of Mrs. Howorth's book—essentially in her own words—but having done so I am left with scant space to comment on it further. In any event I should require many pages to deal with it in detail. I can

only indicate its shortcomings and its virtues by further quotation. "Later, when the speaker at one of the Royal Society Popular Lectures in Canada fell sick, Professor Cox telephoned Rutherford to take his place and this led to his being accorded a Fellowship of the Royal Society of Canada and eventually to the full London Fellowship in 1903" (p. 78), "Superb chemist that she was Marie Curie had foreseen these events, but it was left to Frederick Soddy to establish each one of them by experiment—natural transmutation, 1901, disintegration theory, 1902, displacement law, 1911" (p. 93), "By 1905 it was still not confirmed that the alpha particle was a helium nucleus" (p. 114), "In 1932, Harkins's 'neutron' had been experimentally established by Chadwick. Later Chadwick went to study in Germany under Nernst and Rubens" (p. 129), "when Cockcroft and Walton in the Cavendish Laboratory succeeded in 'splitting the atom' Cockcroft alone received the award [of a Nobel prize]" (p. 188), "What exactly is a beautiful equation?" I asked [Professor Dirac] "Is Einstein's little mass-energy equation beautiful?" "No, that is not beautiful," he replied, "but some equations are very beautiful indeed" (p. 257), "One can say that on Soddy's perception the whole of nuclear science has been built" (p. 267), "The loneliness which such inattention from the scientific world creates is sometimes not easy to bear without resentment. It may be also, in the case of Soddy, that the loneliness of his early days returned. One could imagine that his mother died three times, once in his infancy, once with the death of his wife, and once on his retirement from academic life" (p. 277).

I do not think that the historian of the science of this century will pass over the work and the worth of Frederick Soddy, as he himself found it for a season passed over—or imagined that he found it passed over—in his later years. He is assured of the esteem of posterity, without special pleading. Mrs. Howorth's book contains much that will be of interest to the historian, but her special pleading is likely to pass him by.

NORMAN FEATHER

GUIDE TO MODERN PHYSICS

Handbook of Physics

Edited by Dr E. U. Condon and Dr Hugh Odishaw (McGraw-Hill Handbooks) Pp xxvi+1462 (London McGraw-Hill Publishing Company, Ltd, 1958) 194s

THIS is a magnificent book. It contains about 1,500 pages and weighs nearly 3 kgm, dimensions which are achieved by solid packing of authoritative information, with little padding or wordy introductions. We have considered it from the points of view both of the senior who has had ample opportunity of forgetting his physics, and of the student who is in the process of acquiring it. For both it seems to be an excellent work of reference.

It is divided into nine parts: mathematics, mechanics of rigid bodies, mechanics of deformable bodies, electricity and magnetism, heat and thermodynamics, optics, atomic physics, solid state, and nuclear physics. Each part is divided into about ten chapters, each written by a specialist; there are nearly ninety contributors, practically all from the United States. The list of chapters would be too long

to enumerate here but some idea of the contents can be given by saying that the topics are those in which there is considerable interest at the present time. The book gives a general impression of the rapid development of physics in many different directions.

This development has introduced the usual difficulties in keeping the subject matter up to date, and in the preface the editors express some concern about their success. They need not have worried, most physicists would be only too delighted to keep within hailing distance of the amount of physics in this book.

In fact the main criticism of the book is that it does not seem clear about its own purpose. In the preface the editors imply—but do not clearly state—that they regard the contents as “What every physicist ought to know. Surely the claim is outrageous? There can be very few people who have the mental capacity for absorbing all this material, and it is questionable whether such people would best serve physics by spending the time needed for its absorption.

In our opinion the main purpose of the book is to serve as a work of reference for the expert who has occasion to wander into a field related to his own but unfamiliar to him. He will find the general principles authoritatively and clearly set out and will be able to see the types of mathematical approaches that are used. He will not usually find experimental details—except for occasional chapters on such subjects as experimental stress analysis and vacuum technique—since the book is essentially theoretical.

The mathematical part of the book is perhaps the least satisfactory. It contains some elementary material such as logarithms which seems out of place and some such as the theory of probability which is likely to be of more use to biologists than to physicists. On the other hand the theory of errors is not treated. Nevertheless the main content is extremely good and well set out.

The book is beautifully printed and produced, and we have noted only very few misprints and mistakes. Unfortunately, the very high price—which is quite reasonable for the amount of material contained—will probably rule it out for most individual physicists. It should nevertheless be in every library and more important every physicist should know of its existence.

H. LIPSON
S. G. LIPSON

REACTION KINETICS

Some Problems in Chemical Kinetics and Reactivity Vol. I

By N. N. Semenov. Translated by Michael Boudart. Pp. xii+230 (Princeton, N.J. Princeton University Press. London: Oxford University Press 1958) 36s net.

THIS is the second English translation of the first volume of Prof. Semenov's book on *Some Problems in Chemical Kinetics and Reactivity* to appear in the past few months. Reading it one is immediately struck by the strength of the author's grasp of the fundamental issues of reaction kinetics and by his ability to marshal the evidence in a subject where the experimental results are often confused, and their interpretations conflicting.

The volume under review has no pretensions to being a text-book, and is in fact an extended version of an introduction to a symposium held in Moscow. It thereby retains a certain freshness and is notable for the provocative and stimulating points of view which it takes. It begins with a classification and account of reactions of monoradicals (no nonsense about ‘what is a radical?’), a chapter which is to be commended for its discussions on bond energies and the relation of energy of activation to heat of reaction, and for the cautious but telling way in which the relation of structure to reactivity is dealt with. The next section is on competition between monoradical reactions, and here a clear account of the role of peroxides in oxidation of hydrocarbons is to be found—a great deal of modern Russian work of value much of it unfamiliar to this reviewer is dealt with here. The mechanism of chain decompositions of hydrocarbons is discussed.

In dealing with biradicals a distinction between the physical concept (triplet state paramagnetism) and the chemical concept (absence of activation barriers, tendency to dimerize, weakness of the second bond) is exemplified at the outset although there is a general coincidence. The chemical aspects as would be expected are stressed.

After this survey the second (and final) part of the volume deals with chain initiation and termination. This is divided into chapters on dissociation of molecules and recombination of radicals (essentially by homogeneous processes), initiation by ions of variable valence, and the influence of the walls of the reaction vessel. All these are excellent, the last being particularly recommended. It leads to some interesting speculations on the processes of heterogeneous catalysis.

The standard of production of the book is not high, the typescript being rather unsatisfactory with an irritating and unnecessary symbol for the chlorine atom. The translation is quite good, although marred by a few words like ‘organism’, and expressions such as the ion impact method imagined by V. L. Tal'roze. For a physical chemist however this book of Semenov's should be compulsory reading.

T. M. SUGDEN

CHEMICAL OCEANOGRAPHY

Apparatus and Methods of Oceanography

By Dr H. Barnes. Part I. Chemical. Pp. 341 (London: George Allen and Unwin, Ltd. 1950) 40s net.

THE special methods of analysis used in chemical oceanography and marine biology are to be found in a great many different publications some of which have limited circulations. There is a need for a collection of working methods, preferably with some guidance for the inexperienced. The need is very competently met by this book. Although suitable for the experienced analyst it is also explicitly intended to help biologists with less chemical knowledge, and to be useful to those with small libraries. The author has therefore devoted the first quarter of the book to three chapters on colour comparisons and photometric analysis to errors and precision, and to the calculation of results. It is difficult to judge the value of this part of the book. It is well done—indeed it is admirably clear—but much of it

seems unnecessarily elementary, and some of the instruments described are surely obsolete

The rest of the book is very useful indeed. Separate chapters (several for nitrogen and phosphorus) give methods for determination of chlorinity, pH, nitrogen, phosphorus, silicon, carbon, oxygen, alkalinity (an account of the carbon dioxide system is inter-polated), conservative elements by micro methods, trace metals and plankton pigments. Others describe filtration methods, and sediment analysis. In each chapter, introductory notes explain the application and chemistry of the methods, which are then given tersely in a form easy to follow at the bench. Remarks on matters of technique, interference, and accuracy come last. The methods are well chosen and it is evident that Dr Barnes is drawing on considerable experience. It is a little surprising that he does not mention the determination of pH with indicators, as it is easy to get quite good results with very simple gear. He should be well able to explain and set out the corrections needed for this method, which is still in use.

There are more than 420 references, some 60 of which are in an appendix bringing them up to July 1958. These are invaluable, although there are few from Russian sources. The 45 tables are mostly relevant, but it is not easy to see the need for reciprocals of atomic weights, nor for a complete list of the symbols recommended by the Chemical Society. The index is thorough. The binding and paper seem rather too absorbent for a book which is certain to be used a great deal on the laboratory bench.

F A J ARMSTRONG

ATLANTIC HYDROMEDUSAE

The Carlsberg Foundation's Oceanographical Expedition round the World 1928-30 and Previous "Dana" Expeditions

"Dana" Report No 46. The Hydromedusae of the Atlantic Ocean and Adjacent Waters. By P L Kramp. Pp 283+2 plates (Copenhagen: Andr. Fred. Høst and Son, 1959). 60 Danish kr.

THIS work, by one of the world's most knowledgeable experts on the subject, is a valuable addition to the excellent series of *Dana Reports*. It will partly replace and partly help to guide us to the multitudinous works on medusae in so many scattered journals, although it has not a complete literature list.

One might wonder how far this new volume overlaps Russell's monograph on the "Medusae of the British Isles" published in 1953 and if it is necessary or desirable for both to be at hand. That there is considerable overlap is inevitable and as it should be, but the two serve distinct purposes. Russell is confined to British waters—but not as defined by the Convention!—and it has much more detailed descriptions with details of the hydroids and their development where these are known. Kramp covers a much wider field. An example which illustrates this difference is given by the genus *Phialidium*. Russell describes two species but Kramp twelve and four doubtful ones. Kramp's description of *P. hemisphaericum* is contained in ten lines, and Russell's in ten pages.

This new report is in three sections. The first occupies 74 pages and is a systematic account of the species taken on the *Dana* cruise, 1928-30, and in collections made at the request of the *Dana* Committee. Not

only are very full taxonomic descriptions given, often clearing up doubtful nomenclature, but also brief but useful summaries of distribution, both geographically and in depth. It contains descriptions of three new species and one new subspecies.

The second section, of more than a hundred pages, is a survey of all the hydromedusae which have up to now been found in the Atlantic and adjacent waters, a term interpreted to include the Caribbean, Davis Strait and Baffin Bay, the Mediterranean, Black Sea and the waters north of European USSR. Truly a wonderful coverage. This section will be a boon to those struggling with the systematics of medusae as it has a diagnosis of every family, genus and species, and with keys to all species at present considered valid. It makes extensive use of Russell's book and his Plankton Sheets for those species that are given therein, but its wider field will make it a most valuable aid towards the determination of medusae by workers everywhere. The descriptions are concise and their arrangement helps to make them simple to follow. The keys, too, are clear, and if only the medusae themselves were always as clear their determination would be much easier. It is scarcely the author's fault that medusae are so often damaged that in practice the answer to some of the questions may be just a question mark. Because of the changes during development the section is confined to the adult forms. This is a pity because so often the young stages found in the plankton can be puzzling. I was disappointed to see that Kramp had not done more to link the medusae with their hydroids as there is now a great deal of information on this, but he probably considered it to be outside the particular relevance of the book. Doubtful species are mentioned in case future research should point to their validity. In this section, too, their distribution is concisely mentioned.

The third section is for the ecologist and it describes the composition of the fauna of the hydromedusae within each of the zoogeographical regions of the area—the Black Sea excluded—and based on the distribution of the water masses. The number of regions is generous in its coverage, with details separately given for four ecological groups—neritic, slope, oceanic epipelagic and bathypelagic—each being regionally subdivided. The neritic group is given extensive subdivision, first into eight major regions, for example, Arctic, East Atlantic Boreal, etc., and then into provinces, for example, Atlantic coasts of the British Isles, Channel, North Sea, Baltic, Norway north of Bergen, Iceland. Russell, in 1935, laid stress on the value of certain medusae as 'indicator species', and the detail given in this section of Kramp's book will be invaluable in this respect. It is only to be expected that further research will widen our knowledge of the distribution of many of the medusae, and although it is obvious that Kramp realizes this (for example, at the bottom of p 266), I found some of his statements too dogmatic, and once in error. On page 210 he says that *Ptychogena lactea* is "entirely lacking in the East-Atlantic boreal region". The *Scoia* took this species in the Faroe Channel in June 1958, and indeed Kramp himself confirmed the identification.

Like other *Dana Reports*, the proof-reading and production have been excellent. Those interested in the systematics of medusae or in the ecology of the water masses will certainly want to have this volume, and I have no doubt that their copy will before long be well thumbed.

J H FRASER

An Anthropologist at Work

Writings of Ruth Benedict By Margaret Mead Pp xxii+583+8 plates (London Martin Secker and Warburg Ltd, 1969) 42s

RUTH BENEDICT and Margaret Mead are two of the best-known names in American anthropology, and certainly the best known to the general public because their writings have a popular appeal and have appeared in cheap editions. This is a book by the second about the first, or rather it is a book about Ruth Benedict and her circle among whom Margaret Mead was a prominent figure, as she is in the book. It contains a number of articles—and also poems—by Ruth Benedict interlarded with introductory pages by Margaret Mead. Some of the articles have already appeared in print elsewhere, and the unpublished ones contain so little of scientific interest that it scarcely seems worth while committing them to print, and, indeed it must be said that much of Ruth Benedict's writing fell into the class of higher journalism rather than into that of scientific anthropology. It could, however be said that it is often helpful in evaluating an anthropologist's writings to have some knowledge of him as a person and of his private interests. That would be true, but a brief memoir would have served the purpose better than a book of more than 500 pages and so constructed that the subject of the memoir is constantly interrupted by its editor and the editor by its subject. Moreover even an English anthropologist who might be expected to find an account of his American colleagues of interest, may find as I have the company somewhat dull. Those who are not anthropologists will, I fear, find it tedious for what can be more tedious than the doings and views of persons we have scarcely heard of, and persons of no very great importance? An answer to that question might be the revelation of their feuds and personal antipathies. Some of the gossip may be true and might be spoken, but it ought not to have been published in print so soon—for example what is said about the late Prof Radcliffe Brown for it is not as though relations between other persons mentioned are treated with complete candour. It is a pity that the initial sympathy and admiration which many of us have felt towards Ruth Benedict an able woman who left some important writings behind her, and also towards the centre of the circle, Franz Boas should in the course of reading this memorial volume be lost.

C. E. EVANS PRITCHARD

Nuclear Reactors for Power Generation

Edited by E. Oponshaw Taylor Pp vii+144 (London: George Newnes Ltd, 1958) 21s net

THE basis of this book is a short course of lectures given at the Heriot-Watt College, Edinburgh. The first and the final chapters provide a reasonable survey of the application of nuclear power. The first of these chapters deals with the world energy requirement, and the importance of nuclear power to the United Kingdom, the United States, the U.S.S.R., and the remainder of Europe. The final chapter considers the economic application of nuclear power, dealing with the choice of steam cycle, fuel burn up and the importance of a high load factor. In this latter context pumped storage schemes are discussed.

The five intermediate chapters provide a short technical survey aimed at providing engineers concerned with the construction and operation of nuclear

power plants with a background of information. The text is not intended for the designer. The chapter on materials is the exception, however and is more detailed. Certainly the designer would find it a useful survey of the likely reactor materials. The potential reactor operator would probably advocate more space being allowed for safety and instrumentation, to enable the control systems of the current electricity authorities nuclear power stations to be described in detail.

A considerable training programme for technicians and operators will be necessary as the large nuclear power stations begin to be commissioned from 1960 onwards. This book provides a summary of a typical course.

R. VAUX

Disposal of Radioactive Waste

By K. Saddington and W. L. Tompkins Pp x+102+8 plates (London George Newnes, Ltd, 1958) 17s 6d net

THE disposal of radioactive waste material is a problem which had to be faced when the production of radioisotopes commenced on a large scale both in Great Britain and elsewhere. It will of course, become of increasing importance as the atomic energy power programme expands and the use of radioactive material increases in industry and the medical fields.

The authors have provided a book which should do much to enlighten the general reader and at the same time, act as a useful work of reference for those working in the field of atomic energy.

Although it is claimed that the book is designed to assist sanitary engineers, the main emphasis is on the wastes arising at reactor stations and fuel processing establishments. A more detailed account of the problems arising in industry would have been an advantage.

The important biological aspects are described very fully, perhaps too fully, having in mind the class of reader for whom the book is intended. Certain of the other chapters could have been expanded to provide more guidance to those outside the U.K. Atomic Energy Authority.

It is quite impossible in a book of this size to give a comprehensive account of all the problems and their solutions. Nevertheless the authors are to be congratulated on a good attempt to provide a general survey of the disposal of radioactive wastes.

Selections from Modern Abstract Algebra

By Richard V. Andree Pp vii+212 (London Constable and Co. Ltd, 1958) 42s net

A BETTER title for this book might be "An Easy Introduction to some Ideas in Modern Abstract Algebra". It is often said that abstract algebra demands little manipulative technique but a considerable degree of mathematical maturity, the object of this book is to enable the novice to acquire that maturity starting from little more than basic notions about integers and real and complex numbers. The early chapters discuss logical ideas and concepts such as equivalence classes and congruence in detail with plenty of illustrations and exercises chosen over a wide field, explanations are full and generally careful though the reader may be left in doubt as to whether a postulate is or is not the same thing as an axiom (p. 11) and the description of a series as "convergent perhaps finite" (p. 24) is unfortunate.

Boolean algebra receives adequate discussion with examples from logical puzzles and circuit theory.

Groups, matrices, determinants, fields, rings and ideals are then brought in at a gentle pace, with a wealth of concrete illustration. The author does not disdain to exhibit a diagram of the inter-relations of fields, integral domains, commutative rings, rings, which should help the beginner in the rather tiresome task of remembering the connexions and differences of these concepts. The Cayley-Hamilton theorem for matrices is proved, and in dealing with groups the reader is led to see the importance of the Jordan-Hölder theorem, though the proof is omitted.

The author tells us that the lecture courses on which this book is based have been increasingly popular in the University of Oklahoma, and that engineering students have found the work on Boolean algebra and matrices valuable and stimulating. One can readily believe this, for the style is easy and informal, most readers will be keen to go further, and for them the carefully selected references to more advanced works will be useful. T A A BROADBENT

The Terpenes

By the late Sir John Simonsen and Dr W C J Ross Vol 5 The Triterpenes and their Derivatives—Hydroxy Acids, Hydroxy Lactones, Hydroxyaldehyde Acids, Hydroxyketo Acids and the Stereochemistry of the Triterpenes. With Addenda to Volume 3 by the late Sir John Simonsen and Dr P de Mayo Pp ix+662 (Cambridge At the University Press, 1957) 84s net

VOLUME 5 of this well-known series contains a comprehensive summary, up to about 1954, of work on the subjects named in the title. A few references and rather more ideas date to about 1956. An important section is concerned with the classical stereochemistry of the various then known triterpene skeletons, with some consideration of conformational questions. As in previous volumes, conformational formulae are inadequately used, but the volume marks a distinct improvement in this respect. There is a considerable addendum bringing up to 1956 work on configuration and structure in the sesquiterpene and diterpene series.

Inevitably in a rapidly moving field the book is seriously out of date. For example, a number of structures quoted have been superseded and many others then unknown have since been determined. There is, inevitably, no consideration of important recent methods such as rotational dispersion, but a rather full account of the use of molecular rotation differences. However, it can form a starting point for the research worker and provides some useful summaries of more classical aspects of the subject for teaching purposes. A J BIRCH

Carbon Dioxide in Water, in Wine, in Beer and in other Beverages

By F Justin Miller Pp 49 (Oakland, Calif F Justin Miller, 3166 Birdsall Avenue, 1958) 15 00 dollars

THIS memoir comprises three almost independent essays on (a) a numerical method of representing the gas pressure relationships in various carbonated beverages, (b) the rate at which such beverages become impregnated by the gas, and (c) the rate at which the gas is lost from the carbonated liquids under various conditions. No radically new conceptions are developed but numerous graphical and tabulated data are included and the discussion covers

many vexed questions such as the role of nuclei and agitation in the effervescence of carbonated drinks and the suggestion, not supported in the present thesis, that various forms of bonding of carbon dioxide, for example, to proteins or as "carbonic acid", play a part. Some readers may find the presentation rather verbose and obscure and may feel somewhat perplexed by the description of numerous 'experiments' where it is not always easy to appreciate either the objects or the results. Further more some at least of the ideas will be provocative as, for example, the view that solutions of carbon dioxide in aqueous liquids may be regarded as dispersed systems similar to emulsions. It is further suggested that increasing the level of disturbance during carbonation results in a coarser 'emulsion' so that the gas is entrapped in comparatively large aggregates which are unstable and tend to give rise to over foaming ('wildness' or 'gushing') when the pressure is released. While this view may help in describing the phenomenon of gushing, it leaves out of account much that is known from scientific experiment about this behaviour and moreover does not in any material way contribute towards means of controlling or avoiding the defect. As this is only one example illustrating the general character of this monograph it will be clear that the latter makes no claim to be comprehensive, but, nevertheless, it contains a good deal of interest to the physical chemist as well as much that will be stimulating to the more technical reader. A H COOK

Animal Behaviour

By Dr John Paul Scott (The College Library of Biological Sciences) Pp xi+281+16 plates (Chicago, Ill University of Chicago Press, London Cambridge University Press, 1958) 37s 6d net

THE particular value of this book is that it is comprehensible to reasonably intelligent people who have not steeped themselves in the jargon of the ethologists. It may be used as a text-book because it covers well the general field of animal behaviour, especially in basic social aspects, but the book is also an introduction which will subtly draw the student forward into a wider range of reading. The scientific discipline throughout is commendable.

Animal behaviour is concerned with the activity of the whole organism and groups of organisms: what an animal is doing is as important as what it is, and behaviour is one of the central problems of existence. Dr Scott develops his work from the elements of behaviour, the limitations imposed by anatomy, and the internal causations from physiology, to the subject of learning and the effects of experience. This is straightforward going with field and laboratory illustration, but when the study of organization of behaviour and social organization is reached Dr Scott becomes an inspiring teacher. He is not to be classed with those practitioners in ethology who cannot see wood for trees: he becomes a naturalist seeing individuals and populations in their larger environmental setting. The problems of developing sociality and social disorganization in relation to ecological factors are well chosen and illustrated and the reader is left wondering—a valuable mental state—about the puzzling field of the gene complex in relation to homeostasis and habitat selection in very slightly different races of animals. It is something of an achievement to write so simply without writing down. F FRASER DARLING

THE TANDEM GENERATORS OF THE UNITED KINGDOM ATOMIC ENERGY AUTHORITY

By K W ALLEN and F A JULIAN
Atomic Weapons Research Establishment Aldermaston

W D ALLEN and A E PYRAH
Atomic Energy Research Establishment Harwell

AND

J BLEARS

Metropolitan-Vickers Electrical Co Ltd., Trafford Park, Manchester

THE electrostatic generator, associated with the name of Robert J Van do Graaff, has emerged during recent years as one of the principal instruments in nuclear physics in the range 1-6 MeV. Its advantages are those of flexibility and precision. The type of ion accelerated (proton, deuteron, helium 3, etc.) and its energy can be readily varied while at a given setting the beam energy can be controlled to 0.02 per cent. The principal limitation of the machine is that terminal voltages greater than 6 MV are difficult to attain and until very recently, no electrostatic generator had produced hydrogen ions with energies in excess of 10 MeV. As a result, studies of nuclei using electrostatic generators have been limited to the lighter and medium weight elements. With energies of 12-14 MeV, these studies can be extended to the heaviest elements.

The idea of utilizing the principle of charge-changing to obtain doubling of energy in an accelerator is due to W H Bennett, who patented the idea about twenty two years ago. Renewed interest was shown in the proposal following an article written in 1951 by Alvarez¹, who pointed out many of the advantages associated with voltage-doubling and an important contribution was made by Weismann and Cameron², who developed an ion source which yielded 25 μ amp of negative hydrogen ions.

Briefly, the tandem generator^{3,4} depends on the voltage multiplication which can be achieved by injecting negative ions into an electrostatic generator in which the stack, instead of being single-ended as in a conventional machine, extends throughout the length of the pressure vessel. The negative ion source is thus at earth potential and outside the pressure vessel, a factor which is of importance as we shall see below. Negative ions are conveniently formed by the passage of positive ions through gases at velocities corresponding approximately to the velocities of the outer orbital electrons. These conditions favour the formation

of negative ions at energies of 10 keV. For example a hydrogen ion beam passing through hydrogen gas can emerge with 2 per cent in the form of H⁻. Unwanted particles such as neutrons and electrons, are removed from the negative ion beam by the action of a weak magnetic field before injection into the electrostatic generator. The beam is then

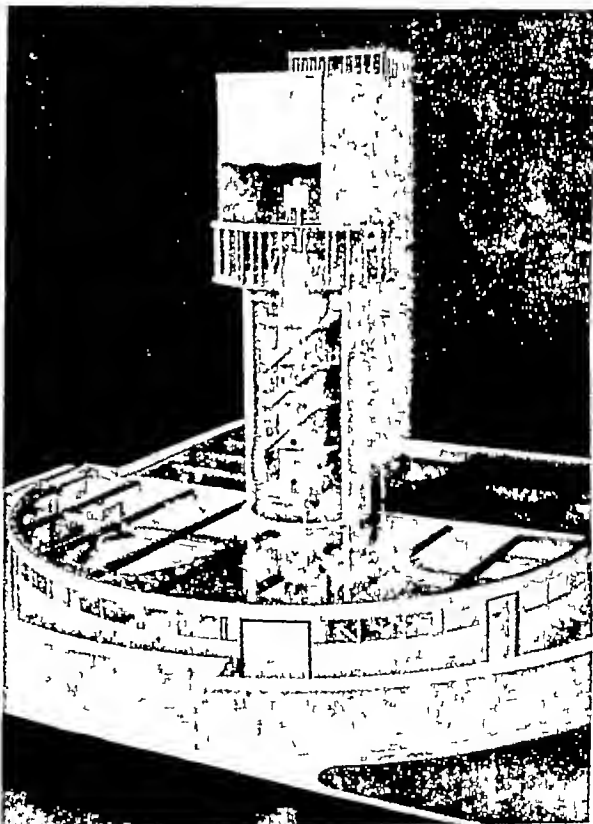


Fig. 1 Model of the tandem generator building at the Atomic Energy Research Establishment Harwell

accelerated by the positive voltage on the central electrode, and as a result of this acceleration, the ions are moving with a centre of mass velocity large compared with that of the outer electrons about the nucleus. In these circumstances, the passage of the ion beam through a thin foil or tube containing gas at low pressure causes electrons to be stripped off, so that the emergent beam consists of positively charged particles. The energy lost by the beam in passing through the stripper is negligible ($<0.5 \text{ keV}$). The positive ions are then further accelerated through the second half of the stack. Thus, an H^- ion of charge e , injected into a stack with a central electrode of V volts, will emerge with energy of $2Ve$ electron volts. Oxygen ions which are injected as O^- and lose, for example, five electrons at the central electrode will finally emerge with an energy $6Ve$, and so on.

The tandem generator has many possibilities. Proton and deuteron beams with energies of $\sim 12 \text{ MeV}$ and oxygen ions with energies of $30\text{--}40 \text{ MeV}$ can readily be obtained. In the more distant future, ion beams of helium, lithium, fluorine and any other element capable of forming negative ions (a criterion which includes about half the periodic table) may be produced. The fact that the ions are generated outside the pressure vessel at or near ground potential means not only that the source of most of the troubles in an electrostatic generator is readily accessible for maintenance, but also that there are virtually no limits to the power consumption, size and complexity of the injector system. Thus, millimicrosecond time of flight techniques, which are important in many experiments, are more readily applied in the tandem generator than in the conventional machines, since deflexion and bunching can be applied to the low-energy beam before injection. Finally, it may be possible in the future to polarize the nuclei of negative ions, and eventually to produce beams of accelerated polarized protons.

A horizontal tandem generator has been developed by the High Voltage Engineering Corporation, of Burlington, Massachusetts, for the Chalk River laboratories of Canada, and came into operation in January of this year, following successful trials in Burlington. In 1956 interest in the tandem generator was growing in the United Kingdom Atomic Energy Authority, because the potentialities of the machine as a tool for nuclear research have a direct bearing on the atomic energy programme. Thus, precision studies of the energy-levels of the heaviest elements can for the first time be made with beams of protons or deuterons from the machine, similar studies can be made of the energy-levels and level densities in the region of the periodic table occupied by the fission products. Finally, the availability of high-energy deuteron beams makes possible neutron

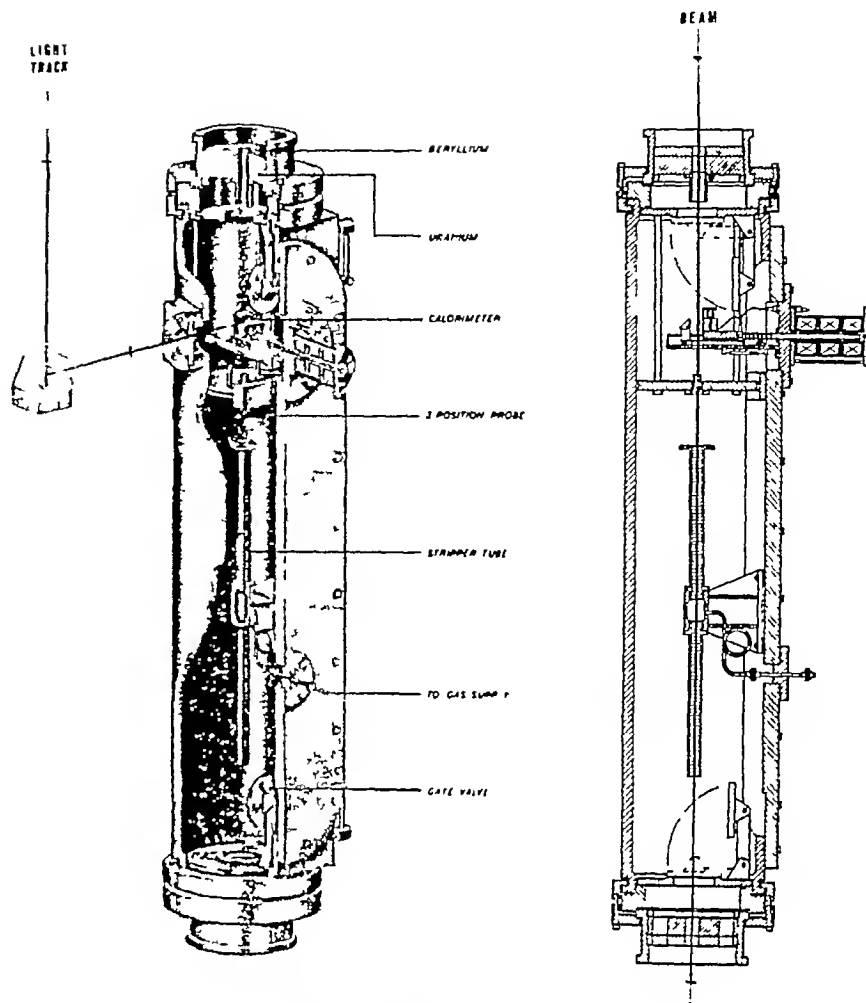


Fig 2 Arrangement of the gas stripper used to convert negative ions into positive ions in the high-voltage terminal

sources in the region of $8\text{--}12 \text{ MeV}$, a region which has hitherto constituted a gap in the energy of neutron sources readily available from conventional machines.

In June 1956, therefore, it was decided to build two machines for the Atomic Energy Authority, one at the Atomic Weapons Research Establishment, Aldermaston, and the other at the Atomic Energy Research Establishment, Harwell. A contract was placed with Metropolitan-Vickers, Ltd., for the engineering components of the British machines, the Atomic Weapons Research Establishment undertook the development of ion sources and strippers, while the provision of accelerating tubes was the responsibility of the Atomic Energy Research Establishment. A vertical design was chosen because there is no experience in Great Britain of the construction of horizontal machines, and it was felt that the engineering difficulties in a vertical machine would be less severe. There are, however, other advantages in a vertical design. In a vertical machine, a much greater weight of equipment can be placed in the centre terminal, so that the possibility presents itself of using the machine as a conventional single-ended machine as well as a tandem. Also, with a vertical machine, the beam can be delivered to any point in a horizontal plane by 90° deflexion in a single rotatable magnet. In Fig 1 is shown a photograph of the model of the tandem generator at Harwell, the target rooms are disposed in a semi-circle, with two shielding walls dividing the area into three

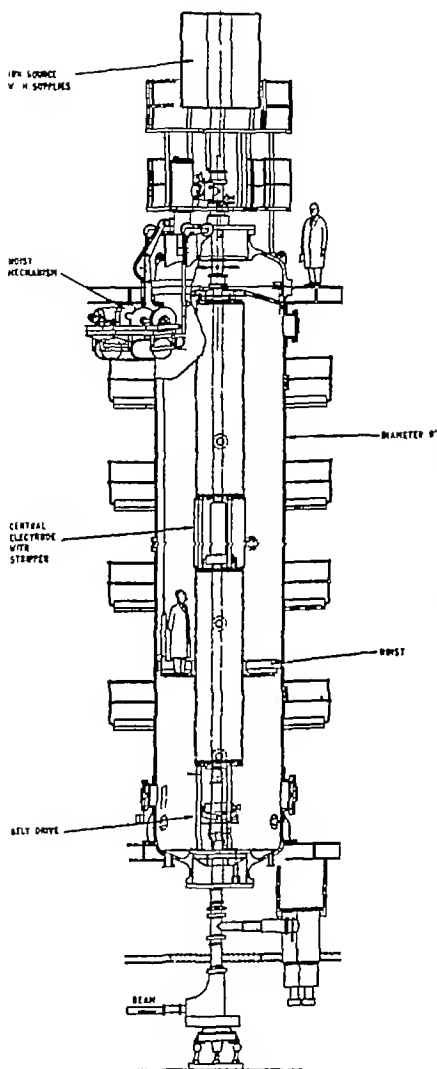


Fig. 3. Vertical section of the tandem generator.

sections. In this way, experimental equipment can be set up in one room while an experiment is in progress in a neighbouring room.

In the Aldermaston machine, stripping of the negative ions in the centre terminal is achieved by passing the beam through a tube 24 in. long and 0.14 in. in diameter containing oxygen gas at low pressure. Precise control of the injected beam is required in order to maintain an accurate focus at the centre of the stripper tube for all centre terminal voltages in the operating range of the machine. The

advantage of the gas stripper is its indestructibility, however, considerable success has been achieved at Harwell in stripping with thin carbon films 4–5 $\mu\text{m}/\text{cm}^2$ thick, and analysed proton beams up to 2 μamp have been focused on targets. The components of either gas stripper or foil stripper are mounted on a flat plate which forms the greater part of one side of the aluminium alloy chamber (Fig. 2) which joins the two accelerating tubes. The type of stripper or any of its components may therefore be changed at will without affecting the overall alignment of the accelerator.

The injector system, which is described elsewhere¹ is based on a Thonemann ion source used in the manner first suggested by Phillips and Tuck.² It is essentially a positive ion source in which electron exchange with neutral atoms takes place in the exit canal. Lens voltages following the canal are reversed as compared with the typical positive ion source so that only negative ions emerging from the canal are accelerated. After magnetic analysis to remove electrons and unwanted ions, the ion beam from the source is further accelerated and focused by electrostatic lenses. It enters the first accelerating tube of the main machine with an energy in the range 40–120 keV, depending on the centre terminal voltage. An optical method, suggested by R. Middleton, of observing the beam in the centre terminal has shown that a focus about 3 mm in diameter can be obtained.

Identical accelerating tubes each 14 ft long are used in the two halves of the machine. The tubes consist of highly polished aluminium electrodes cemented to accurately ground glass rings. As in the Chalk River machine³, the bulk of the gas used in stripping is pumped down the lower accelerating tube. This minimizes the loss of negative ion beam due to charge neutralization in the upper tube.

The engineering of the machine which will be described elsewhere is shown in section in Fig. 3. The pressure vessel is 45 ft long weighs 45 tons, and when fully pressurized contains about 2 tons weight of nitrogen mixed with carbon dioxide or freon. Access to the machine for general servicing is by the manholes at the base from which personnel can be hoisted by a lift with driving mechanism situated outside the pressure vessel near the top.

The accelerators at both Establishments have been operating satisfactorily for several months. Proton and deuteron beams with energies up to 11.5 MeV have been used in experiments, and currents up to 8 μA at somewhat lower energies are also available.

We wish to express our gratitude to our many colleagues in Harwell, Aldermaston and Metropolitan-Vickers who have contributed to the success of these machines. In particular we should like to mention A. J. Marriott, J. R. Henry and F. A. Howe of Aldermaston, R. H. V. Dawson and J. H. Partridge of Harwell and G. W. C. Cogle and J. Roxburgh of Metropolitan-Vickers.

It is also a pleasure to acknowledge the support and encouragement we have received at all times from Sir William Cook and Mr. D. W. Fry, of the Atomic Energy Authority and the Directors of Metropolitan-Vickers.

¹ Alvarez, L. *Rev. Sci. Instr.* **22**, 705 (1951).

² Weinman, J. A. and Cameron, J. R. *Rev. Sci. Instr.* **27**, 244 (1956).

³ Danforth, J. L. *Can. Elec. Eng.* **18** (July 1953).

⁴ Allen, W. D., *Can. Elec. Eng.* **25** (February 1952).

⁵ Collins, L. E. and Riviere, A. C. *J. Vac. Sci. Tech.* **4**, 121 (1952).

⁶ Phillips, J. A. and Tuck, J. L. *Rev. Sci. Instr.* **27**, 97 (1956).

UNIVERSITY OF MALAYA IN KUALA LUMPUR

By PROF R D PURCHON

Professor of Zoology, University of Malaya at Singapore

WITHIN less than ten years from its foundation (October 8, 1949) the constitution of the University of Malaya has been radically altered by ordinances enacted by the Governments of the Federation of Malaya and of the Colony of Singapore. The chief purpose of these enactments was to create a new Division of the University at Kuala Lumpur in the Federation of Malaya. The new constitution came into effect on January 15, 1959, and the University now comprises three bodies.

The University of Malaya (chancellor, the Right Hon Malcolm MacDonald, vice-chancellor, Dr A. Oppenheim). The main functions of the University of Malaya are the maintenance of co-ordination between the two Divisions, and the conferment of degrees. The authorities are the Court, the Central Council and the Guild of Graduates.

The University of Malaya in Singapore (principal, A. A. Sandosham). The authorities are the Divisional Council and the Divisional Senate. This Division of the University continues to function as before, except for the transfer to the newly created Division at Kuala Lumpur of the Departments of Geology and Engineering and of certain Departments in the Faculty of Arts.

The University of Malaya in Kuala Lumpur (principal, F. Mason). This is similarly administered by a Divisional Council and a Divisional Senate, and is accorded equal status with the establishment in Singapore. This Division comprises Faculties of Arts, Science and Engineering, while the Department of Agriculture will doubtless be accorded the status of a faculty in the space of a few years. The Department of Engineering was transferred as a whole from Singapore a year ago, and is now fully developed in new buildings in the Pantai valley at Kuala Lumpur. The Department of Geology is in the process of moving, only first-year students being taught in Kuala Lumpur during the present session, when the move has been completed, this subject will cease to be taught at Singapore, thus diminishing the diversity of subjects taught in the University of Malaya in Singapore. However disappointing this may be, this rationalization is unavoidable, at least in the early years under the new constitution.

Development of the University site in the Pantai valley at present includes the completed buildings of the Faculty of Engineering, one residential college and an estate of staff houses. Plans are already at an advanced stage for the buildings for the Faculties of Arts and Science and for the Department of Agriculture. Although these buildings will not be completed for a year, students have been enrolled into the 'intermediate year' of the science course and teaching has begun with skeleton staffs in temporary quarters in a local school, the Victoria Institution.

The Asia Foundation has made a most generous offer of help regarding the provision of a nucleus of books for the library at Kuala Lumpur. Consideration is being given by the University authorities to the methods whereby the books and journals in the library at Singapore can be made available to students in Kuala Lumpur, but care must be taken to ensure that the one excellent library is not split into two mediocre ones.

Appointments to the newly created chairs in science subjects are as follows.

Agriculture The creation of a Faculty of Agriculture at the present time has been made possible by the generosity of the Government of New Zealand, which provided £NZ250,000 specially for this purpose under the Colombo Plan Technical Co-operation Scheme. It is therefore a happy circumstance that the first professor of agriculture should himself be a New Zealander. Prof G. M. Davies, who was born in Dunedin, graduated at the University of Otago and Massey Agricultural College and then spent a further year at Canterbury Agricultural College. During the Second World War he served with the Royal New Zealand Air Force, and won the Distinguished Flying Cross in 1942. After the War, Mr Davies worked for three years in New Zealand, first as a farm appraiser with the State Advances Corporation and then as senior lecturer in soils and fertilizers at Massey Agricultural College. In 1948 Mr Davies moved to the United Kingdom, where he remained for ten years as a regional grassland husbandry officer in the National Agricultural Advisory Service.

Botany Prof M. E. D. Poore, the first incumbent of the chair of botany, brings to the newly created Department several years of ecological experience. Graduating from the Botany School at Cambridge, Dr Poore gained his doctorate in 1954. He studied for a time with Braun-Blanquet in the Montpellier School and then joined the Nature Conservancy at Edinburgh, where he initiated a survey of Scottish mountain vegetation, for which he is well known. He then joined Hunting Technical Services as a consultant ecologist and spent some three years in the Middle East. Here, Dr Poore surveyed the soils, vegetational units and agriculture of Cyprus, Jordan and Iraq with the view of outlining potentialities for agricultural development in these countries.

Chemistry The University of Malaya in Kuala Lumpur is fortunate indeed to have been able to attract Prof R. A. Robinson to this important appointment. Prof Robinson graduated at the University of Birmingham, where he was awarded the degree of Ph.D. in 1929, and the degree of D.Sc. in 1936. Dr Robinson held a Commonwealth Fund Fellowship at the University of Pennsylvania and at Yale University, and then held a Sterling Research Fellowship at Yale. Dr Robinson had appointments at University College, Exeter, and at Auckland University College until the Second World War. During most of the war years he held a senior post in a Chemical Warfare Department. In 1948 he was appointed to the chair of chemistry at the University of Malaya (in Singapore) and holds that post until he returns from a period of study-leave abroad to take up his new appointment in Kuala Lumpur. During his years at Singapore, Prof Robinson has served a full tour of duty as dean of science, and has also served for a period as acting vice-chancellor. He will therefore bring to Kuala Lumpur an invaluable store of administrative experience. Prof Robinson is best known for his research in the field of electrochemistry, and is the author of a standard monograph in this subject.

Geography Prof Robert Ho, who has been appointed to the chair of geography in the University of Malaya in Kuala Lumpur, graduated from King's College, London. He was awarded the degree of M.A. in the University of London in 1950. He has studied soil survey at Rothamsted, and soil analysis in the Department of Agriculture at Oxford. He was appointed to the staff of the Department of Geography in the University of Malaya (in Singapore) in 1948 and has been acting head of that Department from 1957 until his present preferment.

Mathematics The University of Malaya in Kuala Lumpur is fortunate in recruiting Prof O J Eliezer to the chair of mathematics. Prof Eliezer is of Ceylonese nationality; he graduated from the Department of Mathematics at Cambridge, was awarded the degree of D.Sc. in the University of London, and has occupied the chair of mathematics at the University of Ceylon since 1949. He is a mathematical physicist who is best known for his fundamental research in the field of quantum

mechanics. Having served for three years as dean of science in the University of Ceylon, Prof Eliezer will have much experience to offer in the development of the new Faculty of Science at Kuala Lumpur.

Zoology Prof J R Hendrickson, who has been appointed to the chair of zoology, was trained at the University of Arizona and at the University of California at Berkeley and joined the staff of the University of Malaya (in Singapore) in 1951. He is a vertebrate zoologist with wide experience and with special interests in herpetology and ecology. His study of the biology of the green sea turtle will doubtless become known as a classic example of objectivity in field research under difficult conditions. His practical experience of the fauna of the Malayan jungle will enable him to endow his Department with an appropriate trend in teaching and research while his fluency in colloquial Malay will make him especially acceptable in this virile and newly emergent country.

CONTINUOUS-FLOW CULTURE OF THE FILAMENTOUS MOULD *PENICILLIUM CHRYSOGENUM* AND THE CONTROL OF ITS MORPHOLOGY

By S J PIRT and D S CALLOW

Microbiological Research Establishment, Ministry of Supply, Porton

IN a recent report¹ we described the application of continuous flow technique² to culture of the mould *Penicillium chrysogenum*, which is used for penicillin production. This technique has now been used by us to elucidate the influence of pH value on the morphology of *P. chrysogenum* in submerged culture. The morphology of the mould is considered to be of importance in the process of penicillin production³. The role of agitation in determining the morphology of the mould has been stressed by Duckworth and Harris⁴ and by Dion, Carilli, Sermonetti and Chain⁵ but so far the influence of pH value on the morphology has remained unknown. The elucidation of the influence of pH value has been made possible by the advent of reliable means for the accurate control of pH value in cultures over long periods.⁶

Aberrant Forms of Fungi in Submerged Culture

One of the problems of continuous flow culture which we encountered was that the mycelia of newer strains of the mould (H¹s 49-133 and H²s 64 1255) selected for high penicillin production grew initially in a filamentous form but after a time in continuous culture the pellet form of growth was obtained. The main morphological differences between the filamentous and the pellet types of mycelium can be seen by reference to Figs 1a and 3. The pellet type of mycelium was undesirable because with its steady state growth, that is, a constant mycelium concentration in continuous culture, could not be maintained and also its rate of penicillin production was much lower than that of the filamentous form.

Cameo, Sermonetti and Chain⁵ showed that, in batch cultures the mycelium develops in the pellet form if the inoculum is below a certain size, but in our experiments the inoculum was sufficiently large to ensure that the mould grew in the filamentous form

until after the maximum dry weight concentration was reached.

We found that pellet formation was linked with the production of swollen, distorted short hyphae which mark an aberrant form. Duckworth and Harris⁴ in their observations on the production of this aberrant form, included a series of references which emphasized that agitation played a part in the process. The production of short swollen hyphae in vigorously agitated cultures of *P. chrysogenum* under penicillin producing conditions was confirmed by Dion *et al.*⁵ who attributed it to mechanical damage caused by the shearing action of stirring.

It does not seem to have been pointed out previously that abnormally short much branched swollen hyphae similar to those found to be characteristic of agitated cultures of *P. chrysogenum* have also been found to occur in unagitated cultures of fungi under some conditions. Foster⁷, in a short review of this aberrant form, gives references to it going as far back as 1857. Pasteur (quoted at length by Foster⁷), Wolmer⁸, Froy⁹ and Sakamura¹⁰ have reported the production of this aberrant form by *Mucor*, *Penicillium* and *Aspergillus* species. The many different conditions for example, lack of oxygen or high acidity, considered necessary for the formation of these abnormal cells have been summarized by Foster⁷.

In this article we describe how to produce in a vigorously agitated culture of *P. chrysogenum* either the normal, long thin hyphae or the short, swollen type and also how to prevent pellet formation in continuous culture. The importance of control of morphology in continuous flow cultures and in aeration is discussed.

Continuous-flow Culture Method

Cultures were grown in a continuous-culture apparatus developed from the type described by

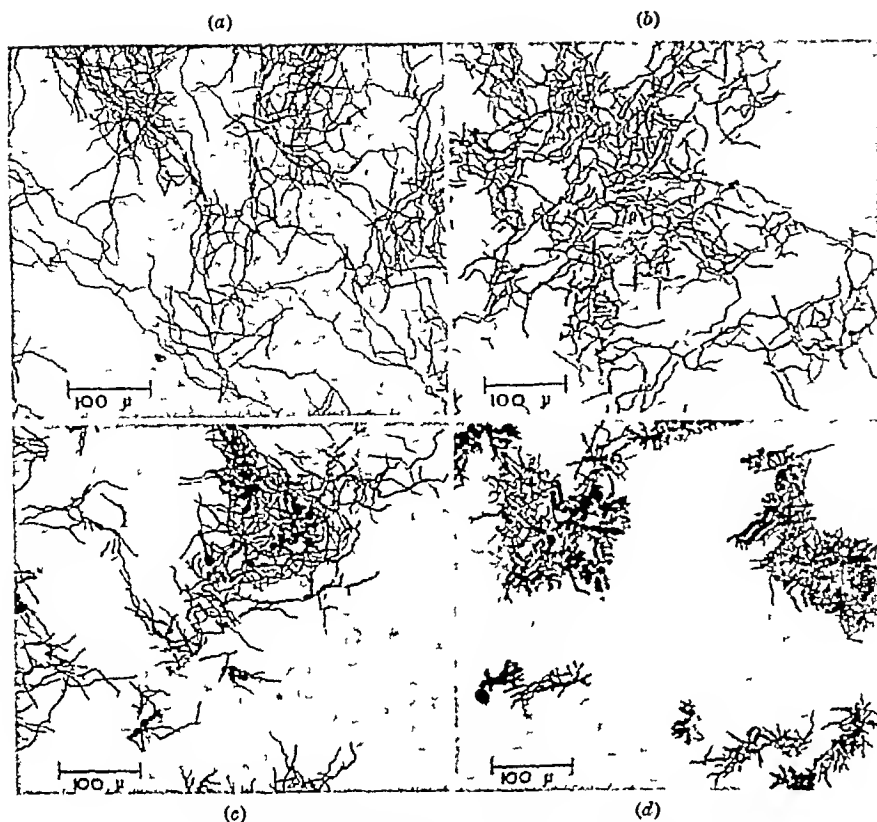


Fig 1 Mycelial forms of strain Wis 54-1255 in cultures grown at different pH values (a) pH 6.0, (b) pH 6.5, (c) pH 6.9, (d) pH 7.4

Elsworth, Meakin, Pirt and Capell¹¹ The pH control system was as described by Callow and Pirt⁵ The composition of the medium was (amounts in gm/l) crystalline magnesium sulphate, 0.25, ferrous sulphate, 0.10, copper sulphate, 0.005, zinc sulphate, 0.02, sodium sulphate, 0.50, manganese sulphate, 0.024, calcium chloride, 0.075, ethylenediamine tetraacetic acid, 0.566, dihydrogen potassium phosphate, 2.0, ammonium sulphate, 6.15, glucose, 20.0, phenylacetic acid, 1.0 The pH value was adjusted with sodium hydroxide In the inoculum culture, which was seeded with spores, phenylacetic acid was excluded from the medium and the glucose concentration was 10 gm/l Growth was limited by the amount of glucose supplied There was an excess of available oxygen Vortex aeration was used with a stirrer speed of 1,200 r.p.m., the impeller diameter was 0.42 times the vessel diameter, the volume of culture in the vessel was 1.7 l An antifoam agent ('Alkatarge-C' (Commercial Solvents, Terre Haute, U.S.A.) 30 per cent (v/v) in liquid paraffin) was added periodically to the cultures at a rate of 0.1 ml every hour The temperature was 25° The dilution rate (flow rate/culture volume) was 0.05 hr⁻¹, so that the average residence time of the mycelium in the culture was 20 hr The duration of culture varied from 200 to 2,000 hr Changes in pH value were made at a rate of 0.1 pH units/hr for the reason given elsewhere¹², and where, also, additional details of the continuous-culture method may be found

The mycelium was stained with cotton blue for the photomicrographs

Morphological Observations

During the initial batchwise growth before flow was started, the mould grew in the filamentous form

until the dry-weight concentration was near the maximum, 0.9 per cent (w/v) Then continuous flow was started and the pH value, which initially was 7.0, was raised to 7.4 in order to bring it near the optimum for penicillin production Under these conditions, for about the first 100 hr, steady state growth was obtained and the dry weight remained at the maximum value The mycelium form was of the aberrant filamentous type described by Dion *et al.*³ The aberrant filamentous form is illustrated in Figs 2b, 4a and 1d The characteristics of the aberrant form were the presence of short, much-branched, swollen and often distorted hyphae For comparison, the normal filamentous type is shown in Fig 1a The normal type is characterized by long, thin hyphae of constant thickness and few branches

After about 100–200 hr in continuous-flow culture at pH 7.4, strains Wis 49–133 and Wis 54–1255 began to form pellets of mycelium and gradually, during a further 100 hr, the aberrant filamentous form gave place almost entirely to the pellet form The initiation

of pellet formation seemed to be agglutination of the hyphae within the individual fragments of mycelium When the mycelium was completely in the pellet form it sedimented like a suspension of sand grains The pellets resembled the sclerotic type described by Thurumalachar and Gopalakrishnan¹³

The strains differed in their ability to form pellets Although all three strains investigated formed the aberrant, filamentous type of mycelium under the conditions stated, strain Wis 47-1564, unlike its descendant strains Wis 49-133 and Wis 54-1255, formed pellets only to a small extent and those that were formed did not persist more than about 100 hr

We discovered, first with strain Wis 47-1564 and confirmed later with strain Wis 54-1255, that pellet formation and the formation of the aberrant and normal filamentous forms were determined by the pH value of the medium The influence of pH value on the morphology of the mould may be seen in Fig 1, which shows the appearance of the mycelium grown at pH values 6.0, 6.5, 6.9 and 7.4 The average length of branches decreased progressively from the order 200 μ at pH 6.0 to 20 μ at pH 7.4 The thickness of hyphae was 2–3 μ at pH 6.0, but at 7.4, owing to the formation of swollen cells, the thickness covered the wider range, 2–18 μ Fig 1d shows the large number of swollen, yeast-like cells produced at pH 7.4 and also the beginning of pellet formation Pellet formation was most marked at pH 7.4 but it did occur to a lesser extent at pH values down to pH 6.7 with strain Wis 54-1255

Lengthening of the hyphae resulted in a marked increase in the viscosity of the culture The culture produced at pH 6.7 and higher values flowed easily like a bacterial culture, whereas the culture grown at pH 6.0 had a porridge-like consistency and flowed with difficulty The dry weights of mycelium in the culture were the same at all pH values



Fig. 2. Normal and aberrant types of mycelium of strain IFis 47-1561: (a) Long thin hyphae (normal type) produced by growth at pH 6.0; (b) short hyphae containing swollen cells (aberrant type) produced by growth at pH 7.4.

The changes in morphology and viscosity accompanying change in pH value were reversed when the pH change was reversed, so that, for example, the pellet or short filamentous form gave place to the long filamentous form when the pH value was lowered and vice versa. Microscope observations showed that the new form of mycelium produced as a result of a pH change arose by new growth from the old form. It was not a transformation of the old form. This was confirmed by the fact that the rate of appearance of the new form was approximately equal to the growth rate after a pH change it took about three days for the old form to disappear almost completely.

The pH value was not the only factor which affected hyphal length and morphology, nutrition also was shown to be a controlling factor. Substitution of the nitrogen source, ammonium sulphate, by corn steep liquor (filtered 4.5 per cent (v/v)) which is a common constituent of the media used in penicillin production increased the hyphal length, reduced the frequency of hyphal branching and prevented the formation of swollen cells at pH 7.4. The effect of addition of corn steep liquor is shown in Fig. 4. These results strongly suggest that corn steep liquor contains some substance which stimulates the production of the normal morphological type.

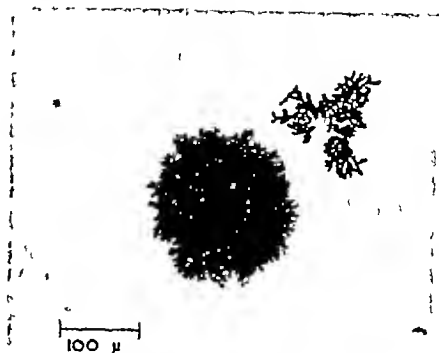


Fig. 3. Pellet mycelium of strain IFis 40-133 produced at pH 7.4.

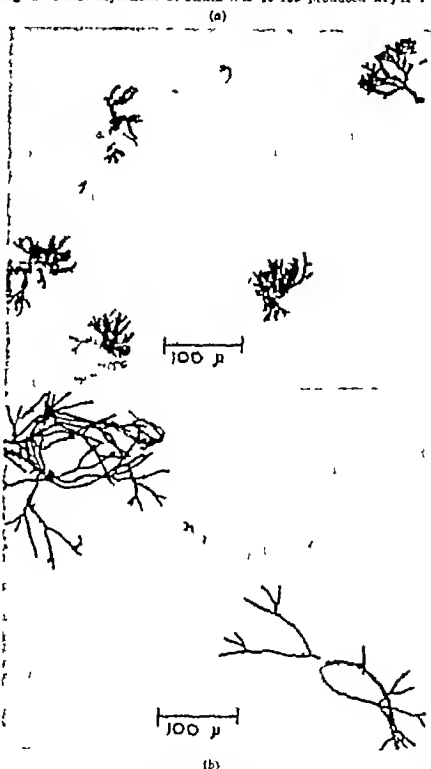


Fig. 4. Mycelium of strain IFis 40-133 grown at pH 7.4: (a) With ammonium sulphate as the nitrogen source; (b) with corn steep liquor as nitrogen source.

Conclusions Possible Role of Cell Wall

The conclusions we draw are that during growth of *P. chrysogenum* in agitated culture the hyphal length decreases with increase in the pH value above

6.0, the hyphal length is a minimum at pH 7.0–7.4 and higher values. Extensive formation of swollen cells occurs at pH values above 7.0, this property and the hyphal length being influenced by the medium composition. Pellet formation occurs at pH values above 6.7 but it also shows dependence on strain.

The increase in the length of hyphae with decrease in pH value we interpret to mean that the resistance of the cells to shear increases with decrease in pH value. We attribute the varying resistance to shear and the production of swollen cells to variation in the cell-wall structure. This idea was suggested to us by the recent bacterial studies which have shown that the mechanical strength of a bacterial cell resides in its cell wall, and by analogy we suppose that the resistance of the fungal cell to mechanical forces is determined by its cell-wall structure. This hypothesis implies that the cell-wall structure or composition depends on the pH of the environment during growth. Also swollen cells could be due to a change in cell-wall structure involving loss of rigidity and consequent inability to resist the internal osmotic pressure.

From the practical point of view the long hyphae produced at a low pH value are undesirable because they make the viscosity of the culture high and consequently lower the efficiency of mixing and rate of transfer of oxygen¹⁴. On the other hand, to prevent the extensive formation of pellets and the swollen aberrant form, the pH value during growth should not be greater than 7.0.

Since the optimum pH value for penicillin production is about 7.4 it seems likely that a continuous-

flow process for penicillin production will require two stages, the first stage for growth of the mould with the pH value not exceeding 7.0 and a second stage with a higher pH value for penicillin production¹⁵.

We are grateful to Prof. M. P. Backus of the University of Wisconsin for the gift of strain *Wis* 54-1255. Strains *Wis* 47-1564 and *Wis* 49-133 were obtained from the National Collection of Industrial Bacteria, Department of Scientific and Industrial Research, Teddington. The technical assistance of Mr. J. E. D. Stratton is gratefully acknowledged.

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TRANSLOCATION OF COBALT-60 AND CAESIUM-137 BY FUNGI IN AGAR AND SOIL CULTURES

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AND

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A LONG-TERM research project has been initiated at the Grassland Research Institute on the mechanism of microbial decomposition of grass swards after ploughing back into the soil. These investigations comprise, among others, studies on the manner by which saprophytes progress through the soil from one food-base, that is, an aggregate of plant debris, to another. This will be determined by the phase in which the fungus exists in the soil—whether as dormant spores and resting bodies or as an actively growing, progressive mycelium. In this connection the mechanism of translocation of nutrients by fungi growing in the soil requires elucidation.

Translocation is the movement of nutrients and other materials from one part of the plant to another. As regards higher plants the mechanism of translocation has been studied extensively, but for fungi comparatively little work has been published. Buller¹ investigated protoplasmic streaming in fungi. On the basis of his own work and that of others he concluded that this phenomenon was the principal agent of translocation of nutrients in fungi. Schutte², after studying translocation by means of dyes and

fluorescein, postulated that fungi can be divided into two groups, translocating and non-translocating, and he, too, associated translocation with protoplasmic streaming. The work of Melin and Nilsson^{3,4} and that of Harley and his collaborators^{5,6} on the transfer of nutrients into the host by means of mycorrhiza indicates a translocation mechanism via the mycelium.

Preliminary notes have been published by Grossbard and Stranks⁷⁻⁹ on their attempt to study the growth of soil fungi *in situ* by inoculating soil with a fungal culture labelled with a nuclide emitting gamma-rays. It was hoped that those fungi which produce hyphae in the soil would form a fresh mycelium growing out from the radioactive inoculum. The new hyphae would in turn become radioactive and their distribution could be detected by virtue of the gamma radiations which have the power to penetrate the soil. This technique would depend primarily on the translocation of the nuclide from the radioactive inoculum into the new hyphae, and could provide not only a useful research tool for tracing the growth of fungi in the soil but also help to elucidate the

mechanism of transport of nuclides through the soil via fungal hyphae. This work has been extended and a brief account is given here.

The fungi used in the latest studies were *Pellicularia filamentosa* (Pat.) Rogers (*Rhizoctonia solani*) kindly supplied by Dr S D Garrett, *Helminthosporium sativum* Pemmi, King and Bekko, kindly supplied by Dr J H. Western, *Phycomyces blakesleeanus* Burgeff Herb Imp Mycol Inst 44142, *Phytophthora cactorum* (Leh and Cohn) Schroet Herb Imp Mycol Inst 02471, *Rhizopus stolonifer* (Jehrbach) Lind Herb Imp Mycol Inst 42844.

The nuclides used were cobalt-60 and caesium 137. They were chosen because they emit γ photons in addition to β particles. The fungi were labelled by culturing in media containing the nuclides ($1 \mu\text{Ci/ml}$), which were readily taken up by the mycelium. When grown in broth cultures, 25–50 per cent activity (varying with the conditions of the experiment) could be detected in the total mat after thorough washing.

The main test organisms for the soil cultures were *P. filamentosa* and *R. stolonifer*. Glass tubes filled with sterile soil were used, though occasionally also rectangular boxes. The inoculum for the soil-growth tubes consisted of a number of disks of a radioactive agar culture mixed with soil. This was divided into two halves of approximately equal activity, one of which was killed by heat. Each half was then placed at one end of the soil column in a growth tube. From this inoculum γ rays were emitted which penetrated the soil. Immediately after incorporation of the radioactive mycelium (living or killed) the tubes were scanned with a directional scintillation counter with a collimator (Ekeco model N 559A). This initial measurement served as a standard to check whether migration of the radioisotope via the fungal mycelium occurred after inoculation and to what extent the radioactive inoculum contributed to the counting rate as observed at points away from the initial reference source. The figures in Table 1, columns 1 and 3 referring to *P. filamentosa* cultures show that the highest counting rate outside the wall of the tube was just above the point where the radioactive mycelium had been incorporated. A similar observation was made with *R. stolonifer* and also with *Phytophthora cactorum*. The inoculum of the latter labelled with cobalt-60 was buried several cm deep in soil in a box and the preliminary scan was performed laterally and longitudinally. In soil box cultures of *H. sativum* labelled with caesium 137 the greatest number of counts was also obtained just above the inoculum. This method is useful and can locate with considerable accuracy the position of a radioactive inoculum through soil and the lid and wall of the container.

After inoculation the growth tubes were incubated and counts were made at weekly intervals. Columns 2 and 4 in Table 1 show the counts after 3 weeks. No significant change in counting rate could be observed as compared with the first scan. Also the ratio of activity between 'living' and 'dead' inoculum tube was the same after 3 weeks. However, by that time a fresh mycelium had grown out which could be seen to penetrate the entire soil column. This was particularly evident in the *Pellicularia* culture. However, radioactivity could not be detected in this fresh growth. Similar observations were made with the fungi which were inoculated into soil boxes. The failure to detect any radioactivity in the fresh mycelium by scanning with the scintillation counter may have been due to one of three causes. First the fungi

Table 1 SCANNING RESULTS OF SOIL GROWTH TUBE OF *Pellicularia filamentosa* (Co-60)

| Distance from inoculum (cm.) | Counts/sec. | | | |
|------------------------------|-------------|--------------------------|--------------------|--------------------------|
| | (1) Initial | (2) Living After 3 weeks | (3) Killed Initial | (4) Killed After 3 weeks |
| 0 | 800 | 800 | 780 | 780 |
| 2 | 300 | 320 | 300 | 285 |
| 4 | 140 | 150 | 145 | 140 |
| 6 | 90 | 90 | 92 | 84 |
| 8 | 70 | 70 | 65 | 65 |
| 10 | 55 | 55 | 55 | 55 |
| 12 | 45 | 45 | 44 | 44 |
| 14 | 40 | 39 | 37 | 36 |
| 20 | 22 | 22 | 22 | 22 |
| 22 | 16 | 16 | 16.5 | 16.5 |
| 24 | 11.5 | 11.5 | 12.5 | 12.5 |
| 26 | 9.5 | 9.5 | 9.5 | 9.5 |
| 44 | 7.4 | 7.4 | 7.4 | 7.4 |
| 60 | 0.5 | 0.5 | 0.5 | 0.5 |

The counts were recorded on a ratemeter Ekeco type N322 and include background counts of 2.4/sec.

tested lacked the capacity to translocate cobalt-60 or caesium 137, second the scanning technique with the scintillation counter was inadequate and third, the dilution of radioactivity by the outgrowing hyphae was so great that insufficient activity was produced in the volume being scanned to enable detection.

Regarding the first point no information could be found in the literature on whether fungi in general are capable of translocating cobalt 60 or caesium 137 in a manner similar to that reported for higher plants as regards caesium 137¹¹ and cobalt 60¹². It was therefore necessary to study translocation in fungi in agar and broth cultures.

Beginning these studies with *P. filamentosa* the transport of cobalt-60 from submerged into aerial mycelium was studied by autoradiography employing Pelco's¹³ stripping film technique. Cobalt is often considered to be a microbial toxin. However the addition of cobaltous chloride to the medium—whether as the stable or the radioactive isotope—enhanced the growth of *P. filamentosa*. Details of the experimental technique were described by Grossbard¹⁴, who suggested that accumulation of cobalt 60 occurred inside hyphae submerged in radioactive agar, for as the autoradiograms showed, the density of silver grains inside the hyphae was greater than in the agar film between the mycelium. Yet, in autoradiograms of aerial mycelium growing just above the active submerged mycelium the grain density within the aerial hyphae was similar to that of the background. This suggested that the tracer was not transported into the aerial hyphae. Similar negative results were obtained from aerial mycelium in broth cultures. It was therefore at first believed that *P. filamentosa* inherently lacked the capacity for transporting cobalt 60 through its system and was one of the group of fungi which—after Schütte¹⁵—had no translocation mechanism. However, when using the stripping film technique very thin preparations have to be made and a few hyphae only were used. The absence of silver grains in the aerial mycelium may have been due merely to the fact that the dilution of the nuclide when transported from the submerged into the aerial hyphae was so great that not enough tracer was available for a positive autoradiogram to be formed. That this reasoning was correct was shown when an autoradiogram was produced of large quantities of mycelium placed on an X-ray film. Adapting a technique described by Schütte¹⁵ a small dish of agar containing cobalt 60 was placed

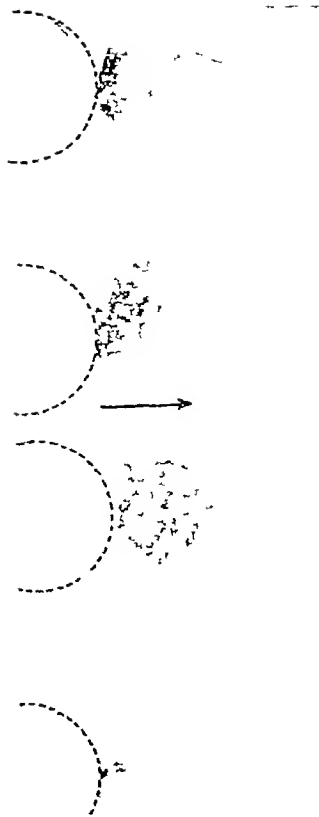


Fig 1 Autoradiogram of *Pellicularia filamentosa*, 'Cellophane strips + mycelium'
 > Original outline of container (diagrammatic) with agar + cobalt-60 and inoculum of fungus
 Arrow indicates inactive agar with fresh mycelium which became labelled with cobalt-60
 Gradual decrease in intensity of blackening with increase in distance from active container

inside a large one filled with similar but inactive agar. In the centre of the radioactive dish *P. filamentosa* was inoculated. The mycelium grew out of the dish over the glass edge on to some 'Cellophane' strips situated on top of the inactive agar of the outer container. The strips together with the mycelium were removed and fixed on microscope slides which in turn were placed in close contact with an X-ray film 'Industrial B' (Ilford). After exposure for 3 weeks a clear image of the mycelium developed, suggesting translocation of cobalt-60 from the inner container via the mycelium (Fig 1). The blackening was most intense at the points where the 'Cellophane' strips were nearest to the container with the radioactive agar and decreased in intensity with an increase in distance. However, when tufts of hyphae were removed from the 'Cellophane' strips at intervals of 5 mm the resulting autoradiograms were negative. These observations indicate that a translocation mechanism for cobalt-60 and probably other materials does occur in *P. filamentosa* but that it cannot be demonstrated readily in individual hyphae.

Translocation was then studied in some Phycomycetes, that is, in *R. stolonifer* and *P. blakesleeana*. These two fungi were grown in flasks with a layer of radioactive agar at the bottom. Individual sporangiophores or tufts were removed and fixed to a glass slide

with collodion and autoradiograms prepared. Figs 2a and b show the sporangiophores of *P. blakesleeana* labelled with caesium-137 and cobalt-60, respectively.

The sporangiophores as well as the sporangia of both fungi displayed considerable grain density giving rise to intense blackening which formed a true image of the morphology of the fungal structures. However, in the sporangia the blackening was far more intense. From these observations it was inferred that the nuclides were readily transported from a food base, frequently 5-6 cm away, through the sporangiophores and that they accumulated in the sporangia. It is tentatively suggested that the two nuclides were translocated by means of protoplasmic flow. Many workers have reported on this phenomenon in *Rhizopus* and other Phycomycetes and have observed that the direction of the protoplasmic streaming was towards the sporangia in which the protoplasm became concentrated prior to spore formation. The analogy with the movement of cobalt-60 and caesium-137 is thus apparent. Furthermore, Grossbard¹⁰ reported that where cobalt-60 labelled hyphal fragments of *Phytophthora cactorum* were ruptured, the tracer could be found in the cell content which had oozed out but not in the empty fragments. The fact that the translocation of cobalt-60 could be demonstrated in individual fungal structure far more readily in the aseptate Phycomycetes than in the septate *Pellicularia*, when using a medium with the same activity, provided further support for the hypothesis of transport by protoplasmic flow. Buller¹ has shown that both *R. stolonifer* and *P. filamentosa* displayed protoplasmic streaming, but he postulated that the type of streaming and the rate differed because of the presence of septa in *Pellicularia*. The flow passed only via a single pore in the septum and thus was slowed down, and this may have affected both the rate and efficiency of translocation. It seems likely that cobalt-60 is held firmly by the protoplasm and moves through the fungus only in chemical combination with the protoplasm (by co-ordination of cobalt with the amino functions of proteins, etc). This fits in with the results of Abelson and Aldous¹¹, who, working with cobalt-59, showed in the case of *Escherichia coli* that the nuclide was "very tightly bound, within the experimental error no tracer was lost by either the exchange with magnesium or inactive cobalt". They suggested as one alternative a "non-specific, non-metabolic attachment to the proteins and other groups of the organism". Thus, if cobalt-60 is transported through the mycelium it is assumed that it is carried along by the protoplasm as an integral part of it.

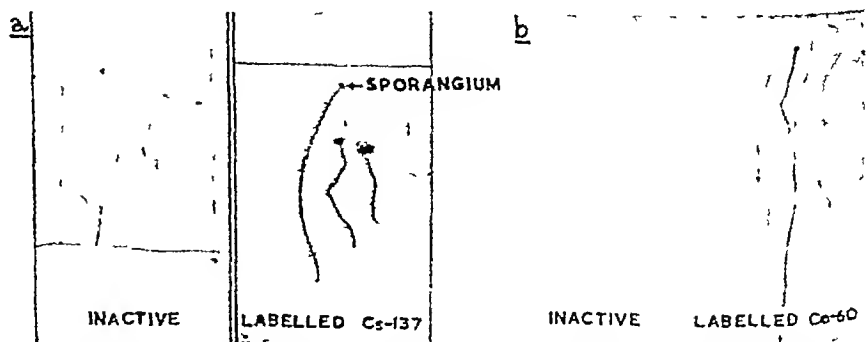


Fig 2 Photographs of autoradiograms of sporangiophores of *Phycomyces blakesleeana*
 a Stripping film technique. Inactive preparation is merely a photograph of the actual slide while the labelled shows intense blackening especially in the sporangia. b, Apposition on X-ray film. Inactive preparation formed no image at all.

The above results suggest that all the fungi tested display a translocation mechanism for the two nuclides in agar media though this is probably more efficient in the case of the Phycomycetes. Failure to detect radioactivity in the new mycelium growing from a labelled inoculum in the soil cannot therefore be explained satisfactorily in terms of an inherent lack of a translocation mechanism in the fungi tested.

While the scanning technique with the scintillation counter could be depended upon to locate a radio active inoculum in the soil, it may not have been sensitive enough to trace small alterations in the distribution of activity, especially in view of the fact that the strong radiations emitted from the inoculum may obscure any small change in counting rate due to genuine radioactivity. Having established that both *P. flamentosa* and *R. stolonifer* have the ability to translocate cobalt 60, a more direct method for testing transport via the fungi in the soil was employed. The soil columns after incubation for several weeks were cut into sections of 2.0 cm. in the case of *P. flamentosa* and 4 and 6.0 cm., respectively, in the case of *R. stolonifer*. Aliquots of 0.5 gm. of soil of each section were extracted with concentrated nitric acid (10 ml.) and the extract counted in a standard G.M.C. liquid Geiger counter tube (Table 2). In addition a very thin smear was made on a glass slide of 0.5 gm. of very finely ground soil taken from each section, placed on an X ray film backed with a 1/16 in. lead sheet and exposed for 3 weeks. Figs. 3a and b show a representative photograph and corresponding autoradiogram of a preparation and Table 2 summarizes the results.

From both the counts and the autoradiograms, it can be concluded that some slight migration of the nuclide occurred from the soil section containing the inoculum but over a short distance only. This was observed both in the tubes with the killed and living inoculum. Frequently though not always movement of cobalt 60 tended to be greater from the killed inoculum. This may be explained in terms of increased permeability of fungal cells after death. As the inocula consisted of disks of agar cultures the nuclide might also have diffused from the agar and not from the fungal structures only. The agar disks were used, because by providing a food base the subsequent growth of the mycelium was greatly enhanced. Other inoculation methods such as by washed mycelium from a broth culture are under investigation in order to eliminate this complication. What migration has taken place may be interpreted on one hand as diffusion of the nuclide from both the agar base and the mycelium and then through

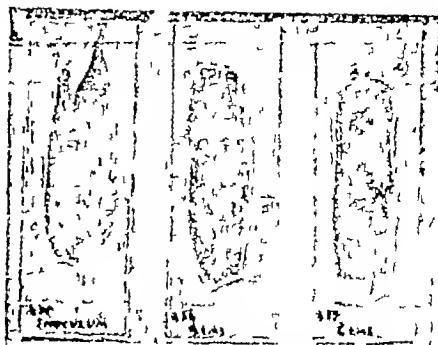


Fig. 3. Photograph (a) and autoradiogram (b) of soil smears from a soil growth tube of *Rhizopus stolonifer* (killed inoculum cobalt-60). Soil with inoculum gives the most intense image; a true reproduction of the soil smears. At a distance of 4 cm. the image is much weaker and at 6 cm. none is formed.

the soil, or else as a case of genuine translocation. There is some indication that the migration rate was somewhat slower in *Pellicularia* than in *Rhizopus* since in the former activity was rarely found farther than 2 cm. from the inoculum. An analogy with the more efficient translocation mechanism of *Rhizopus* as observed in agar culture suggests itself but further confirmatory experiments are necessary before drawing final conclusions, for the migration rate is dependent on many environmental factors not easily standardized. Whatever the mechanism of the

Table 2. RELATIVE RADIOACTIVITY OF SOIL SAMPLES FROM GROWTH TUBES OF *Rhizopus stolonifer* and *Pellicularia flamentosa* (Co-60) BASED ON COUNTS OF SOIL EXTRACTS AND AUTORADIOGRAPHY OF SOIL SMEARS

| Exp. No. | Organism | Inoculum | Distance from inoculum (cm.) | | | | | | | |
|----------|----------------------|----------|------------------------------|--------|---------------|--------|---------------|--------|---------------|--------|
| | | | Act (percent) | A.R.G. | Act (percent) | A.R.G. | Act (percent) | A.R.G. | Act (percent) | A.R.G. |
| 1 | <i>R. stolonifer</i> | Living | 100 | ++ | | | | | | |
| 2 | | Killed | 100 | ++ | | | | | | |
| 3 | | Living | 100 | ++ | | | 1.66 | + | 0.16 | 0 |
| | | Killed | 100 | ++ | | | 5.5 | + | 0.7 | 0 |
| 1 | <i>P. flamentosa</i> | Living | 100 | ++ | 0.75 | | 0.02 | | 0.14 | 0 |
| | | Killed | 100 | ++ | 8 | | 2.47 | | 0 | 0 |
| 2 | | Living | 100 | ++ | 0 | 0 | 0 | 0 | 0 | 0 |
| | | Killed | 100 | ++ | 0 | 0 | 0 | 0 | 0 | 0 |
| | | Living | 100 | ++ | 0.33 | + | 0 | 0 | 0 | 0 |
| | | Killed | 100 | ++ | 0.8 | + | 0 | 0 | 0 | 0 |

A.R.G. autoradiograms. Act. (per cent) percentage of radioactivity as compared with that of the inoculum. * see Fig. 3 (a) and (b). + a living inoculum was used but no growth occurred. ++ intense image; + weak image; 0 no image.

migration of cobalt-60 and whatever the difference in rate between killed versus living inoculum or *P. filamentosa* as compared with *R. stolonifer*, the percentage of cobalt-60 and the distance over which it is transported are very small indeed. In every case most of the activity is retained in the section of the soil containing the inoculum. There the nuclide may be held by either adsorption on the soil colloids after having diffused through the cell wall of the fungi or within the hyphae of the original inoculum, possibly bound to the protoplasm.

Regarding the first point, this would fit in with the observation of Jones *et al.*¹⁵, who have shown that in a soil with moderate exchange capacity cobalt-60 remains close to the surface even after repeated applications of water. These workers placed the cobalt-60 directly in the soil, while in the experiments described here it was introduced via the fungal inoculum, the soil used was one of moderate exchange capacity.

On the second possibility, Harley and McCready⁶ have shown that in the case of excised mycorrhizal roots of the beech 90 per cent of phosphorus-32 absorbed from aerated media was found to be held in the fungal sheath and only 10 per cent diffused into the core. This ratio varied with environmental conditions⁶. By analogy it could be assumed that cobalt-60 also is firmly held within the fungal tissue, especially in view of the observations that migration is of lower order from the living than from the dead inoculum. Thus, the possibility is not ruled out that the small migration which had occurred from

living inocula was due to some extent to active transport inside the fungal tissue, perhaps by protoplasmic flow. This is a hypothesis, and more work is required to distinguish between migration by diffusion or by active translocation. Probably both factors will operate simultaneously.

Our thanks are due to Dr William Davies for his interest in this work, for encouragement and guidance and for providing facilities to carry out these studies. We are indebted to Mr G. E. Barton for his valuable collaboration and technical assistance, without which this work would not have been possible, and to Mr D. Smith for the preparation and counting of soil extracts.

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OBITUARIES

Prof Kaj U. Linderstrøm-Lang, For Mem. R. S.

THE death of Prof. Kaj Ulrik Linderstrøm-Lang on May 25 was a great and irreplaceable loss, not only to his colleagues and friends but also the scientific community at large. The Chemical Division of the Carlsberg Laboratory in Copenhagen, which he led with such force and inspiration for twenty-one years, is perhaps unsurpassed in terms of the number of individuals who identify it as a major scientific home.

Linderstrøm-Lang was born in Frederiksberg, Copenhagen, in 1886, the son of Dr C. F. Linderstrøm-Lang. His education at the Danmarks tekniske Højskole led to a degree in chemical engineering in 1919, following which he became assistant to Prof. S. P. L. Sørensen at the Carlsberg Laboratory. In the environment of Sørensen's fundamental research on the physical chemistry of proteins in solution, Linderstrøm-Lang's natural talents for mathematics and laboratory experimentation led him to conceive in 1925 his classical paper "On the Ionisation of Proteins", which stands to-day as the fundamental theoretical treatment of protein titration curves.

During the period 1926-27 he studied in the laboratory of Prof. R. Willstätter in Munich, and there he developed his continuing interest in the chemistry and mode of action of proteolytic enzymes. Upon his return to Copenhagen he completed his earlier investigations on the electrophoretic properties of proteins and presented his doctoral dissertation in 1929.

His investigations of the nature and determination of proteolytic enzymes, developed in collaboration with the increasing flow of visiting scientists in the Laboratory, became directly applicable to the work

he afterwards undertook in collaboration with Dr. Heinz Holter, who went to the Laboratory in 1930. Linderstrøm-Lang and Holter developed, over the succeeding ten years, a tremendous array of delicate and sensitive techniques for the study of the distribution of a large variety of enzymes and other constituents in cells. These micro methods, now standard procedure in many laboratories throughout the world, made possible an enormous advance in our understanding of many aspects of cellular physiology. It is characteristic of the methods that Linderstrøm-Lang developed that they were based on extremely simple but basic physical principles. Well-known examples are the Cartesian diver technique for the measurement of metabolism in single micro-sections of tissue or of individual cells, and the extremely sensitive gradient technique for the determination of the densities of minute quantities of material. A whole generation of young chemists and biologists was strongly influenced by these methods and profited enormously by direct collaboration with Linderstrøm-Lang during this period of his scientific career.

When S. P. L. Sørensen retired in 1938, Linderstrøm-Lang was chosen as director of the Carlsberg Laboratory. Continuing along the lines begun by Sørensen, which had already made the Laboratory world-famous in protein chemistry, Linderstrøm-Lang initiated an outstanding series of studies on the internal structure of protein molecules. Using as probes such phenomena as the volume contraction occurring as a result of proteolytic cleavage of peptide bonds, he began to develop during this period his strong interest in the limited modification of proteins as one means of elucidating internal structure, and

published many fundamental papers on such systems as the conversion of chymotrypsinogen to chymotrypsin and ovalbumin to plakalbumin. An example of his inexhaustible ingenuity in the development of experimental techniques was the 'deuterium exchange' technique, which permitted the estimation of the relative rates at which individual hydrogen atoms within the primary, secondary and tertiary structures of a protein molecule could reach equilibrium with deuterium atoms in the water in which the samples were dissolved.

Linderström Lang's scientific talents, combined with his characteristics of warmth and perception, brought him early and frequent recognition by many organizations both scientific and civic. In addition to receiving numerous honorary degrees from universities throughout the world, he was a member of the Royal Swedish Academy of Sciences, the Academy of Sciences of the U.S.S.R., the Royal Society of London, the Finnish Scientific Society and the National Academy of Sciences of the United States, to mention only a few. He was, at various periods during his life, president of the Danish Academy of Technical Sciences, the Akademiet for de tekniske Videnskaber, and in 1958 of the International Union of Biochemistry.

The list of honours and accomplishments scattered through his career are too numerous to list in detail. Perhaps even more important than these tangibles, however, was the impact of his warm personality on everyone who knew him. Kaj Linderström Lang had talents in many areas of human endeavour and, had he not chosen science as his major interest, could clearly have contributed prolifically in a variety of pursuits including music, art and literature. Those who know him will not forget his unique combination of wisdom, humour and intellectual integrity. With his death the world lost not only a great scientist but also a great man. C B ANDERSEN, JYU

Dr M Copisarow

MAURICE COPISAROW, who died on April 16, in his seventieth year, was a scientist of quite outstanding ability. His university education was acquired between 1909 and 1913 in the School of Chemistry at Owens College, where I knew him as a fellow student. He stayed on for postgraduate study as Dalton Research Scholar during 1914-16, working with Chaim Weizmann on "Phthalides of the Benzene, Naphthalene and Carbazole Series" (published in 1915). Afterwards, as Honorary Research Fellow (1916-19) he launched out into independent inquiries concerned mainly with reactions promoted by aluminium chloride.

During the First World War, Copisarow worked for the Ministry of Munitions and was responsible for a change in the method of washing TNT which greatly reduced the risk in handling this explosive. At the end of the War he experimented on the conversion of various explosives and also phoagens into products for which industrial uses could be found, and in these operations his eyesight suffered severe injury. Most unpleasantly the damage was progressive and in a relatively short time, while still at the outset of his career, he became blind. However, by 1925 he had to his credit nineteen publications of high quality, and in that year he was awarded the D.Sc. of the University of Manchester.

In his work as a chemist he could never have confined himself to narrow specialization. His mind

ranged over whole fields of scientific activity, and his keenness of perception allied to his uncommonly active imagination gave rise to a versatility which is well exemplified by his generalized theory of allotropy (*J Chem Soc*, 1921) and by his work on the phenomenon of periodic precipitation, reported between 1927 and 1932 in various scientific journals. These publications illustrate admirably his ability to recognize certain apparently unrelated chemical processes and structures as forms of expression of a unifying principle and to enunciate it.

After he had lost his sight, Dr Copisarow's scientific activities became restricted principally to the preparation of review articles and essays dealing with matters calling for theoretical consideration. His blindness seemed indeed to intensify his insight, and he extended his thinking to such subjects as the functioning of certain oxidation enzymes, the effects of radiation on enzymes and the biochemistry of virus infection. He studied these matters with the ultimate object of selecting and co-ordinating knowledge which might throw light on problems associated with the malignant growth of cells. Observations on biochemical work in the field of cancer research were published over a period of years in several journals, including a comprehensive review on the "History of Human Cancer", which appeared in the *Edinburgh Medical Journal* in 1952. Copisarow's writings on these matters were prompted by his great desire to contribute all he could to the furtherance of progress in the war on disease.

Further evidence of his feeling for the well being of his fellow-countrymen is afforded by the interest he had in the application of appropriate scientific knowledge to agricultural pursuits, and during the Second World War he was active in advising on methods for grassland improvement and for the reclamation of bracken-covered areas. In all he published eighty-three scientific papers and in recognition of special services to his country he was placed on H.M. Civil List.

Dr Copisarow was a man dedicated to the work he had chosen, and though in later years, he had to endure much ill health and many worries, he remained courageous in adversity, sustained to no small degree by religious faith and by the devotion of his wife and family. T K WALKER

Dr D S Gracie

VOLUNTEERING in the Royal Scots at seventeen, David Smart Gracie was badly wounded on July 1, 1910 at the Somme, and spent the rest of the First World War as a prisoner in Ruhleben, an experience which marked him for life.

In the late 'twenties, after graduating at Edinburgh with a medal and lecturing on agricultural chemistry, he went to the Colonial Service and carried out a notable "Preliminary Survey of the Soils of Kenya" before the Colonial Agricultural Service had been reconstituted.

Moving to the Egyptian Ministry of Agriculture in 1930, Gracie spent two decades investigating the fascinating problems presented by a soil which has sixty centuries of cultivation history, capped by its change to irrigation all the year round during the past hundred years. As the last survivor within that Ministry in 1949 of what had once been a strong team of some twenty British scientific expatriate workers, he finished with a chattering Brinsgale by collating

and analysing his results from sixteen continuous years of field experiments on the cotton crop. One side-issue during the Second World War from his work on other crops was to economize tonnage of merchant shipping by showing that imported artificial fertilizers produced much more food for the Egyptian than grain imported as such, which the British army had to bring in for its own use.

In 1949 Gracie started afresh in the dusty precincts of Amman with scanty resources, locating cultivable areas in the Jordan valley and the desert for the United Nations Arab Relief. In 1955 he transferred to Iian with better resources, where he created a large efficient laboratory organization for the United Nations Technical Assistance Board at Teheran. In 1958 he broke down from heat exhaustion, and retired to his Edinburgh home too late, dying there on May 31 of this year, leaving his wife Vera and one son.

With all his work done overseas, in countries not notorious for gratitude, merely increasing the resources of those countries by many acres of cultivation or many more tons of annual crop, he is likely to be one of those for whom there is but little remembrance—a depressing reflexion on those fine political projects for under-developed countries.

Gracie has been described as “a fierce seeker for truth, who could never suffer a rogue gladly”, though he might tolerate a fool. He held on to his standards of precision, and made sure that his native assistants did the same.

Out of thirty years joint experience, a mutual friend writes of “the qualities of integrity, judgment, and application in good and indifferent health which he brought to his work. He had none of the narrowness with which specialists are sometimes charged, he was widely read in a diversity of subjects and worth listening to on any of them. Unbending in his uprightness with an inner light which lit for him so clearly the path he held in all affairs, yet he was not stiff, human, kindly, generous, and considerate, his friendship was one of the wholly good things a man could be blessed with.” W. LAWRENCE BALLS

Dr W W Francis

DR WILLIAM WILLOUGHBY FRANCIS, librarian of the Osler Library at McGill University, Montreal, since 1929, died on August 10, aged eighty-one. A relative of Sir William Osler (his mother was Osler's first cousin, and Osler always spoke of him as a nephew), he was born at Montreal on April 2, 1878, and was educated at Trinity College School, Port Hope, and at Johns Hopkins University, Baltimore, where he graduated A.B. in 1898 and M.D. in 1902. After further study in Montreal, Baltimore, Vienna and London, he returned to Montreal in 1906. In 1912 he was appointed assistant editor of the *Canadian Medical Association Journal* and secretary-treasurer of the Canadian Medical Association, and in 1915 he went overseas with No. 3 Canadian General Hospital (McGill) as registrar. On demobilization in 1919, he lived in Oxford (where Osler was regius professor of medicine) before he became editor of the *International Journal of Public Health* at Geneva.

Dr Francis's *magnum opus* was started in 1922, when he joined R. H. Hill, Archibald Malloch and Leonard Mackall in compiling the catalogue of Osler's magnificent library at Oxford. Working for 14–16 hr a day for seven years, he succeeded nobly in inter-

preting Osler's dream of an ideal biobibliography of epoch-making books and in staging it as a pageant. The catalogue under the title “*Bibliotheca Osleriana*” was published by the Oxford University Press in 1929, and the Osler Library at McGill was officially opened on May 29 of that year. Dr Francis was president of the Medical Library Association during 1935–37, and honorary consultant to what was then called the Armed Forces Medical Library at Washington.

Bearing a striking resemblance to Osler in the shape of his head, his olive complexion, his dark, humorous eyes, the lightness of his step, and several of his mannerisms, ‘Bill’ or ‘Billy’ Francis was a charming man. Someone said of him that he was born under a dancing star and sang his way through life. His learning was vast and bizarre, but never pedantic, his memory was rich and retentive, his humour was spicy and puckish. His seemingly infinite leisure was at the disposal of the young and old who went to him for inspiration and for help. A classical scholar, a painstaking bibliographer (“his meticulousness exceeds anything you ever met with”—Osler), and an unsurpassed writer of whimsical letters, Dr Francis married in 1921 Hilda Colley, who survives him, with his daughter, Dr Marian Kolen.

W. R. BETT

Prof A Preece

THE William Cochrane chair of metallurgy in the University of Durham at King's College, Newcastle upon Tyne, became vacant last November with the untimely death of Prof Archibald Preece at the age of fifty-three.

Preece was educated in South Wales and graduated from University College, Swansea, in 1926. He first joined the Pressed Steel Company of Great Britain as metallurgist, and later became a research officer to the South Wales Siemens Steel Research Association, but he returned to academic work in 1933 when he became a lecturer in metallurgy in the University of Leeds. There he pursued researches on the effect of high temperatures upon steel. The importance of his work was recognized by the award of the Sir Robert Hadfield Medal by the Iron and Steel Institute and by his promotion to a readership in the University of Leeds in 1946.

In 1948 he was appointed to succeed C. E. Pearson as professor of metallurgy in King's College, Newcastle upon Tyne. He took charge of a small but active department of teachers and research workers who carried out important work on the scaling of metals, temper brittleness and the solidification of steel castings, which were Preece's particular interests, though he encouraged others to work on a wide variety of different metallurgical topics. Just before his death he had the satisfaction of moving his Department into more commodious quarters and installing new equipment.

Prof Preece was a deeply religious man who could be stern or kindly as the occasion demanded. He set himself extremely high standards both in his work and in his dealings with students and colleagues. Probably the most outstanding quality by which he will be remembered was his unwavering integrity and his strict adherence to the truth as he saw it. He was deeply devoted to his work and to his Department, and his sudden death was a great loss to all who came in contact with him.

A. F. BURSTALL

NEWS and VIEWS

Commonwealth Scientific and Industrial Research Organization Dr F W G White CBE

Dr F W G WHITE, deputy chairman of the Commonwealth Scientific and Industrial Research Organization Australia, has been appointed chairman in succession to the late Sir Ian Clunies Ross. Dr White who is a New Zealander, went to Australia in 1941 at the invitation of the Commonwealth Government to help in Australia's effort to provide radar equipment for the Australian and United States Forces. When the Organization was formed in 1949 he became chief executive officer, and in 1957 deputy chairman. During the period of reconstruction following the War Dr White played a leading part in building up the laboratories of CSIRO, which have since then assisted in the growth of Australia's secondary industries. He was largely responsible for the establishment of laboratories for meteorological physics, coal research and building research. He has been active in sponsoring the formation of industrial research associations and in helping firms to create their own research facilities. Dr White has taken a direct interest in the development and work of the Organization's laboratories concerned with biological research and has travelled widely to study agricultural and pastoral problems at first hand. Since 1946 when special funds were made available for wool research he has devoted a considerable effort to the founding and development of the CSIRO Wool Research Laboratories, which have done much to sustain wool in the competitive fibre markets of the world.

Dr White graduated as MSc in 1928 in the University of New Zealand and later went to do research work at the Cavendish Laboratory, Cambridge. He was awarded the PhD degree of the University of Cambridge in 1932. After a period as a University teacher in the University of London, he was appointed professor of physics at Canterbury University College in New Zealand.

Dr R. N. Robertson

Dr R. N. ROBERTSON, a distinguished Australian plant physiologist has been appointed a full-time member of the executive of the Commonwealth Scientific and Industrial Research Organization in succession to Dr F W G White. Dr Robertson is an outstanding research worker who has an unusually wide interests in both basic and applied aspects of plant physiology. Many of the complex problems facing the farmer and the fruit-grower can only be solved if we know how the plant functions—how it absorbs minerals from the soil and how it uses them to build up its structure. Dr Robertson has been concerned with these basic problems throughout his career and particularly in his present position as leader of the Plant Physiology Research Unit jointly operated by the Division of Food Preservation and Transport of the Commonwealth Scientific and Industrial Research Organization and the University of Sydney. Work by Dr Robertson and his colleagues on the growth and development of apples has led to an understanding of the reasons for the poor keeping quality of large fruit and fruit from light crops. His

investigations on the maturity of pears have been of particular importance to the vegetable canning and freezing industries. During the Second World War Dr Robertson gave valuable help to the food control authorities through his investigations on the causes of heating in stored wheat. Dr Robertson has spent the past year as visiting professor of horticultural science at the University of California and is at present on a short visit to the University of Cambridge.

Dr Robertson was born in Melbourne in 1913. He graduated in science with first-class honours in botany at the University of Sydney in 1933 and continued postgraduate research at that University as Lunnan Macleay Fellow. He was awarded a research scholarship of the Royal Commission of the Exhibition of 1861 and went to work at the University of Cambridge, receiving the PhD degree for research in plant physiology. In 1945 he joined the staff of the Division of Food Preservation and Transport of the Commonwealth Scientific and Industrial Research Organization and took charge of work on the storage of fresh fruit and vegetables. When a Plant Physiology Research Unit was formed in 1952 as a co-operative venture between the Division and the Botany School of the University of Sydney, Dr Robertson became its leader. Dr Robertson is a Fellow of the Australian Academy of Science and a corresponding member of the American Society of Plant Physiologists. The Royal Society of New South Wales awarded him its Clark Memorial Medal in 1954. For many years Dr Robertson was secretary to the Australian National Research Council.

Agricultural Chemistry in Aberystwyth

Prof R O Davies

PROF DAVIES has retired from the chair of agricultural chemistry, University College of Wales Aberystwyth. His services to the University College of Wales and to the agricultural industry of the Principality have extended from 1920 when he was appointed lecturer in agricultural chemistry, in 1939, he became head of the Department of Agricultural Chemistry in the College, which then also served as the agricultural advisory centre for the Mid Wales area. On the establishment of the National Agricultural Advisory Service in 1946 he relinquished his post as advisory chemist and devoted his activities wholly to College work and to his interests in research.

Prof Davies has been especially concerned with problems of the nutritive values of lowland and upland swards and of milk composition, particularly in relation to their mineral constituents. His early work with A L Provan and W J Pugh established that an increase in the protein and mineral constituents of milk occurred when cows were changed from winter rations to lowland pasture. Experimental work on upland swards with W I J Milton (of the Welsh Plant Breeding Station) was begun in 1930. It shows that the mineral deficiencies of these swards can be rectified without resort to ploughing and reseedling. Long term treatments of upland swards have led to the extinction of the native hill herbage and its replacement by species of high productivity and mineral content which have become established.

voluntarily in the favourable environment created through the improvement of soil status and the control of the grazing animal. More recent work with D I H Jones has shown that the mineral content is one factor that influences the nutritive value of the organic nutrients in upland swards, and that the digestibility and the utilization of the digested nutrients of unimproved hill herbage can be increased by feeding calcium carbonate with the grass.

Prof T W Goodwin

PROF R O DAVIES has been succeeded by Dr T W Goodwin, who since 1949 has been senior lecturer in biochemistry in the University of Liverpool. Dr Goodwin's early work on vitamins A and C has led on to a wide interest in the biosynthesis of carotenoids and in comparative biochemistry, in these fields, the range of his own studies and those in co-operation with other workers has formed the basis of notable developments as well as for a wide series of reviews and contributions to reference texts. He has had considerable opportunities of contacts with overseas research in his own particular and cognate fields of plant biochemistry, having held a Rockefeller Foundation travel grant in 1954, when he worked in the University of California with Profs Fox and Mackinney, visited many other American universities, and later having taken part in symposia and lectured in several of the leading research centres in European countries. At Liverpool he has been concerned in the presentation of fundamental and applied biochemical principles, not only to honours BSc students but also in the schools of medicine, dentistry and veterinary science. Dr Goodwin's wide experience in teaching and research will enhance the resources of the Rural Science Departments at Aberystwyth, which, with the closely associated Welsh Plant Breeding Station, have long had special interests in problems of crop, grassland and animal production.

British Gelatine and Glue Research Association :

Dr D A Sutton

DR D A SUTTON, chief biochemist of the South African Council for Scientific and Industrial Research Pneumoconiosis Research Unit at the South African Institute of Medical Research, Johannesburg, has been appointed director of research of the British Gelatine and Glue Research Association in succession to Mr A G Ward, who is going to the University of Leeds as professor of leather industries (see *Nature*, 182, 1707, 1958). Dr Sutton graduated with first-class honours in chemistry at the Imperial College of Science and Technology, London, and after holding posts with the British Rubber Producers' Research Association and the Paint Research Station, went to Pretoria in 1949 where, until 1956, he was head of the Division of Organic Chemistry of the Council for Scientific and Industrial Research, in charge of groups working on various aspects of industrial organic chemistry. He has since been in charge of investigations of the collagen in various living constituents, the chemotherapy of silicosis, and carcinogen liver protein bonding.

Uranium as Fuel

GREAT BRITAIN's nuclear power programme is based on the Calder Hall type of nuclear reactor which 'burns' natural uranium as fuel. Uranium ore is mined in Australia, South Africa, Canada and the United States and processed to an oxide known as 'yellow cake'. Material from the Commonwealth

is shipped to Great Britain and processed at the Springfields factory of the UK Atomic Energy Authority into uranium metal and then into fuel elements for British reactors. A special feature of the March 1959 issue of *Atomic World* (10, No 3) is a series of three articles linked by the theme "From Mine to Fuel Element, 1959", in which the procedure from the initial mining of the uranium ore to the final fabricated fuel element is described. In the first article, "Mining and Processing at the Mary Kathleen", the mining and treatment of the ore to the 'yellow cake' at the recently completed £13 million installation at Mary Kathleen in Australia is considered. This is followed by an account of the processing at the Springfields factory where new plant is being commissioned, and the final article in the series, entitled "Fabricating the Fuel Elements", describes how the billets of natural uranium are cast into rods which are then machined, heat treated and canned in 'Magnox' (an alloy of magnesium and aluminium) to give the fuel elements used at Calder Hall and Chapel Cross. The complete series of operations has been summarized in a composite flowsheet drawn by the staff artist of *Atomic World*. The drawing, 11 in. x 22 in., is very suitable for use in science sixth forms in schools and in technical colleges, and copies may be obtained (price 2s 6d) from the publishers.

Time Ball at Greenwich

AFTER an absence of more than a year, the Time Ball has recently been erected on a new mast on the roof of Flamsteed House, the oldest of the Royal Observatory buildings at Greenwich. A time ball was first erected there in 1833 and it was in 1919 that the aluminium sphere now used was fitted. It was taken down for overhaul in 1958 and as the operating machinery is not yet complete it is not intended to resume daily dropping until the summer of 1960, when Flamsteed House will be opened to the public as an annex of the National Maritime Museum.

The Ageing Worker

IN a report recently published by the Nuffield Foundation ("Age and the Working Lives of Men: an Attempt to Reduce the Statistical Evidence to Its Practical Shape") Studies of Ageing within the Conditions of Modern Industry. Pp 68. London: Nuffield Foundation, 1959. 3s net.) F Le Gros Clark, who has been responsible for a number of monographs on ageing, has addressed himself to answering, as best as present evidence permits, the question, what happens within the conditions of modern British industry to ageing men when failing powers make them no longer fully employable on their normal work. He is concerned, that is to say, not with the psycho-physiological aspects of ageing and the changes that take place in the ageing organism, but with the sociological aspects—the fate of ageing individuals in the contemporary industrial milieu. Reliable evidence on this topic is remarkably hard to come by, and Mr Le Gros Clark has made skilful use of the available statistical data to arrive at his tentative conclusions. Total incapacity for work increases steadily from the age of 55 onwards, and by the age of 65 about 10 per cent of all male workers are totally incapacitated. By the age of 70 this percentage has approximately doubled. The real industrial problem, however, concerns men who are still fit for work, but who because of failing powers need different and less exacting work. At the age of

65 the author estimates that some 20 per cent fall into this category, while a smaller but still considerable number need alternative work well before their mid sixties. There are, of course, wide differences between occupations and the report provides some provisional data relating to thirty occupational groups. The Report suggests that an important question is whether an increasingly mechanized industry will be able to provide the kind of work needed by ageing workers and by those who do not wish to retire at 65. If not, what other social arrangements will be needed to ensure the well being of the ageing man?

Staff for Industry and Commerce

Two important publications dealing with the control and development of staff in industry and commerce have been issued by the Institute of Personnel Management. The first, by E. M. Barling, late director of personnel of the John Lewis Partnership, is concerned with the management of workers whose skills are mainly mental or social rather than manual. Much of the practice described by Miss Barling will be of interest to those dealing with similar problems in large industrial and commercial organizations, Government departments, public corporations, hospitals and scientific establishments. The subjects covered include training and education, pay and incentives, consultation and communications and welfare amenities (Pp 46 London Institute of Personnel Management, 1959 4s 6d). The second, by F. I. de la P. Garforth, of the Department of Work Study and Staff Training, Engineering and Allied Employers' West of England Association, provides a systematic approach to the provision of supervisors and managers. The subjects covered in the broadsheet include organization charts, staff reviews and appraisals, forecasts of vacancies, recruiting policy, further education and training for staff, job rotation and exchange and a section on the initiation and operation of a systematic management development policy (Management Development: A Systematic Approach to the Provision of Supervisors and Managers Pp 72 London Institute of Personnel Management, 1959 15s 6d).

I.C.S.U. Review

The activities of the International Council of Scientific Unions have greatly expanded during recent years. Joint Commissions have been appointed covering fields of interest common to two or more of the constituent unions and other committees have been formed to organize specific programmes of research. The recent International Geophysical Year was initiated and sponsored by the Council through a special committee appointed to supervise the programme. Despite these outstanding achievements there is still widespread ignorance concerning the organization and activities of the International Council of Scientific Unions. The lack of adequate information concerning its affairs has been felt to be detrimental to the continued growth of the Council. As a step towards remedying this state of affairs and with the view of encouraging the flow of information between individual unions the Executive Board of the Council has approved the establishment of a new quarterly journal to be called the *I.C.S.U. Review* to provide information to members of the Council and to all who are interested in international co-operation in science about the activities of the Council and of the scientific unions. The *I.C.S.U. Review* will contain

reports of meetings of the Bureau, the Executive Board and the General Assembly of the I.C.S.U., information about special activities, reports of some of the more important symposia, reviews of certain publications, special articles on various aspects of international co-operation in science, and announcements about forthcoming meetings, symposia or congresses organized by the unions. In the first issue (May 1959) Pp 1+50 Subscription 16 florins 30s or 4.50 dollars per volume of four issues. Amsterdam: Elsevier Publishing Co., 1959. Prof A. von Muralt, treasurer of the International Union of Physiological Sciences and former president of the International Council of Scientific Unions, has written an article entitled 'What does ICSU stand for?' There are other articles on international collaboration in science by L. V. Berkner, on the International Geophysical Year by Prof Sydney Chapman on the marine sciences by Roger Revelle, and a review of some aspects of the origins of life considered in the light of the Moscow international symposium of August 1957, by N. W. Pirie. With the increasing importance of international co-operation in science in recent years, and the growing status of the International Council of Scientific Unions as an essential part of the organization of scientific activities on a world wide scale the *ICSU Review* will undoubtedly fill an important niche in the literature of science, and will find a place on the shelves of all scientific libraries and information services.

Russian Journal of Inorganic Chemistry

A TRANSLATION of the Russian *Zhurnal Neorganicheskoi Khimii*, the only Russian journal devoted exclusively to inorganic chemistry, is being published by the Chemical Society, under the title *Russian Journal of Inorganic Chemistry*. In an introduction to the first number the President of the Chemical Society states that it marks a further step in a plan to make Russian chemical literature more generally available. Many chemists have become aware of their loss in being unable to read in the original the numerous important scientific papers now being published in the U.S.S.R. Although increasing attention is being paid to the teaching of Russian, the need for English translations will inevitably persist for a long time. The publication has been made possible by the far-sighted support of the Department of Scientific and Industrial Research. The Council of the Chemical Society believes that the venture will not only be of direct value to many research workers, but that it will serve to strengthen still further the sense of international partnership in the advancement of chemical science. The translation is by experts. The distributors are Cleaver Hume Press Ltd., 31 Wright's Lane, London W 8. The ordinary subscription rate is £30 (90.00 dollars in the United States) per annum to libraries of universities and technical colleges £22 10s (67.50 dollars in the United States) in both cases inclusive of postage. The first number has 103 pages in the large format of the *Journal of the Chemical Society* and includes thirty-nine papers and eight brief communications in all cases in full. The topics cover a wide range of interests in inorganic chemistry, some of the papers bordering on physical chemistry, and the standard is high. As indicating the general interest of the journal, mention may be made of one paper in which a MnS is shown to be photo-oxidized during the recording of the powder X-ray pattern and the published data on a Mn^{4+} are wrong.

Digest of Soviet Technology

A *Digest of Soviet Technology* is being published each month by Engineering Information Services, Ltd (No 1, April 1959 8 Victoria Road, Kirkham, Preston). The subscription rate is £6 6s annually. Such a new digest, with an editorial policy of giving "express information on recent technological developments in the Soviet Union and Eastern Europe", should be of great value to all persons concerned with technical progress in industrial and academic research. It is claimed that the information supplied is obtained by critical reading of a large number of periodicals and non-periodical literature published in Soviet countries. The fields of coverage are essentially mechanical engineering, production processes and methods, instruments and automation. The material is divided into the following sections: Design and Production, Metallurgy, Welding and Foundry Production, Instruments and Automation, General News, including inventions and book reviews. In the third number (June), the editors state that in future greater attention will be paid to 'non-periodicals'. This follows when one realizes that a considerable proportion of Soviet technical information is given in books before it appears in periodicals. Certainly when this policy is brought into force the *Digest* will be able truly to provide "express information".

Journal of Research of the National Bureau of Standards

It is announced in the April issue of the *Journal of Research of the National Bureau of Standards* that the Journal is now to be published in four separate sections. Section A (Physics and Chemistry), to be issued bi-monthly, will cover a broad range of physical and chemical research, with major emphasis on standards of physical measurement, fundamental constants, and properties of matter. Section B (Mathematics and Mathematical Physics), to be issued quarterly, will be devoted to pure and applied mathematics, including mathematical statistics, theory of the design of experiments and numerical analysis, theoretical physics, chemistry and engineering, with emphasis on the mathematical content, and logical design, programming, and computers. Section C (Engineering and Instrumentation), to be issued quarterly, will include new developments in instrumentation, data processing, test methods, and some of the work in acoustics, applied mechanics, building research and cryogenic engineering. Section D (Radio Propagation), to be issued bi-monthly, will report research in radio propagation, communications, and upper atmospheric physics. The separate sections may be subscribed for individually.

British Scientific Instrument Research Association Publications

It is announced in a recent issue of the *Bulletin of the British Instrument Research Association* that several changes are to be made in the regular publications of the Association. Henceforth, the *Bulletin*, *Stra Technical News* and *Research Reports*, together with other office matter, are to be printed by the Association. For this purpose an office type composing machine (supplied by Vari-Typer Ltd, London) and a Rotaprint rotary printing machine have been installed. The type faces used for the *Bulletin* and the *News* will differ from those at present, but the 10-point size will be retained. The

Bulletin, which was originally intended to be circulated to members of the Association only and which now is generally available, contains abstracts from current literature relating to the construction and use of scientific instruments, and news of the Association's activities in a section entitled "Association Notes". However, since March 1953, the second monthly publication, *Stra Technical News*, with a circulation limited to members only, has been issued, the specific aim of which is to tell the members about the Association's work. "Association Notes" will therefore, in future, be transferred from the *Bulletin* to *Stra Technical News*, and the title of the *Bulletin* is to be changed to *Instrument Abstracts*.

Feltmaking Research

THE eleventh annual report of the Director of Research of the British Hat and Allied Feltmakers Research Association for the year ended August 1958 (pp 20 Manchester British Hat and Allied Feltmakers Research Association, 1959) refers to the inclusion of research on finishing processes as a full time activity. Work on the carotting of furs has shown that the quality of the felt produced is related to the method by which it is obtained and further work has established the importance of body size, weight and build, relative to the size and substance of the hat. Work is to start on the stoving of skins in the carotting process and work on wool noils indicates that only 35 per cent of the overall variability of the felt-quality parameters can be explained by chemical tests for damage. Further work was carried out on the determination of the solubility in alcohol of grades of lac, and a study of a new multiroller machine for both settling wool and felting fur bodies indicates that multirollers can be made to give a rapid rate of felting without adversely affecting the quality of the felt, by using a balanced combination of pressure, jig amplitude and frequency, together with a pre determined traverse rate and controlled temperature and acidity. A detailed study was made of the technology of a fur-hardening machine as it affects the quality of the hardened forms and hat bodies produced, and in further work on the use of polyethanoxo compounds as dyeing assistants a relation was found between dyeing properties and the partitioning of the dyes into a layer of ethanoxo compound above water. Dyes with the highest partition coefficients gave the best results on dyeing. Studies on frictional properties of felt indicate that frictional behaviour against wood depends on the surface roughness, whereas against phenol-formaldehyde resins, the nature and structure of the fillers are important. Work was initiated on the measure of hat felts for tensile properties.

The Regional Research Laboratory, Hyderabad

THE annual report for 1957-58 of the Regional Research Laboratory, Hyderabad (pp ix+136 Hyderabad, 1958), emphasizes the further reorientation of the research programme both for team-work and the grouping of schemes into projects. For the internal planning and conduct of research the operational research approach has been followed, and this is outlined in the report. A striking feature of the year was the increase in pilot-plant work, and particular attention is also directed to the work on 'Citicide', a powerful new insecticide from turpentine developed in the Laboratory; on 'Hykole', active carbons produced from coke, the production of phenylacetic acid and phenylacetamide, for use in

the production of penicillin, and on 'Louniginin', a flavouring agent which has twenty times the strength of vanillin. Besides brief notes on progress in the various research schemes, arranged under some thirty project headings, the report includes notes on X-ray instrumentation and physico-chemical studies, analytical work, equipment and machinery, as well as a list of publications and patents, colloquia held during the year, and lists of research staff. Executive Council and Scientific Advisory Committee. Somewhat fuller details are given of the castor-oil project, which embraces the refining of the oil, the preparation of trimonoolein, using hexane as solvent, the hydrogenation of castor-oil and the preparation of surfactants, the cotton-seed project (including refining, storage, pilot-plant processing and hydrogenation to fatty acids), the fatty acids project, the dehydrated castor oil project, entomological studies on insecticides, the hand made paper project, the utilization of the products of low temperature carbonization of coal (including the preparation of pitch and road tar, preparation of creosotes for wood preservation, recovery of motor spirit recovery and fractionation of tar acids and their chemical examination) and the glass and ceramics development project.

Fencing Posts in Australia

MILLIONS of miles of fences divide and subdivide grazing and farm lands in Australia. Their construction, replacement and maintenance form a major cost item for primary producers. A survey carried out a few years ago by the Commonwealth Scientific and Industrial Research Organization Division of Forest Products, with the assistance of the State Departments of Agriculture, gathered essential information on materials, methods, costs, fence-life and causes of failure of fences on hundreds of farms across the country (Rural Research in CSIRO, 27 Melbourne, March 1959). Much of the cost is in the posts, and years earlier the Division had begun testing small, round, wooden posts to see if they would be suitable. After some thirty years trial they proved to be efficient if preserved against decay and insect attack by treatment with creosote. An alternative method of treatment using water-soluble preservatives has been developed more recently. The Postmaster General's Department has adopted full length preservative treatment for its telegraph poles and, as a consequence, expects an average saving of £2 million a year over the next forty years. This figure shows the savings that could be made if all farmers used round preserved posts for their fencing requirements. Those who are already using such posts have considerably altered their outlook on fencing. An important step in reducing fencing costs has been made. Other aspects, such as design, have been neglected and appear to offer fruitful fields for research.

Inflorescence Inception and Leaf Size in Gramineae

At BONNELL, in a study of the successive leaves on the flowering shoots of *Glyceria*, *Lolium* and *Triticum* has observed that the blades of successive leaves were progressively longer eventually reaching a maximum after which the blades of the last few leaves produced before heading were shorter. When the longest leaf blade was elongating, dissection of the shoot apices showed that inflorescence initiation was taking place. Epidermal cell measurements in *Triticum* indicate that differences in blade length are due to

differences in the amount of cell extension. It appears that a correlated change occurs in blade morphology associated with the onset of the reproductive state of the shoot apex brought about through changes in the amount of cell extension. A study of the effect of different amounts of low temperature and different day lengths on the relation between inflorescence inception and the production of the longest leaf blade showed that, under some conditions, this relation can be disturbed (*Annals of Botany* NS 23, 217 (1959)).

Belgian Oligocene Foraminifera

THE second of a series of studies on the Belgian Paleogene by a team of micropaleontologists at the University of Utrecht consists of a memoir by D. A. J. Batjes on 'Foraminifera of the Oligocene of Belgium' (Institut Royal des Sciences Naturelles de Belgique Mémoire No 143. Pp 188+13 plates Bruxelles 1958). Hitherto very little was known about them although the Belgian Oligocene includes the type areas of the Tongrian and Rupelian divisions. The samples investigated were collected both from surface outcrops and from borings and mine-shafts, so that essentially the whole Oligocene was covered. Further, some German and Dutch Oligocene and Belgian and German Miocene deposits were examined. Altogether some 140 species (of which two are new) are described, all, with the exception of *Nummulites germanicus* (Bornemann) belonging to the smaller foraminifera. The author considers that some might may be index fossils for the Oligocene or in any event for the Boom Clay and Septaria-clay. One *Cassidulinia carpathina* Hedberg widely distributed in the Tertiary of the Caribbean Antillean area, is described for the first time from Europe. The faunal assemblages have close affinities for much of Oligocene time with those of north western Europe and not with those of areas farther south. Dr Batjes also made detailed observations on the lithology and lateral variation of the deposits in different parts of Belgium. Correlating these with the foraminiferal assemblages, he is led to postulate that parts of the Tongrian and Rupelian deposits are of the same age and that similar relations may exist between the Rupelian and Châtian.

A Reinterpretation of Charnockites

SINCE the publication of Sir Thomas Holland's classic memoir on the charnockite series of peninsular India nearly sixty years ago, similar rocks have been discovered and studied in many parts of the world and various theories of their origin have been put forward without, however, a thorough knowledge of the type area near Madras from which these rocks were first recorded. A detailed re-examination of the rocks of this area has been made by A. P. Subramaniam (*Imperial Science*, 257 331 May 1959). Mineralogical, petrographical, and chemical data are presented which indicate that Holland's 'Charnockite Series' in fact contains members which are genetically unrelated to one another. Charnockite is redefined as a hyporthene quartz feldspar rock with or without garnet characterized by greenish blue feldspars and greyish blue quartz. The term 'charnockite suite' is suggested for a group of related alaskite, charnockites (birkomites), endermites and hypersthene-quartz syenites all of which are partly metamorphic. This series corresponds to the Acid division of Holland's 'Charnockite Series'. The 'Intermediate' division of Holland consists of an assemblage of hybrid rocks

derived by interaction between charnockite magmas and pyroxene granulites of the basement. The "Basic" division of Holland consists principally of pyroxene granulites and interstratified quartzo-felspathic garnetiferous sillimanite gneisses (khondalite), while his "Ultrabasic" division is represented by pyroxenitic schlieren, neither the "Basic" nor "Ultrabasic" divisions being related to the charnockite suite. The charnockite suite of rocks is considered to be of primary igneous origin, and to have been emplaced as thick sheets and lenses in gently folded basement rocks, all the rock units have later suffered intense regional deformation.

Automatic Centrifuge

AN eight-page folder issued recently by Ivan Sorvall, Inc., Norwalk, Connecticut, illustrates and describes the super-speed Servall SS-3 Automatic Centrifuge and the SS-4 Enclosed Centrifuge. Both instruments are table-top models with a marked versatility in accepting any one of five different rotors covering a wide range of batch capacities, speeds and gravitational forces. After the desired operating speed, running time, and rate of deceleration have been pre-set on the SS-3's conveniently angled control panel, the circuit is actuated by the push of a button. A particular advantage of the automatic controls is the accuracy with which a given operation may be repeated and complete uniformity of result maintained. The SS-4 is a manually controlled instrument and the complete control panel is removable for remote operation. This is convenient when work demands operation in cold rooms or fume hoods. Both centrifuges are designed for rapid adaptation to continuous flow operation with the Servall 'Szent-Györgyi and Blum' system, which allows the collection of small amounts of precipitate, in tubes, from gallon quantities of samples.

University News Queen's University of Belfast

THE following appointments to lectureships are announced: Dr C J M Stirling, organic chemistry, Dr J S Pate, botany, Dr B V Jayawant, electrical engineering, N C Mitchel, geography, W D Ryan, light electrical-engineering.

Bristol

THE appointment has been announced of Dr W M Shepherd, reader in the University, to the chair of theoretical mechanics. The following have been appointed to lectureships: P W Bothwell, public health, D R Coles, medicine, D G Osmond, anatomy, R Park, civil engineering, N G Sanerkin, pathology.

London

THE following appointments have been made: Prof J L D'Silva, professor of physiology at London Hospital Medical College, to the Halliburton chair of physiology tenable at King's College, A H J Rams, senior lecturer in the University of Birmingham, to the chair of surgery tenable at Charing Cross Hospital Medical School. The following have been appointed readers: Dr G R Hilson, bacteriology, and Dr D Dexter, morbid anatomy, tenable at St George's Hospital Medical School, J F Smith, morbid anatomy, tenable at University College Hospital Medical School. R E M Thompson, bacteriology, tenable at the Middlesex Hospital

Medical School, Dr P J Grant, engineering science, and Dr B W Martin, applied thermodynamics, tenable at the Imperial College of Science and Technology, E M Rawstron, geography, tenable at Queen Mary College. The title of reader in the University of London has been conferred on T E Hughes, zoology, in respect of his post at Birkbeck College, Dr J Wynn Reeves, psychology, in respect of her post at Bedford College, Dr J H Trounce, therapeutics, in respect of his post at Guy's Hospital Medical School.

University College of North Staffordshire

THE U S Rubber Co has founded a second post graduate research studentship at the College. J Penfold (Nottingham) and J Beard (Southampton) have been appointed to these studentships. The Phillips Petroleum Co of Bartlesville, Oklahoma, has founded a postgraduate research studentship at the College, to which C J Panton (Southampton) has been appointed. All three research students will work with Dr P H Plesch on problems related to cationic polymerization.

Announcements

THE Institute of Physics is to hold a conference on Some Aspects of Magnetism during September 22-24 at Sheffield. Further information may be obtained from the Secretary, Institute of Physics, 47 Belgrave Square, London, S W 1.

AN informal Discussion on Flow Properties of Blood and Other Biological Systems, sponsored jointly by the British Society of Rheology and the Colloid and Biophysics sub-Committee of the Faraday Society, will be held in the Department of Physiology, Oxford, during September 23-24. Further information may be obtained from Dr A L Copley, Medical Research Laboratories, Charing Cross Hospital, Strand, London, W C 2, or from Dr G Stainsby, British Gelatine and Glue Research Association, 2a Dalmeny Avenue, London, N 7.

A SYMPOSIUM on Depression will be held at the University of Cambridge Post-Graduate Medical School during September 22-26. Information may be obtained from the Secretary, Medical School, Tennis Court Road, Cambridge.

THE 250th anniversary of the successful use of coke in ironmaking is to be celebrated by a meeting at the University of Birmingham and at Coalbrookdale, Shropshire, during September 23-25. Further information can be obtained from the Secretary, Iron and Steel Institute, 4 Grosvenor Gardens, London, S W 1.

THE Institute of the Rubber Industry is to hold a conference on Industrial Technical Organization at the Palace Hotel, Southport, during October 9-10. Information can be obtained from the Conference Secretary, Institution of the Rubber Industry, 4 Kensington Palace Gardens, London, W 8.

THE Committee on Geodesy and Geophysics of the Academy of Sciences of the U S S R published in 1957 a short report of 75 pages on the recent work done in the Soviet Union in the field of seismology, seismo-geology, seismological survey, physics of the earth, tectonophysics and the age determination of minerals and rocks. A list of seismological stations, abstracts of some of the papers and bibliographies of others are given.

BRITISH CAST IRON RESEARCH ASSOCIATION

OPEN DAYS

THE British Cast Iron Research Association, Alvechurch, Birmingham, held two open days on May 28 and 29. The first day was arranged for visits by representatives of member firms and the second day for visitors from other research associations, Government laboratories, universities, technical colleges and local schools.

The president of the Association, Mr E. Pleyer, inaugurated a new experimental cupola installation. The cupola is a shaft furnace in which metal, coke and fluxes are charged alternately and air is blown through tuyères up the furnace shaft. This furnace is likely to remain the most important melting unit for cast iron in Britain for very many years. The reactions occurring are highly complex and the unit is capable of innumerable variations in design. This experimental installation is on a full industrial scale, has mechanical charging and an extensive stockyard. Use can be made of cold or hot blast, the latter being achieved by means of a separate oil fired blast heater built with radiation and convection sections. It is expected that air blast temperatures of up to 800° C will be achieved in the experimental work. This range of blast temperature is far higher than that on which there is any industrial experience at present. The furnace will melt up to about six tons an hour and the molten metal produced will be disposed of by means of a pig-casting machine. Interchangeable well and melting zone sections have been provided so that the melting zone profile can be changed and the furnace operated without a refractory lining in the melting zone and with water cooling. The equipment is fully instrumented so that materials and thermal balances can be accurately computed.

Dr J. G. Pearce, formerly director of the Association, opened a new laboratory block to be devoted solely to study of fume and dust in iron foundries and its elimination. This laboratory has a large experimental hall covered by a gantry crane, and is equipped for full scale studies of the various dust extraction and ventilation problems which arise in iron foundries. There is also a dust-estimation laboratory with a comprehensive range of instruments for sampling industrial dusts. Estimation of the free silica content of collected dusts is carried out by X-ray diffraction. Demonstrations were made of various devices developed by the Association for the control of dust produced during the manufacture of iron castings.

In the chemical analytical laboratory the most important display dealt with the application of liquid/liquid solvent extraction and the removal of iron by extraction as chloride, and the acetylacetonate complex was demonstrated. In connection with slag analysis the extraction of heavy metals as diethyl dithiocarbamate complexes is being applied to the determination of aluminium. Another important display in this laboratory dealt with the determination of trace elements. For the determination of aluminium in cast iron the element is separated as the cupferron complex after removal of interfering elements by extraction with diethyldithiocarbamate and chloroform. The separation of cobalt, copper,

lead and bismuth was also illustrated. The determinations were completed by cathode ray polarography or spectrophotometry. The demonstration of special methods of analysis was augmented by the display of a cathode ray polarograph modified by the British Cast Iron Research Association to improve its utility, and a spectrophotometer modified for single beam recording spectrophotometry in the ultra violet region and for use as a high sensitivity recording flame spectrophotometer.

The work of the Association not only covers the material cast iron, but also the material used for the moulds into which the molten metal is cast. These are usually clay bonded silica sands, and the production of castings with good surface finish and free from defects involves consideration of their behaviour when rapidly heated by molten metal. The simulation of this cannot be achieved in the laboratory by heating moulding sand test pieces in normal laboratory furnaces since, because of the low thermal conductivity of the materials, any organic or carbonaceous materials are destroyed before the test pieces are uniformly heated. These carbonaceous materials contribute in an important manner to the properties of moulding sands and are substantially not destroyed before a casting solidifies in a normal mould. To overcome this difficulty a testing machine using dielectric heating has been developed which enables sand test pieces to be rapidly and uniformly heated to any desired temperature. Load/deformation curves can be automatically recorded when the test piece has reached the required temperature. One such unit has now been thoroughly tested and an attempt is being made to build similar equipment using a higher frequency and greater power input for still more rapid heating rates. The technique should be of interest for the testing of other ceramic and refractory materials at high temperatures, particularly where rapid rates of heating are important.

Cast iron is a complex alloy capable of developing a wide range of properties depending upon the manner in which solidification proceeds. The properties of grey cast iron are determined by the dispersion of the graphite phase which originates at a eutectic transformation during solidification. The displays indicated that the solidification of this eutectic had received detailed study in terms of nucleation and growth. It appears that elements which reduce the interfacial energy between graphite and the melt increase the number of nuclei growing at a given degree of undercooling. Sulphur and hydrogen appear to reduce the rate of growth of the eutectic cells. The technique by which the nucleation of the iron is estimated by means of eutectic cell counting was demonstrated and stereophotomicrographs of the graphite skeleton within each eutectic cell were shown to illustrate the growth mechanism. A special cooling-curve furnace used for solidification studies was also displayed. This employed a molybdenum heating element and was constructed so that there was always a constant temperature difference between the surroundings and the sample during solidification and recalescence.

The application of the results of the fundamental work on nucleation to practical problems was well illustrated, particularly in connexion with the soundness of iron castings. Increasing the degree of eutectic nucleation increases the tendency to shrinkage defects, and methods for reducing eutectic nucleation are being tried. The laboratory findings have been well confirmed by industrial trials.

Fundamental work is also proceeding on the interplay of thermal and nucleation effects in the production of chilled castings, and also on the mechanism of solidification of white cast irons in which the eutectic of austenite and iron carbide can appear in various patterns related to the nucleation of the melt and the amount of undercooling before solidification. The detection of eutectic cells in white cast irons has proved difficult and the use of the reflecting polarizing microscope has so far proved to be the most useful tool.

The mechanism of the corrosion attack on cast iron in diesel engine waterways has been studied and the special test rig used was demonstrated. Evidence at present shows this to be caused by the accumulation of acidic oxidation products of the glycol in the coolant, the chief of which is formic acid. The formation of formic acid is probably accelerated by the loss of the copper corrosion inhibitor.

The problem of phosphorus in foundry pig iron was illustrated. To a large extent British iron ores of low phosphorus content are exhausted, and foundry pig irons produced from home ores generally contain more than 1 per cent phosphorus. This element has many harmful effects in cast iron when present in such amounts and the Association has just completed an extensive survey of the possibility of utilizing high phosphorus iron ores for the production of low phosphorus foundry pig iron. It has been possible to demonstrate that by top-blowing with oxygen in a rotary Kaldo converter, the phosphorus of phosphoric pig iron can be substantially eliminated and the iron cheaply recarburized.

Cast iron in steam engineering applications is generally limited to temperatures not exceeding 450° F. The Association has just completed the first part of an investigation showing that this is an unrealistic limitation since almost all cast irons have dimensional stability up to at least 750° F. Creep tests are in progress to provide additional evidence.

Cast iron is not a truly elastic material. When stressed the strain can be shown to involve a recoverable anelastic component and an irrecoverable component. By a study of the stress/strain curve the latter has been shown to involve true plastic deformation and also a mechanism by which the graphite voids are increased in size. The application of triaxial stress systems by means of mild notches is shown to modify the mechanical properties. Typical results obtained in this investigation were demonstrated.

For many years the Association has been studying the influence of the gaseous elements in cast iron, and the practical implications of this work were illustrated. In particular, the influence of aluminium in cast iron in causing the decomposition of water vapour, leading to the solution of hydrogen, was emphasized with many industrial examples.

The Association maintains a Foundry Operations Section to provide the iron-founding industry with an advisory service on productivity and working efficiency. Recently, considerable interest has been displayed in a form of time-lapse ciné photography known as 'Memo-motion' and the equipment used and typical results obtained on foundry operations were demonstrated.

The exhibition material was designed to demonstrate that the work of the Association involved largely applied research undertaken specifically in support of the iron-founding industry, its materials, processes, working conditions and productivity. Many examples were given illustrating how the worker in a more or less fundamental field could receive inspiration and ideas by contact with the day-to-day problems of industry.

H MORROGH

ATOMIC MECHANISMS OF FRACTURE

A CONFERENCE on "The Atomic Mechanisms of Fracture" was held at Swampscott, near Boston, Massachusetts, during April 12-14, organized by the National Academy of Sciences—National Research Council. More than 400 people attended, including about twenty from overseas, and twenty-five papers were presented.

Although the main emphasis was on the properties of metals, there were a number of papers dealing with non-metallic crystals, and non-crystalline solids. In the last category interest centred on dynamic effects. H. Schardin presented some rather precise results on the measurement of crack velocities in glasses of various compositions which showed that, although it is approximately true that the maximum crack velocity is proportional to the speed of longitudinal elastic waves, there are significant discrepancies which appear to be correlated with the chemical constitution of the material. H. Kolsky discussed the similarities in behaviour of plastics and viscous liquids when subjected to tensile-stress pulses of short duration, caused by the stress waves from an explosion. At the other extreme end of the time-

scale, R. J. Charles discussed the dependence upon time of the strength of silicate glasses under static loading. Attributing this to the chemical action of atmospheric water vapour at the tip of a crack, he adduced supporting evidence from the behaviour of crystalline oxides under similar conditions.

In the main field of interest of the conference, it was clear that the complexity of the process of fracture is now agreed. Four types can usefully be distinguished: (1) ductile, (2) brittle, (3) creep, (4) fatigue. It should, however, be emphasized that this is no more than a classification of convenience, each heading probably covers a variety of processes, and when any particular body changes from one piece into two pieces a selection of these processes may have been involved, according to the conditions of the experiment. An extreme case arises when a crystal of a soft metal draws down, in tension, to a chisel edge or a point. The mechanism, doubtfully included under the general heading of fracture, is the flowing of material away from the developing neck, by single or multiple glide processes. It was suggested that the central, fibrous part of the typical

cup and-cone tensile fracture of, say, a copper bar might be essentially similar to this. A paper by C Crussard *et al* emphasized the value of the electron microscope in the study of such fracture surfaces—a value which arises not so much from its high resolving power as from its great depth of focus. Crussard showed that in such a fibrous ductile fracture there is evidence of repeated nucleation of new cracks ahead of the growing tip of the major crack, such nucleation taking place usually at minute inclusions in the metal. The new cracks may then join with the major crack by a process of repeated necking down as just suggested.

R W K Honeycombe and C J Beevers showed that by suitable choice of conditions, such necking can be suppressed, even in single crystals of a face centred cubic material, and that when this is done one obtains a mode of separation which can be more properly called a true ductile fracture, the separation of the two parts taking place along a previously heavily deformed glide plane and being apparently controlled by the resolved shear stress on this plane. On the other hand single crystals of iron tested at low temperatures by N P Allen and B Edmondson, either neck down to 100 per cent reduction of area, as already described, or else cleave along the {100} cleavage plane without obvious prior slip. The choice between the two modes of behaviour is determined by the direction of the tensile stress relative to the crystal axes and the transition is quite sharp.

The topic which received the greatest amount of attention during the conference was the well known ductile-brittle transition in polycrystalline iron which normally takes place rather below room temperature. A paper by G T Hahn, B L Averbach, M Cohen and W S Owen reported an extensive series of observations on the tensile fracture of mild steels, of various compositions and grain sizes, over the temperature range 20–230°K which showed that the phenomena are more complex than had perhaps previously been realized. In particular the authors claim that different processes are important in different ranges of temperature—other things being equal—and that mechanical twinning plays a decisive part at the lowest temperatures.

Microscopic observations of specimens broken, or almost broken, under conditions near those obtaining at the brittle-ductile transition showed the existence of numerous micro-cracks each usually confined to a single grain. The frequency of occurrence of such cracks varied systematically with the conditions of the test and the authors maintain that it is necessary to subdivide the process of fracture in this transition range into: (a) true initiation in which some plastic deformation is probably essential, (b) growth within the original grain, (c) propagation through the rest of the specimen. A useful concept which arises is that the 'effective' value of the surface energy of the newly formed surfaces may be much larger—the authors deduce 10 times larger—for (c) than for (b). This is indeed reasonable in the light of some of the fractographic studies of J R Low, which show very clearly the change of character of a cleavage surface which can take place when the crack passes from one grain into another less favourably oriented for cleavage.

A contribution from N J Petch summarized his own extensive work, relevant to the more metallurgical aspects of the same problem. In addition to the grain size, temperature, and strain rate, which are commonly recognized as important variables, he

discussed also the mechanisms by which the carbon, nitrogen and other elements commonly present in steels affect the various stages of the fracture process and the ways in which their influence can be modified by previous mechanical and thermal treatment. The introductory paper by A H Cottrell also dealt with the brittle-ductile transition at some length, in addition to giving a general survey of the whole subject of the conference. Although some points of controversy remain and although much detailed work remains to be done, it appears that the broad outlines of the explanation of the ductile-brittle transition are becoming settled.

The two main contributions on creep fracture namely on slow fracture at temperatures which are high relative to the melting point came from N J Grant and R C Giffens. The features which distinguish this type of failure from the others are the considerable importance of grain boundary sliding and grain boundary migration, the comparative ease of dislocation climb processes and the possibility of deformation by the migration of point defects under the action of stress. It was made very clear that these four processes can be interrelated in several ways and that they can all be interrelated to any deformation by dislocation glide which may be taking place in the body of the grains. Failure is often, but not always intergranular, and is often, but not always associated with the presence of 'voids' in the grain boundaries. The fracture behaviour was reported to be particularly sensitive to the presence of small amounts of impurity in a nominally pure metal. The paper by Giffens summarized some of the earlier experimental work which is considerable in quantity and not always self-consistent. It is clear that it is likely to be some time before the present confusion approaches anything approximating to a unified body of knowledge although the general lines of the pattern are beginning to emerge.

The problem of fracture during fatigue is perhaps in the least satisfactory state of all. Of the papers presented at the conference most were concerned with the early stages of the process. W A Wood described the interesting results obtained by a taper sectioning method applied to a partially fatigued copper specimen. As with so many other papers on other topics, the impression given by this work is that the mechanism of fracture is more complex than had hitherto been supposed. The emphasis is on the events taking place close to the surface of the solid and leading up to the formation of a true crack. E S Machlin and A J McEvily described experiments on four inorganic crystals which seem to show an interrelation between liability to fatigue fracture and the ability of the crystal to become deformed by cross slip, the possibility of the formation of 'extrusions' from the metal surface also seems to be correlated with both these features. A similar point emerges from a comparison of two papers on copper by W A Backofen and N Thompson respectively, one of which dealt with the effect of crystal orientation on liability to fracture while the other related crystal orientation to extrusions.

Mention must also be made of the contribution by E R Parker on the cleavage fracture in tension of single crystals of magnesium oxide. These observations and similar work by Stokes *et al* mentioned in the course of discussion demonstrate the advantages to be gained by experimenting on ionic rather than metallic crystals and emphasize a point that was made on a number of occasions. This is that on

close examination, no crystal breaks in a truly brittle manner, the fracture is always preceded by some small amount of plastic deformation. This is one of the key points in connecting theories of fracture with current views on the mechanical behaviour of crystalline solids. The other general feature of the

proceedings, already mentioned, was the evident fact that in no circumstances is fracture a simple process. The realization that "when a problem is difficult, it is probably two problems" is perhaps the most important step on the road to a solution.

N. THOMPSON

OXIDATION OF ORGANIC COMPOUNDS

A SYMPOSIUM on the oxidation of organic compounds was held in the Stern Hall at Queen Mary College, University of London, during April 13-14.

In his opening address Mr D. A. C. Dewdney, director of Esso Petroleum Co., Ltd., spoke of the importance of a free exchange of scientific information and the need of still further fundamental research into basic problems, an improving standard of living and higher productivity are largely dependent on the commercial application of original scientific discoveries. In welcoming visitors to the symposium, he referred especially to those from the USSR and Czechoslovakia.

The first part of the scientific discussion was concerned with the course of the oxidation of saturated hydrocarbons by chromic acid in acetic acid containing some sulphuric acid. From the papers and the discussion which developed there was general agreement that the first recognizable stage in the oxidation is hydrogen abstraction from the hydrocarbon, and that the factors which influence the speed of the reaction are mainly steric and configurational. The same factors also determine the rate of oxidation by chromium trioxide in anhydrous media.

Dr J. Roček (Institute of Chemistry, Czechoslovak Academy of Science, Prague) reported that *n*-paraffins are oxidized at a rate directly proportional to the number of methylene groups, the rate constant for any individual member being $k_n = k_{CH_2}(n-2)$, where n is the number of carbon atoms and k_{CH_2} the rate constant for the oxidation of a single methylene group. The relative rates of oxidation of the methyl, methylene, and methine groups in open chain hydrocarbons have been found to be 0.015:1:32-77. Measurements of the rate of oxidation of *cycloalkanes* disclosed some interesting anomalies.

The oxidation-rate of the tertiary CH-group is found to vary somewhat with the bulk and structure of the neighbouring alkyl groups, these variations are due mainly to polar factors and are similar to changes in rates of solvolysis of the corresponding tertiary chlorides. Only in special cases has steric retardation been found, steric acceleration does not play any detectable part in the acyclic series. It is concluded that the rate-determining step is the formation of a carbonium ion by way of a hydride ion transfer from the hydrocarbon molecule to an oxygen atom of the oxidizing agent.

Prof K. B. Wiberg (University of Washington) from a study of the rate of oxidation of diphenylmethane and of its nuclear substituted derivatives in 95 per cent acetic acid concluded that the oxidation proceeds by initial removal of a hydrogen atom to give a benzhydryl radical which is then oxidized directly to benzophenone. In support of such a mechanism, oxidation of optically active 3-methylhexane gives an optically active tertiary alcohol, a result which seems to exclude the initial formation

of a carbonium ion. The formation of camphenilamic acid by the oxidation of isocamphane is also cited in support of that view. Further evidence of an indirect nature is derived from a study of the action of chromyl chloride on propylbenzene- β - d_2 , benzyl methyl ketone is among the products, and it was found to have one deuterium atom in the α -position, indicating a deuterium shift during the reaction.

The oxidation of tertiary paraffins by chromic acid in presence of sulphuric acid is known to lead to tertiary alcohols, and the course of the reaction can be interpreted in terms of dehydration of the alcohol to olefin. In a study of the oxidation by Dr W. J. Hickinbottom (Queen Mary College, London) the conditions were selected so that tertiary alcohols could not be formed, by using chromium trioxide in acetic anhydride. Under these conditions, paraffins gave products which were qualitatively identical with those from the corresponding olefins in presence of weak acids. Further, some of the paraffins gave unsaturated products. From these results and from quantitative measurements of the rates of oxidation it was concluded that tertiary paraffins are attacked preferentially at the tertiary carbon atom with the subsequent formation of an olefin.

A possible key to the oxidation of paraffins by chromic acid may lie in the behaviour of the alcohols which may be derived from them by oxidation. Our knowledge of the course of the oxidation of alcohols is based on the work of Prof F. H. Westheimer (Harvard University). In continuation of this work, he described, with Y. E. Chang, a study of the oxidation of pinacol and its monomethyl ether. A feature of the pinacol oxidation is that it proceeds 2.7 times as fast in deuterium oxide as in water. This was interpreted to mean that the hydroxyl bond is not cleaved in the rate controlling step of the oxidation. The relative merits of an ester mechanism and hydride abstraction were discussed and many useful ideas exchanged.

Dr W. A. Waters (Oxford) reviewed the relationship between vanadate and permanganate oxidations. The role of trivalent manganese and of organic free radical intermediates in permanganate oxidations was reviewed. Features diagnostic of one-electron oxidations were brought to notice. It was stressed that lack of diagnostic evidence need afford no grounds for the rejection of a reaction mechanism.

Dr J. W. Ladbury (ICI, Ltd., Plastics Division, Welwyn Garden City) and Dr C. F. Cullis (Imperial College of Science and Technology, London) discussed the oxidation of inorganic and organic compounds by permanganate. The development of reaction rate with time depends on the nature of the compound undergoing oxidation. The observed types of behaviour fall, broadly speaking, into four categories according to the shape of the reaction-time curves. Thus there may be (1) a continuous decrease in rate with time, usually not strictly according to a

second-order knot law, (2) an initial autocatalytic development of reaction rate followed eventually by a decrease due to consumption of reactants (3) an initial high rate of reaction which rapidly decreases almost to zero and is then followed by an autocatalytic reaction of type (2) (4) an initial high rate followed by a linear reaction - time curve. These various kinds of behaviour were discussed and reasons proposed for the characteristic differences observed according to the nature of the substrates. In the discussion on this Prof N M Emanuel (Moscow) directed attention to the resemblance between type (3) and the oxidation behaviour he had observed using oxygen.

Dr S Littler and Dr W A Winters (Oxford) reported that pentavalent vanadium becomes an oxidizer in acid solution, the active agents being cations, for example, VO_2^+ , $\text{V}(\text{OH})_2^{2+}$, depending on the acidity which reduces only to the oxidation level of quadrivalent vanadium with organic compounds. Kinetic studies were reported of some glycol isomers and of the oxidation of *cyclohexanol*. In the latter case an initial rapid esterification seems to be involved though the rate-determining stage involves C-H bond fission. Isotope effects in *cyclohexanol* depending on the oxidizing ion were discussed and a cyclic mechanism proposed.

The oxidation of saturated hydrocarbons in the liquid phase by air is now a matter of both industrial and theoretical importance. Prof A N Bashkurov (Moscow) described his work on the oxidation of the higher paraffins. In this he described a very important development, namely, that the oxidation can be arrested at a predetermined stage. By using barium salt and selecting suitable conditions—a temperature of 105–170°C and a nitrogen-oxygen mixture containing 3–4.5 per cent of oxygen—the higher paraffins can be converted into the corresponding alcohols in 70 per cent yield. There is practically no degradation of the hydrocarbon molecule and all the possible secondary alcohols are formed.

Prof N M Emanuel (Moscow) discussed a number of interesting aspects of slow branched-chain oxidation reactions of hydrocarbons and reference was particularly made to the capacity for auto-acceleration and self propagation and the control of these reactions by homogeneous catalysts. Some of the ideas

developed in this paper were shown to have application in biological processes such as retardation and suppression of the growth of malignant tumours in animals.

Prof H B Henbest (Queen's University, Belfast) reported that trialkylamines are readily oxidized by a large variety of reagents, the initial products being usually N-oxides, enamines or carbinolamines. Depending on its structure and the reaction conditions a compound of the last type may be oxidized further to an amide or may cleave to a mixture of a secondary amine and a carbonyl compound. Analogous compounds may be formed in the oxidation of dialkyl anilines but in this series additional products are possible if nuclear positions become involved in the reaction.

A general survey of the field was presented followed by a more detailed discussion of some of the reactions of trialkylamines and dialkylanilines with N-bromo succinimide, ceric salts, p-quinones, di-tert-butyl peroxide, and benzoyl peroxide. The results with dialkylanilines suggest that the three primary oxidation processes of electron removal, hydrogen atom removal, and hydride ion removal can all occur, the choice for any particular amine being mainly dependent on the type of oxidizing agent used.

Some known features of oxidations by persulphates were summarized by Dr R G R Bacon (Queen's University Belfast) and new data presented. Persulphates may be employed (a) as aqueous solutions, undergoing thermal or photo induced decomposition; (b) in strongly acidic solutions; (c) in alkaline solutions; (d) in redox systems, where persulphate acts in conjunction with, for example an oxidizable metal ion. The use of persulphate in redox systems was discussed with emphasis on the value of silver ion as the redox partner. Applications of this method to oxidations of alkylbenzenes, phenols, alcohols, carboxylic acids, and amines, were described.

In summing up the proceedings of the symposium, it can be said that its success as a scientific meeting depended very largely on the free and uninhibited exchange of ideas and the discussion of current and unpublished work now in progress.

W J HICKINBOTTOM
R F GARWOOD

GAS CHROMATOGRAPHY

THE Gas Chromatography Discussion Group associated with the Hydrocarbon Research Group of the Institute of Petroleum has now completed its reorganization following an inaugural general meeting last autumn held at University College London, on September 23, 1958 and the first annual general meeting at the Imperial College of Science and Technology, London on April 10, 1959. Both meetings were held in conjunction with an informal symposium and were attended by more than two hundred participants.

The success of the new organization may be judged from the total enrolled membership, which is now about 220 of which some fifty are from the Continent or the United States. The Group has now organized four one day informal symposia in Britain and the second formal symposium in Amsterdam in the spring of 1958 which was attended by nearly

five hundred participants from twenty one different countries. In addition it has published two papers and arranged for the manufacture and sale in the United Kingdom of specially prepared stationary phases and supports in an endeavour to standardize experimental procedures for determining and methods of presenting gas chromatographic data. Arrangements are being completed for the collection and distribution of the latter to members together with abstracts of papers on the technique from more than sixty journals. The future programme tentatively includes another informal symposium to be held at Bristol in the autumn of 1959 and the third formal symposium in Edinburgh during 1960. The outstanding contributions of Dr A J P Martin both in originating gas-liquid chromatography and in many important later developments have been recognized by the Group by bestowing on him honorary life membership.

The technical part of the meeting at University College, London, on September 23, 1958, was introduced by Prof E D Hughes, who gave a short welcoming address commenting on the rapid growth of the Group. Dr D Ambrose, the local organizer, then presented proposals on behalf of the Group for the determination of retention volumes under standard conditions. Various practical points about the experimental procedures were discussed, including temperature control and the life of columns.

Dr G A P Tuey described the work done in his laboratories in preparation for the sale of standardized materials for use as stationary phases. Extensive tests had been made of volatility in an apparatus which simulates conditions in the chromatographic column but allows a gravimetric determination of the loss at a particular temperature. The rate of loss with time was determined and a final specification includes a figure for initial loss, the steady rate of loss and relative and specific retention data.

The comparison of detectors for gas chromatography was the subject of a paper presented by Dr I G McWilliam. Detectors were discussed in terms of sensitivity, response time, relationship of detector output to molecular parameters and ease of construction and operation. The sensitivity is best stated in terms of gas concentration, and the unit gm/ml of carrier gas was advocated. Base-line noise (μV) and drift ($\mu\text{V/hr}$) should also be stated. The response time must be small enough for negligible distortion of the true peak shape to occur. If the relationship between detector output and some molecular parameter is known, quantitative analysis without calibration is facilitated. Although all these factors must be considered in selecting a detector, the final choice frequently depends upon the ease of construction and operation. Of those in use, Dr McWilliam considers the single-jet flame ionization detector the simplest.

Dr K R Garrett presented a report on a programme of co-operative analysis of hydrocarbon gases organized by the Institute of Petroleum. Cylinders containing sales butane and a cracked C_4 -mixture have been circulated among participating laboratories, where they have been analysed using a range of techniques. Preliminary results indicate the importance of standardization of methods of taking samples from the cylinders and enable some assessment to be made of the reproducibility of possible standard procedures.

An interesting study of alumina as a packing was described by Mr C G Scott. Several methods of achieving different levels of adsorption activity had been tried, but the most promising seemed to be the addition of small quantities of water and silicone oil. With optimum proportions it was possible to maintain the ability of the adsorbent to separate hydrogen and methane but with much reduced retention volumes for the higher hydrocarbons. An analysis of a gas mixture containing hydrogen, C_1 , C_2 , C_3 , C_4 and C_5 -hydrocarbons was therefore possible in a single run at constant temperature.

Prof R M Barrer welcomed the Group to the Imperial College of Science and Technology, London, on April 10, 1959, congratulating it on the excellence of the meetings it organized and the vigour and enterprise shown by such a comparatively new organization. The local organization of this meeting was carried out by Dr G J Minkoff. The first paper, presented by Dr A Goldup, was concerned with the potentialities of the new coated capillary columns in

the petroleum industry. He described a compact practical apparatus with which capillary columns had been operated at temperatures up to 250°C . Column efficiencies in excess of 100,000 theoretical plates had been obtained with metal tubes ten thousandths of an inch in diameter and 250 ft long coated with squalane or 'Apiezon' grease. A novel sample introduction device was described in which the very small samples required for the column were obtained by a dynamic division of the carrier gas at the column head. The use of these high-efficiency columns in the analysis of various petroleum products and in geochemical prospecting was illustrated. Mr B H F Whyman, another of the authors of this paper, in a prepared contribution to the discussion, described a simple apparatus for drawing long lengths of coiled glass capillary, which show certain advantages over metal capillary.

Mr R P W Scott then described the use of fine nylon tubes (0.01 in, 0.02 in and 0.1 in in diameter) as capillary columns. Simple coating procedures were used, the transparency of the nylon being helpful in adjusting the rate of flow of the solution of the stationary phase through the tube. A column 1,000 ft in length of 0.02 in diameter coated with dinonyl phthalate gave a maximum of 750,000 plates, but the efficiency tended to fall off rapidly with increasing retention time to about 250,000 plates. Operating temperatures were limited to about 100°C with present tubing, but 180°C seemed feasible with other polymers. A very active discussion took place following these two papers and it is obvious that there is much interest in these new capillary columns, which M J E Golay described for the first time in the autumn of 1957.

A new detector employing changes of dielectric constant developed primarily for preparative-scale gas chromatography was described by Mr D W Turner. For this application, where high sensitivity is not so important as for analytical work, the detector has the advantages of being largely independent of flow-rate, non-destructive and reasonably robust. It employs a novel circuit which is very sensitive to the minute capacity changes produced in the detector cell, and with slight modifications is easily used with solutions such as are encountered in liquid chromatography.

Mr V Willis presented a paper on the application of gas chromatography to process stream monitoring, where an instrument is required automatically to sample and analyse a gas or liquid stream over long periods. A column-life of two years is aimed at, but is difficult to attain with many stationary phases. Although a useful survey of requirements was given, unfortunately few constructional details were available.

Finally, in the last paper Dr S H Langer discussed his work on improvement in stationary phase selectivity. He exemplified this with his results using tetrahalophthalate esters for the separation of the aromatic hydrocarbons. These esters had been selected in an endeavour to exploit the complex formation known to exist between tetrachlorophthalic anhydride and condensed aromatic hydrocarbons. Effective separations of the lower aromatic hydrocarbons had been obtained and separation factors and activity coefficients were compared with other stationary phases. It seems likely that the electron-deficient tetrahalo-substituted ring interacts with the aromatic compounds by a charge-transfer mechanism.

D H DESTY

RADIATION SAFETY AND HEALTH PHYSICS

By J W LUCAS

THE Windscale reactor incident of October 1957 involving the release of radioactive fission products into the atmosphere¹, undoubtedly served to focus the attention of the general public on to the hazards of ionizing radiation and to the increasing risks of exposure. Interest has also been aroused by the publication of reports by the Ministry of Health, Medical Research Council² and the UN Scientific Committee³. The rapid expansion of the nuclear power programme coupled with the increasing employment of sources of ionizing radiation in industry, medicine and research institutions, and also nuclear weapon testing demands an increasing vigilance and knowledge of the risks and safety precautions on the part of many people. The U.K. Atomic Energy Authority has an excellent record of safety both with respect to its own staff and to the general public in the vicinity of its establishments and has also exercised a rigorous control over the discharge of waste radioactive products into the environment⁴. The Fleck Committee set up to inquire into the organization for control of health and safety⁵ nevertheless recognized the need for a rapid expansion of health physics and safety staffs in the Authority, and recommended that the Research Establishment at Harwell should set up a national training centre for health physics and nuclear safety staff to cater for persons both inside and outside the Authority.

A number of short courses on "Radiological Protection" have already been held at the Isotope School Harwell, but it was felt that there was scope for a college of technology to undertake similar work. An approach was therefore made to the United Kingdom Atomic Energy Authority, Industrial Group, at Risley, in the spring of 1958 with the view of introducing courses in the Liverpool College of Technology later in the year. A scheme was prepared in conjunction with the Authority and this article provides a brief interim report based on experience of three courses which have been run in late 1958 and early 1959.

Each course is of a fortnight's duration. The available places on the three courses have been taken up by representatives of the U.K. Atomic Energy

Authority, public health departments, factory inspectorate, local industry, insurance and education, members attending include medical officers, physicists, engineers, insurance accident surveyors, chemists, public health inspectors and safety officers.

The aim of the courses has been to provide an introduction to and a general survey of, the problems of radiological protection against all forms of ionizing radiation. The very specialized problems of reactor safety and the processing of nuclear fuel elements have not been dealt with specifically, except in so far as environmental effects may be involved. Special attention in both lectures and practical work is however given to subjects such as the comparative properties of radiations, the sources of radiation including background and fall-out, the effects of radiation on plants, animals and man, contamination and decontamination, waste disposal, health physics instrumentation and monitoring, procedures for absorption of radiation and shielding. Table I summarizes the lecture and practical topics which have been covered on the early courses; the programme is rounded off by visits to local institutions and works by the exhibition of films, and by discussions.

The programme of practical work has been devised to provide a series of short term experiments underlining the basic problems of a comprehensive protection service. Some aspects of the practical work and the results which have been obtained have already proved of considerable interest and are briefly described. It is hoped to publish the detailed observations at a later date.

The experiments in radiobiology have been singularly successful in demonstrating the fate of various radioisotopes when brought into contact with biological organisms to be found in a natural environment. The techniques have been previously described by D G Pickering and myself⁶. The experiments with blanket weed (*Microspora*) have demonstrated conclusively the ability of the algae to concentrate many isotopes from their environment and have particularly served to emphasize the importance of properly planned disposal procedures. A safe procedure for radioactive liquid waste is afterwards demonstrated to members of the course.

Table I. SYLLABUS OF LECTURES AND PRACTICAL WORK

| Lectures | | | Practical | |
|--|--|-------------|---|--------------------|
| Section | Topics | No of hours | Subject | No of hours |
| Radiation and its sources | Comparative properties, units and calculations of dose; background and fall-out; nuclear reactors; particle accelerators | 6 | X-ray equipment and sealed sources. Techniques with open isotopes—counting and identification | 1 |
| Measurement and detection of radiation | Principles of measurement types of counter and I.P. instruments | 6 | Calibration and operation of H.I. instruments. Dosage calculations | 3 |
| Interaction of radiation and matter | Radiation chemistry; radio-biology—genetics; metabolic processes | 6 | Radiobiology | - |
| Radiological protection | I.C.P.L.s and M.I.C.s: control of internal and external radiation in laboratories and plants; medical care; waste disposal; legal requirements; industrial practice; X-ray units | 10 | Contamination—prevention and removal Waste disposal Shielding Radiation monitoring Air sampling | 4 3 10 10 |

Lectures have been presented by members of the Health and Safety Branch of the U.K. Atomic Energy Authority Industrial Group, Factory Inspectorate and the Universities of Leeds and Liverpool in addition to College staff.

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An interesting study of alumina as a packing was described by Mr C G Scott. Several methods of achieving different levels of adsorption activity had been tried, but the most promising seemed to be the addition of small quantities of water and silicone oil. With optimum proportions it was possible to maintain the ability of the adsorbent to separate hydrogen and methane but with much reduced retention volumes for the higher hydrocarbons. An analysis of a gas mixture containing hydrogen, C_1 -, C_2 -, C_3 -, C_4 - and C_5 -hydrocarbons was therefore possible in a single run at constant temperature.

Prof R M Barrer welcomed the Group to the Imperial College of Science and Technology, London, on April 10, 1959, congratulating it on the excellence of the meetings it organized and the vigour and enterprise shown by such a comparatively new organization. The local organization of this meeting was carried out by Dr G J Minkoff. The first paper, presented by Dr A Goldup, was concerned with the potentialities of the new coated capillary columns in

the petroleum industry. He described a compact practical apparatus with which capillary columns had been operated at temperatures up to 250°C . Column efficiencies in excess of 100,000 theoretical plates had been obtained with metal tubes ten thousandths of an inch in diameter and 250 ft long coated with squalane or 'Apiezon' grease. A novel sample introduction device was described in which the very small samples required for the column were obtained by a dynamic division of the carrier gas at the column head. The use of these high-efficiency columns in the analysis of various petroleum products and in geochemical prospecting was illustrated. Mr B H F Whyman, another of the authors of this paper, in a prepared contribution to the discussion, described a simple apparatus for drawing long lengths of coiled glass capillary, which show certain advantages over metal capillary.

Mr R P W Scott then described the use of fine nylon tubes (0.01 in, 0.02 in and 0.1 in in diameter) as capillary columns. Simple coating procedures were used, the transparency of the nylon being helpful in adjusting the rate of flow of the solution of the stationary phase through the tube. A column 1,000 ft in length of 0.02 in diameter coated with dinonyl phthalate gave a maximum of 750,000 plates, but the efficiency tended to fall off rapidly with increasing retention time to about 250,000 plates. Operating temperatures were limited to about 100°C with present tubing, but 180°C seemed feasible with other polymers. A very active discussion took place following these two papers and it is obvious that there is much interest in these new capillary columns, which M J E Golay described for the first time in the autumn of 1957.

A new detector employing changes of dielectric constant developed primarily for preparative scale gas chromatography was described by Mr D W Turner. For this application, where high sensitivity is not so important as for analytical work, the detector has the advantages of being largely independent of flow-rate, non-destructive and reasonably robust. It employs a novel circuit which is very sensitive to the minute capacity changes produced in the detector cell, and with slight modifications is easily used with solutions such as are encountered in liquid chromatography.

Mr V Willis presented a paper on the application of gas chromatography to process stream monitoring, where an instrument is required automatically to sample and analyse a gas or liquid stream over long periods. A column-life of two years is aimed at, but is difficult to attain with many stationary phases. Although a useful survey of requirements was given, unfortunately few constructional details were available.

Finally, in the last paper Dr S H Langer discussed his work on improvement in stationary phase selectivity. He exemplified this with his results using tetrahalophthalate esters for the separation of the aromatic hydrocarbons. These esters had been selected in an endeavour to exploit the complex formation known to exist between tetrachlorophthalic anhydride and condensed aromatic hydrocarbons. Effective separations of the lower aromatic hydrocarbons had been obtained and separation factors and activity coefficients were compared with other stationary phases. It seems likely that the electron deficient tetrahalo-substituted ring interacts with the aromatic compounds by a charge-transfer mechanism.

D H DESTY

titles, a card index is issued free to members and can be bought by others. It consists mainly of films on pure and applied science, but no subject is ignored which is within the scope of a university. Medical films are also listed, but the Committee tries to avoid duplication of the work of the Film Committee of the British Medical Association and related organizations. Catalogues are, as a rule, easily accessible in university reference libraries, and many member institutions have as many as three copies in constant use. Index cards are 2d each to non-members (minimum 5s) and a revised list was published early in 1957. The Council also publishes the *University Film Journal* about three times a year which contains relevant articles of interest to

staff and students in universities, important reprints and as much news material from home and overseas as possible. At the time of writing, inquiries are being circulated throughout all member universities on the quality and kind of film needed by lecturers and professors, and what special film equipment is being held and would be available to colleagues.

The Council has successfully sponsored special conferences on the use of films in such diverse fields as modern languages (at the Institut français), arts subjects (at the Institute of Education, London), chemical engineering (at Birmingham), psychology (at University College, London). It has also in the past, assisted in the selection of films for the annual British Association meetings. J. HORNE

UNIVERSITIES AND ADULT EDUCATION IN BRITAIN

THE total number of courses conducted in Britain by university extra mural departments during 1957-58 were rather fewer than during 1956-57, but still above the figure for 1955-56. Although this may give cause for modest satisfaction, the slight decline which took place was not evenly spread over the whole of the work but affected with disproportionate severity tutorial classes and residential courses, two branches of work which universities have traditionally cherished*. Since the beginning of the current decade the tendency has been for the number of tutorial classes to decline, but the sharp drop during 1957-58 is without recent precedent.

There are signs that the policy of financial limitation initiated a few years ago is now affecting extramural work particularly in the type of course provided. In such work it is difficult to stand still; an attempt to curb developments inherent in the work is apt to lead to retrogression. Many extra-

mural departments were just able to hold their own, or reported small increases in the number of classes (usually shorter classes) in spite of grant problems.

At Glasgow it was reported that during the past year some of the emergency cuts which had to be made, such as the reduction of the library grant, are likely to have a harmful effect on the quality of the work unless they can soon be restored. Nottingham had to reject ten requests from classes because of shortage of funds. At Oxford also there were financial problems. "The University Chest found itself forced to cut its grant for extra mural work, with the result that the adult scholarship scheme was suspended and the number of classes fell more sharply than at any other university." The Delegacy for Extra Mural Studies stated, in a memorandum submitted to the Hebdomadal Council, its firm belief in the value and importance of extra mural studies, and "its regret that the work must be contracted at a time when the need for it had become even more urgent."

* Universities Council for Adult Education. Report on the year 1957-1958. Pp 28. (Ristol) W. E. Salt, Hon. Secretary and Treasurer. The University 1959.)

THE CENTRAL AGRICULTURAL RESEARCH STATION, CARAPICAIMA, TRINIDAD

By DR. A. J. VLITOS

Director

THE new Central Agricultural Research Station located at Carapichaima, Trinidad, is an institution intended to foster fundamental and applied research relative to sugar cane. Supported by private funds (Caroni Ltd. and Ste. Madeleine Sugar Co., Ltd.) the new Research Station is concerned with the agronomy, physiology, pathology, entomology, and biochemistry of sugar cane with the ultimate aim of applying in the field new information which may be forthcoming from the basic investigations.

The main section of the Station houses the physiology, pathology, entomology, and biochemistry units in an air conditioned laboratory, fully equipped with the facilities required to carry out the research programmes. Adjacent to main laboratories are dark rooms and a temperature-controlled light room suitable for the growth of plants under controlled environmental conditions. A library, containing the pertinent scientific journals is located in the east wing of the main building.

An agronomic programme, more applied in nature, will complement the fundamental studies in physiology. A major effort is being directed towards the control of froghopper (*Aeneolamia varia saccharina*) and the other major insect pests of cane in Trinidad. Chemical weed control, as well as new methods of cultivation, are also under investigation. Physiological and biochemical studies are concerned with the auxin relations in the developing cane seedling, from seed to flowering. In addition to the auxin studies, several investigations on mineral nutrition and photosynthetic efficiency will round out the physiology programme. The pathology programme is devoted to a thorough study of the rhizosphere of sugar cane, including a taxonomic investigation of the microflora and microfauna residing in the immediate vicinity of the root system as well as an analysis of the interrelationships between the secretions of the root system and the microbial population.

THE LISTER INSTITUTE

THE report of the Governing Body on the work of the Lister Institute for 1959 describes a wide range of investigations*. In the field of microbiology the Guinness-Lister Unit continues its exploitation of the genetics of *Salmonella* bacilli, mainly in terms of the biochemistry and genetic control of the synthesis and function of flagella, using the bacteriophages that infect these bacilli to transduce genetic material from one kind of bacillus to another. The bacteriophage transduction technique has been extended to staphylococci. The other purely biological study concerns the cytology of certain free-living, flagellated protozoa.

Studies by Institute staff into the immunology and pathology of infective diseases are concerned with infections by viruses, pleuropneumonia-like organisms, bacteria and protozoa.

The isolation of the viruses of trachoma and of inclusion blennorrhoea has opened up a large field of study, both in Gambian laboratories of the Medical Research Council's Trachoma Unit, where the epidemiology of trachoma is being studied, and in the Council's Unit in the Department of Virology. The ready infection of the baboon's conjunctiva with the virus of inclusion blennorrhoea provides an experimental model in which to study the practicability of prophylactic immunization in the related infection by trachoma virus. In the Smallpox Vaccine Department, there is continued progress towards making vaccine from vaccinia virus grown in tissue culture, as an alternative to virus harvested from the skin of infected sheep.

The investigation of a bacterial urethritis in man established a genital type of pleuropneumonia-like organism as a possible cause. In man, however, the incidence of antibodies to pleuropneumonia-like organisms was not correlated with the presence of the organisms in the genitalia, so a detailed study of the relation of the pleuropneumonia-like organism antibody response to infections by the organism is being made, in the first place in experimental infections of the rat.

The immunological study of bacterial infections shows further progress in identifying the two antigens of the whooping cough bacillus responsible for prophylactic immunization and the exclusion of the histamine-sensitizing antigen as being immunogenic as well as a search for immunizing somatic antigens in the diphtheria bacillus and an analysis of the iota toxin of *Clostridium welchii*, a bacillus that may play an aetiological part in infective haemorrhagic fever. The study continues of the biologically active substances formed when diphtheria anti-toxins are refined by proteolysis, and of the actual enzymic process of refinement.

With pathogenic protozoa, the antigenic analysis of *Trichomonas* species continues and a new field has been entered in an attack on the immunology of trypanosomiasis. Soluble trypanosome antigens, formed during experimental trypanosomiasis of the rat, are under investigation and the *in vitro* culture of trypanosomes is being attempted to provide bulk material for antigenic analysis of these protozoa.

The refined serological methods devised to identify the animal source of food for blood-sucking insects continues to provide valuable facts about the feeding habits of tsetse flies and mosquitoes in regions where these insects are vectors, or possible vectors, of disease.

Work on the relation of early tissue reactions to defence against microbial infection continues. The tissue response to various kinds of injury, including infection, was explored to determine the role, if any, of the serum proteases which increase capillary permeability. The investigation of early non-specific resistance to bacteria was extended to infections by tubercle bacilli.

The biochemical researches mainly concern three kinds of substances—the blood group substances, the cellular phospholipids and starches.

During the year the problem of homogeneity of the blood-group specific substances isolated from secretions and digests of tissue has received careful attention and new methods of analysis have revealed that in the natural secretions blood specificity is associated with at least two types of mucopolysaccharide molecule. Progress was made in the separation and purification of enzymes which destroy the serological activity of the blood-group substances, and the chemical changes associated with loss of activity were investigated.

The phospholipid study is at present directed to defining the constitution of tissue phospholipids which, although ill-described, are known to be metabolically active. The structure of one of these, cardiolipin, has been elucidated and work is proceeding on the fatty constituents of the plasmalogens and the polyglycerophosphates.

The plant enzymes established as responsible for the synthesis and degradation of starch have been characterized in terms of their individual actions on starch. These enzymes were studied particularly in respect of their combined actions in systems thought likely to reproduce the conditions in which starch is synthesized *in vivo*, and of their separate actions on chemically modified substrates, designed to yield information on the specificity of the enzymes.

On human plasma proteins, the Institute's work is concerned with the isolation, refinement, characterization, assay and in some cases clinical trial of the various biologically active proteins of human plasma.

The difficulties of specifying the potency of preparations of anti-haemophilic globulins for use in haemophiliacs has necessitated a re-examination of modes of assay; clinical studies of the efficacy of the human preparation are in progress. The therapeutic value of γ -globulin in the treatment of hypogammaglobulinaemia is the subject of another clinical study. Studies of the isolation of active proteins include that of plasmin for clinical use and the conditions of its activation from the precursor plasminogen during the fractionation of serum as well as that of oxidase caeruloplasmin. Pathological studies include investigations of the so-called 'macroglobulins' that occur in hyperglobulinaemic sera and of the proteins that appear in the urine of man and animals poisoned by heavy metals.

* Lister Institute of Preventive Medicine. Report of the Governing Body 1959. Pp 34 (London: Lister Institute of Preventive Medicine, 1959).

A THEORY OF THE ABRASION OF SOLIDS SUCH AS METALS

By J GODDARD, H J HARKER and H WILMAN

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ABRASIVE wear is particularly important in machine bearings and gears¹ as well as in the mechanical surfacing of metals. Nevertheless, hitherto there has been no adequate theory to account quantitatively for the observed friction and wear of metals during abrasion. In particular, no simple relation between wear and friction has been observed. We have now observed such a clear and interpretable relation (see equation 1, below) and this has led us to develop the theory outlined below, which accounts well for the abrasion phenomena in the case of metals and similar solids, where the deformation is mainly plastic.

As the hard abrasive surface we have used emery papers having a mean particle diameter of 5, 10, 15, 35, 45, 70, 100 and 150 microns (grades 0000 to 3) since these represent at least approximately defined degrees of roughness down to a fineness not easily obtained by machining. The metals (copper, silver, platinum, aluminium, iron, molybdenum, tungsten) were blocks having about 3 cm² nominal bearing area and these were slid at about 5 cm/sec under loads (W) of up to 2 kgm on these emery papers. Practically identical results were obtained with the emery either dry or wet with propyl alcohol, except in the case of aluminium which showed negligible pick up of emery when wet, but extensive pick up and abnormally high friction when dry.

Figs 1 (curves a and b) and 2 show for example in the case of copper and tungsten the typical variation of the coefficient of friction, μ , and the wear per unit distance M respectively, with the mean diameter D of the emery particles.

Spurr and Nowcomb² made similar experiments but with loading via a lever arm on which the specimen (3/16 in diameter rod but probably about 0.1 cm diameter of bearing surface) was fixed and under which the emery paper passed on a trolley. Instead of the form of variation of μ with D shown in Fig 1 (curves a and b), with its fall at low D to a value close to that for the metal sliding on a similar metal surface they concluded μ increased linearly with D the rise (~ 0.1) being due to the ploughing component³ μ_p , which was assumed to be zero at $D = 0$, and proportional to D . In our more general conditions we have used specimens of considerable length (~ 2 cm for curves a and b in Fig 1) in the sliding direction. We conclude that on the finer grades of emery (D small), only in a limited front region of the specimen bearing face are there effective contacts and indentations of the emery particles into the metal. This region is estimated to be only ~ 0.1 cm for 0000 emery, but it must increase (roughly proportionally) with increasing diameter of the abrasive particles. In the remaining rear part of the face, the metal is mainly in contact with metal which has been worn away from the front specimen region and is almost completely clogging the emery in the operative bearing area. In agreement with our quantitative theoretical estimations, we find the variation of μ with D is much less (approximately that found by Spurr and Nowcomb²) when a shorter

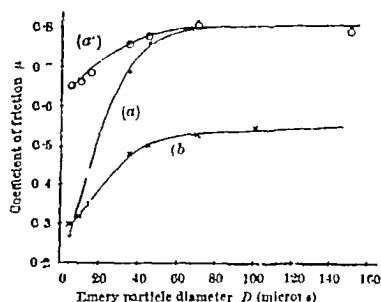


Fig 1 μ for copper (—●— 2 cm specimen length —○— 0.18 cm specimen length) and tungsten (—x— 2 cm specimen length) sliding on various grades of emery paper

copper specimen (0.18 cm) is used as in curve a of Fig 1.

We find a corresponding form of variation of M with D (Fig 2), also not previously described. The data of Figs 1 and 2 also give Fig 3 indicating an effectively linear variation of M with μ . Since M is also proportional to the load W , we have

$$M = k W (\mu - \mu_s) \quad (1)$$

where k is a constant (different for different metals) and μ_s is also a constant which we find is virtually identical with the coefficient of friction of two surfaces of the given metal sliding against each other at similar loading. (Experiments in this laboratory by P V K Porgess, J N King and P S Dobson have shown however, that for the non metals graphite, molybdenum disulphide and sodium chloride, the M vs μ locus is curved.)

In considering the abrasive process theoretically, we conclude that if the abrasive particles were

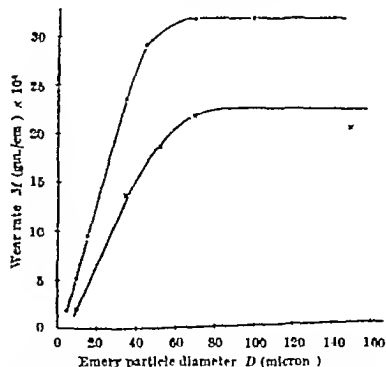


Fig 2 Wear of 2 cm copper and tungsten specimens on various grades of emery paper (—●— copper 1 kgm load —x— tungsten 1 kgm load)

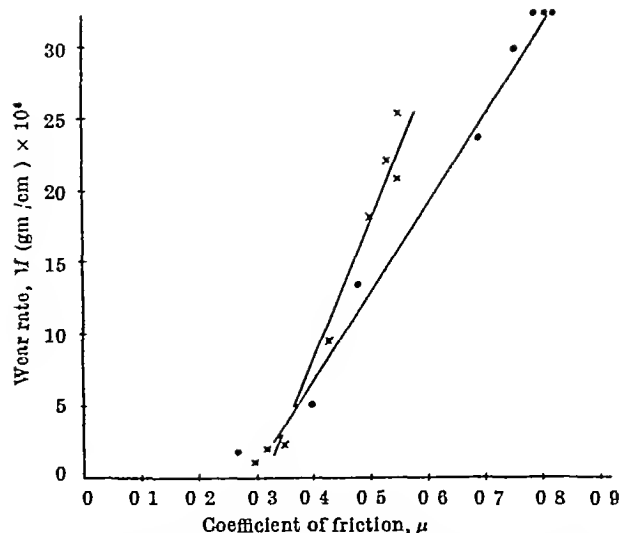


Fig. 3. The linear variation of M with μ for the copper and tungsten specimens: \times — \times , tungsten, 2 kgm. load, \bullet — \bullet , copper, 1 kgm. load.

spherical, and all those contacting the metal shared the load equally, then μ would indeed be very small, the ploughing component μ_p being correspondingly small and of the order suggested by Spurr and Newcomb's results (~ 0.1), but that it would be practically constant, independent of D . We find, in agreement with these views, that μ is, in fact, very small, ~ 0.15 (and thus μ_p still smaller), for metals such as copper and silver sliding under 1–2 kgm. load on a two-dimensional array of glass spheres of about 125 microns diameter ($\sim D$ for grade 2 emery) bonded on to a backing sheet (namely, "Scotchlite" reflective sheeting). Correspondingly, a negligible wear is observed in this case, although shallow, smoothly rounded grooves are formed, and little wear would be expected in view of the small inclination of the sphere surface to that of the metal near the contact, due to the low degree of indentation into the metal in the present conditions.

On the other hand, for metals such as copper and silver sliding on a glass-paper or emery-paper sheet having this order of particle diameter (~ 125 microns), μ was high, ~ 0.8 , and practically independent of D for values of D between 50 and 150 microns. We conclude (see below) that of this μ , μ_p is about 0.5, much higher than Spurr and Newcomb's suggested. The wear rate was also high and approximately constant for D within this range. The individual angular abrasive particles caused grooves in a smooth silver surface (sliding under 1 kgm. load) largely by removal of more or less curved, waved or coiled strips of metal of length up to about ten times the groove width (which was $\sim 1/3$ – $1/7$ of D). These metal strips were often observed still integral with the metal at the front ends of the grooves. The high μ and M that we observe in this range of D is thus evidently due to the emery (or glass) particles being mostly angular (as can be seen in the microscope) and not spherical.

Theoretically, if n pyramidal or conical particles share the load W equally and are indented into the metal surface with their axes along the direction of the loading, then the sum of the areas of contact (between the particles and the metal) projected on to the plane normal to the loading direction must be constant and equal to W/p_m , where p_m is the maximum flow pressure of the metal. Thus, n is determined by W and p_m , together with θ , the angle

between the pyramid axis and one of the radial edges. For square pyramids, azimuthally randomly oriented, we find that

$$\mu = \mu_p + \mu_a = (2/\pi) [\sqrt{2}(p'_m/p_m) \cot \theta + (s/p_m) (2 \operatorname{cosec}^2 \theta - 1)^{1/2}] \quad (2)$$

and for equilateral triangular pyramids:

$$\mu = \mu_p + \mu_a = (2/\pi) [2.25(p'_m/p_m) \cot \theta + 1.473 (s/p_m) (1.333 \operatorname{cosec}^2 \theta - 1)^{1/2}] \quad (3)$$

while for conical particles

$$\mu = \mu_p + \mu_a = (2/\pi) [(p'_m/p_m) \cot \theta + (s/p_m) \operatorname{cosec} \theta] \quad (4)$$

where μ_a is the adhesion- or shear-component of μ , s is the tangential force required to shear unit area at the operative surface where shear occurs, and p'_m is the apparent p_m for forward ploughing against an increased pile-up of metal ahead of the moving particle. We conclude that s/p_m is about 0.3, that is, about equal to the coefficient of friction of the metal (oxide) on the metal (oxide), that is, μ_0 . Although $p'_m > p_m$, we can take these as approximately equal.

To account for the observed maximum $\mu \sim 0.55$ for tungsten (see Fig. 1), the mean θ would thus have to be about 70° for square pyramidal particles ($2\theta = 140^\circ$, minimum profile angle 125°) giving $\mu_p = 0.33$, 75° for triangular pyramidal particles (min. profile angle 137°) giving $\mu_p = 0.37$, and 62° for cones (profile angle 124°) giving $\mu_p = 0.33$. This corresponds well to the sort of obtuse angularity of the particles mostly seen in the microscope. This theory thus accounts well for the observed μ , which is much larger than for the case of the more shallowly indenting spheres, which approximate to cones of nearly 180° angle, that is, $\theta \sim 90^\circ$.

The constant value of μ observed at $D > 70$ microns appears, in general, to be smaller the harder the metal, for example, ~ 0.78 for copper, nickel, silver and gold, 0.65 for platinum, ~ 0.6 for molybdenum, chromium, iron, beryllium, and ~ 0.55 for tungsten. This variation is partly associated with the differing values of s/p_m (this variation is apparently small), but it appears to be mainly due to the ratio p'_m/p_m varying from 1 for the hard metals such as tungsten to ~ 1.5 for the softer metals such as copper, silver and tin.

The above model could be made more general by including the case of pyramids or cones having their axes inclined away from the direction of loading, but this would still be only an idealized approximation to the extremely complex actual case of irregularly shaped abrasive particles. Our model shows, however, that in the absence of clogging, μ is independent of the particle size of the abrasive, and that μ_p forms the major part of the observed total μ .

Now considering the wear rate, M , suppose a part, fW (where $0 < f < 1$), of the load W is supported on n identical emery particles, and the remaining load $(1-f)W$ is supported on metal-to-metal contacts. Let A_1 be the groove cross-sectional area (normal to the direction of sliding), A_0 being the equivalent part of this area corresponding to metal removed from the groove space but finally remaining on the specimen (for example, as the pair of piled-up ridges at the sides of the groove, and also as re-adhering wear particles). Then we conclude that

$$M = (fW\rho/p'_m) \propto \{1 - (A_0/A_1)\} \mu_p \quad (5)$$

$$= (W\rho/p'_m) \propto \{1 - (A_0/A_1)\}$$

$$[1 + (\mu - \mu_0)/\mu_p]^{-1} (\mu - \mu_0) \quad (6)$$

where ρ is the density of the metal p_m is the maximum flow pressure across A_1 to cause ploughing, and α is the fraction of the emery particles shaped and oriented favourably for producing wear particles. Comparing the observed linear form, Fig 3 and equation (1), with this theoretical relation (6) shows that A_0/A_1 is independent of the emery particle diameter. Using an equation such as (2), (3) or (4) to express μ_p in terms of θ , equation (5) gives M directly in terms of θ and the properties of the metal, that is, ρ , p_m , p_m , etc.

Since $M = \alpha n p (A_1 - A_0)$, and $n A_1 = f W / p_m$ we may write as an alternative to equation (5) a more direct expression of M in terms of the properties of the metal

$$M/p = \alpha K (f W / p_m) \{1 - (A_0/A_1)\} \quad (7)$$

$$= C (f W / H_D) \{1 - (A_0/A_1)\} \quad (8)$$

where K is a constant defined as A_1 , divided by the horizontal component A_h (that is, normal to the direction of loading) of the mean contact area per particle supporting the load during sliding—thus K depends on the shape of the particles, H_D is the diamond pyramid indentation hardness number of the immediate surface region (which is very heavily work hardened by the ploughing action of the abrasive particles), and C is a constant. Equation (8) shows that if A_0/A_1 is the same for all metals, at constant W , then

$$(M/p) H_D = \text{constant} \quad (9)$$

Our results in Table 1 give an approximate check on the constancy of A_0/A_1 for various metals using equation (7) to calculate $M p_m / W = \alpha K \{1 - (A_0/A_1)\}$, taking $f = 1$ and $p_m =$ three times the ultimate tensile strength for the metal in a heavily work hardened state (cf. $p_m \sim 90$ kgm/mm² for copper)*. It is seen that $\alpha K \{1 - (A_0/A_1)\}$ is of the same order for copper silver platinum and iron. The small differences are probably due to the uncertainty of the value of p_m applicable to the work hardened surface layer and the more widely differing results for aluminium, molybdenum and tungsten seem likely to be mainly due to this uncertainty in p_m .

Further circumstantial evidence of the constancy of A_0/A_1 for all pure metals is given by our interpretation of the results of Kruschov† (see below). The constant K depends on the shape of the abrasive particles and is ~ 0.5 in our case where $0 \sim 60 \sim 70^\circ$, and $0.5 < \alpha < 1$ from direct observation, and by consideration of the experimental $M/(\mu - \mu_0)$ values

Table 1

| Metal | W | Mo | Fe | Cu | Ag | Pt | Al |
|---|------|------|------|------|------|------|------|
| Density (ρ) g/cm ³ | 10 | 9 | 7.8 | 8.9 | 10.5 | 21.3 | 2.7 |
| Ultimate tensile strength kgm/mm ² | 420 | 250 | 37 | 34 | 31 | 34 | 15 |
| $M(f=1)$ gm/cm ² 10^{-4} | 22 | 30 | 13 | 32† | 0.9 | 12.5 | 60‡ |
| $M p_m / W = \alpha K$ $(1 - (A_0/A_1))$ | 0.07 | 0.14 | 0.02 | 0.04 | 0.04 | 0.03 | 0.04 |

* Measured Vickers hardnesses (kgm/mm²) were W 450 Mo 242 Fe 100 Cu 98 Ag 73 Pt 118 Al 27

† Data from "Handbook of Chemistry and Physics, 30th edn pp 2022 ff (Chemical Rubber Publishing Co. Cleveland Ohio 1957-58)

‡ p_m is taken as $\sim 3 \times U.T.S.$

§ Results using 1 kgm. load, all others at 2 kgm.

|| Data using emery paper flooded with propyl alcohol all other data for dry emery paper

in the light of equation (6). The values of $M p_m / W$ in Table 1 thus indicate that $A_0/A_1 > 85$ per cent

Khruschov† showed experimentally that for all metals in the annealed state (of hardness H_D), sliding on the same grade of abrasive cloth (corundum particles $\sim 80 \mu$ diameter) under the same load the volume of wear per unit length, M/p in our notation, is proportional to $1/H_D$. He further observed however, for various metals that M is actually practically independent of the degree of work hardening of the initial metal, and as he concluded this shows that the process of abrasion work hardens the surface region of the metal (which undergoes further abrasive wear) to about the maximum possible extent, though this maximum hardness (H_D)_{max} was not defined. Our theoretical result (8), that (for not too small distances of abrasion) M/p should be proportional to the reciprocal of this hardness of the abraded surface, can be considered as showing in conjunction with Khruschov's observation of $M/p \propto 1/(H_D)$ that this (H_D) _{max} is practically proportional to (H_D) for all pure metals the factor A_0/A_1 being also the same for all pure metals.

The work described has been carried out under the terms of the extra departmental contract between the Mechanical Engineering Research Laboratory of the Department of Scientific and Industrial Research and the Imperial College of Science and Technology, University of London.

* Pigott, M. L., and Wilman, H. Paper 18 Conference on Lubrication and Wear Inst Mech Eng. London October 1957.

* Byatt, R. T., and Newcomb, T. P. Paper 24 Conference on Lubrication and Wear Inst Mech. Eng. London October 1957.

* Bowden, F. P., and Tabor, D. "The Friction and Lubrication of Solids" 2nd edn (Clarendon Press Oxford 1954).

* Khruschov, A. I. Paper 46 Conference on Lubrication and Wear Inst Mech Eng. London October 1957.

A CAPACITANCE METHOD FOR FOLLOWING VINYL POLYMERIZATIONS INITIATED BY γ -RAYS

By G. J. K. ACRES and F. L. DALTON

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DILATOMETRY has long been accepted as the most satisfactory method of following the course of vinyl polymerization. The change in volume as the monomer polymerizes is measured by following the fall in the level of the monomer in a capillary tube using a cathetometer. Direct optical measurement is

impossible when radiation is used for initiation, and although the use of a mirror system is sometimes feasible, parallax errors tend to reduce the accuracy of the method. Also, since polymerization reactions often require several hours for their continuous recording method is

A dilatometer in which the capillary is filled with mercury was developed by Schultz and Harborth¹ to obviate difficulties in following the movement of the surface of highly viscous fluids, and later modified by Burnett for use under high vacuum², we have adapted this dilatometer by using the falling-mercury column as one plate of a condenser, the other plate being a sheathed metal rod parallel to the capillary. Polymerization is followed by measuring the change in the capacity of this condenser using a commercially available capacitance bridge and feeding the output signal to a recorder. The equipment has been designed for use with the radiation sources at Wantage Radiation Laboratory these have been described in detail by Dove, Murray and Roberts³.

The sample is prepared in a breaker-seal tube under high-vacuum conditions and sealed off. Above the breaker seal a B 7 socket is attached and the sample may be connected to the body of the dilatometer by means of this joint as shown in Fig 1. The bore of tap T_1 is filled with mercury, and with T_2 open and T_1 closed the apparatus is connected to the high-vacuum line and evacuated via the B 7 cone A. Reservoir R_1 is filled with mercury and tap T_2 closed. T_1 is then partly opened and the mercury in R_1 allowed to spray slowly into reservoir R_2 . This procedure was found to 'flash off' any small quantities of air trapped in the mercury. After the mercury has run into R_2 , T_2 is opened cautiously and the mercury allowed to flow into the dilatometer until it reaches the level B. The seal is broken by an upward movement of the breaker C, T_2 re-opened and mercury allowed to fill the entire vessel. Air is allowed into the system above A, the reaction vessel removed from the high-vacuum line and reservoir R_1 detached. A capillary tube of appropriate diameter fitted with a B.7 socket and with an earthing connexion sealed through it is held by two short lengths of rubber tubing against a $\frac{1}{8}$ -in. steel rod covered in polythene. The polythene shield prevents fluctuations due to surface adsorption of water vapour by the capillary tube. The steel rod has a small metal plate attached to one end for connexion to the capacitance bridge.

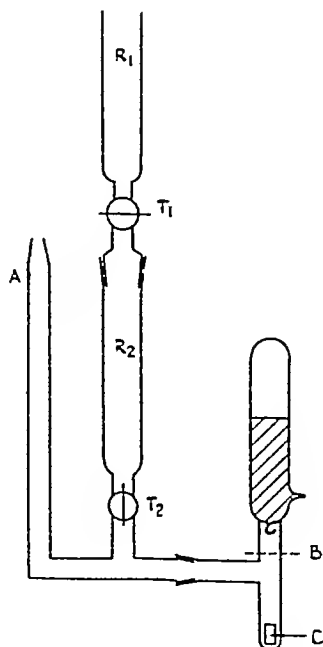


Fig 1. Diagram of dilatometer

The capillary and fittings are shown in Fig 2. This capillary is connected by means of its B 7 socket to A. picein wax is used to seal the joint. By applying compressed air pressure above R_2 and opening T_2 , mercury is forced through A into the capillary tube. T_2 is then closed and the whole apparatus immersed in a water thermostat in the radiation source.

It was found essential that the measuring capillary should be above the surface of the thermostat water, since otherwise a balance of the proximity meter could not be obtained, also, since stabilized glass tanks were not available, it was an advantage to have the capillary above the level of the thermostat tank so that the initial and final mercury-level could be accurately measured with a cathetometer.

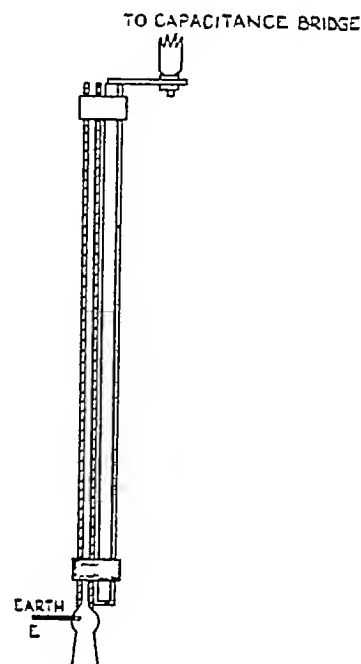


Fig 2. Capillary and electrode

Fig 3 shows the dilatometer in position. The capacitance bridge used was a Fielden PM2 proximity meter (Fielden Electronics, Ltd, Wythenshawe, Manchester). This instrument offsets the large constant capacity of the system and measures only changes in capacity. Since the length of the probe is only 6 ft the meter remains inside the radiation cell and is shielded by conventional interlocking 4-in. lead bricks. The sensitivity may be changed during the run if the fine sensitivity control is removed from the instrument case and mounted outside the cell. This enables the first few per cent of reaction to be followed in detail at high sensitivity, if the sensitivity is then lowered an overall conversion curve may be obtained from the same sample. To enable the proximity meter to be attached to a recorder, a 10-ohm resistance was put in series with the 1-m amp meter of the instrument and the voltage drop across this resistor fed to a Sunvic single-pen 10-millivolt recorder, clearly other values of this resistance may be chosen to suit any available millivolt recorder. To obtain stable readings of the recorder it was found essential to earth the mercury and this was done by connecting E (Fig 2) to the earth of the mains. Earthing of the thermostat tank, clamps and any other metal near the apparatus was found to be necessary. A series of calibration graphs

were made for various settings of the sensitivity control and various capillary diameters. The dependence on sensitivity setting for a 1 mm capillary is shown in Fig 4. The use of narrower capillaries tends to lower the sensitivity of the equipment slightly. In practice, initial and final mercury levels were measured with a cathetometer in order to avoid any slight errors in the sensitivity setting.

At Wantage the apparatus has been used to follow the emulsion polymerization of styrene and methyl methacrylate, and the preparation in emulsion of graft co polymers of polystyrene and methylmethacrylate and poly methylmethacrylate and styrene. It has also been used to follow the bulk polymerization of acrylonitrile and the graft polymerization initiated by gamma rays of acrylonitrile on to poly-dimethyl siloxanes. In use, the following precautions have been found necessary:

(1) A stable power supply is required, and it is therefore advisable to supply the proximity meter from a voltage stabilizer. Mains fluctuations at

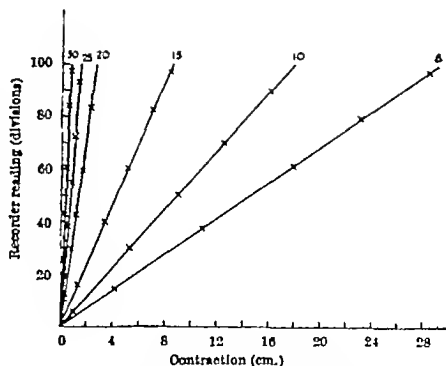


Fig 4 Calibration plot for 1 mm capillary

Wantage are exceptional, however, and this precaution may not be generally necessary. (3) The proximity meter should be allowed at least 30 min. to warm up before each polymerization run. (3) It is essential to earth the mercury, the thermostat tank, source tube and other metal equipment near the capillary to the instrument earth.

The equipment has been used to measure contractions 0.6–30 cm. in capillaries the diameters of which range from 2 mm. to 0.5 mm. The limit of 0.6 cm. is imposed by the maximum sensitivity of the proximity meter. Contractions greater than 30 cm. have not been used in order to keep the size of the capillary small and for contractions greater or less than these values for any given capillary, change in capillary diameter was used. The limit of this process, so far as small contractions are concerned, appears to be the stability of the thermostat tank, since if the capillary is made too narrow, fluctuations due to the slight rise and fall in temperature of the tank amounting to perhaps 0.01 or 0.02 deg. C, are observed. Greater sensitivity may also be obtained by increasing the diameter of the steel rod (Fig 3).

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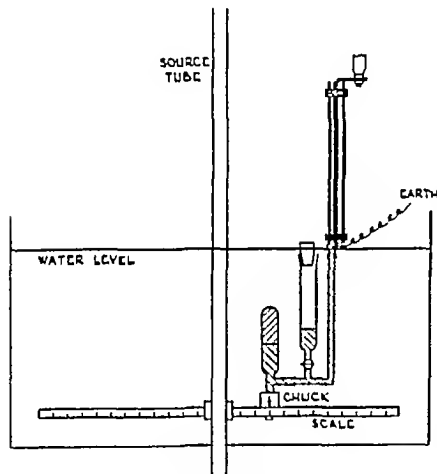


Fig 3. The dilatometer in position

PRODUCTION OF COLICINE BY SINGLE BACTERIA

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COLICINES are bactericidal substances produced by certain strains of Enterobacteriaceae and active on others¹. Colicins in many respects resemble bacteriophages; but, unlike them, do not multiply in the cells they kill. A single particle or molecule of colicin therefore does not produce a 'colony' (plaque) in the confluent growth of a sensitive strain, as does a single phage particle. From the analogy with the production of phage by lysogenic strains it has been surmised that all the colicin produced by a colicinogenic culture, either spontane-

ously or after induction² by ultra violet irradiation is synthesized and released by a fraction of the bacterial population, and that these cells are in consequence non-viable. No direct test of this hypothesis has been possible because colicin production has hitherto been tested only by observation on the antibiotic activity of mass cultures. We have now demonstrated the release of colicin by individual bacteria: (1) through the production by single bacteria of small clear spots in the confluent growth of a colicin-sensitive strain. (2) by the bactericidal

action of products released into micro-drops of broth by single colicinogenic bacteria isolated by micro-manipulator. The results obtained by these techniques support the above hypothesis.

The colicinogenic strains used were derivatives of *Salmonella typhimurium* strain LT2 made colicinogenic by growth in mixed culture with colicinogenic *Escherichia coli* or *Shigella* strains¹, or by phage-mediated transduction². The colicine-sensitive indicator strains were *E. coli* strain ϕ^3 and antibiotic-resistant mutants derived from it.

To demonstrate the clear spots caused by the colicine released by single bacteria we used a modification of the soft agar layer method used in phage work. 3 ml of soft agar (0.35 per cent) seeded with about 10^8 cells of the indicator strain and about 10^4 cells of a young broth culture of *S. typhimurium* producing colicine E2⁴ were poured on to a nutrient agar plate, after 5 hr incubation at 37° about 100 small clear spots, 0.2–0.8 mm in diameter, were visible in the confluent growth of the indicator strain. No such spots were produced by cells of a non-colicinogenic *Salmonella* strain, nor with an indicator strain resistant to colicines of the E group. Colicine E2 is destroyed by trypsin, crystalline trypsin (200 $\mu\text{g}/\text{ml}$) in the soft agar prevented the appearance of clearings. Although the spots looked like phage plaques, no lysis was observed when they were cut out and tested on a fresh plate of indicator bacteria.

It thus appeared that the clear spots resulted from the production of colicine E2, either by the colicinogenic bacteria inoculated, or, perhaps, by their descendants. The following results show that a clear spot can be produced by the colicine synthesized and liberated by a single bacterium.

Colicinogenic bacteria when plated with a streptomycin-resistant indicator in soft agar containing sufficient streptomycin to prevent their growth still produced some clear spots. Similar results were obtained with chloramphenicol. Furthermore, some clear spots were produced even when the colicinogenic cells had been killed by treatment with chloroform for 5 min at 37° before inoculation. The number of clear spots produced in the presence or absence of streptomycin was directly proportional (about 1 per cent) to the number of cells of the colicinogenic strain incorporated into the soft agar layer. Blender treatment, sufficient to break up any cell clumps, applied to the colicinogenic culture just before its inoculation into the soft agar, did not affect the number of clear spots produced. The number of clear spots appearing in the presence of streptomycin was 10- to 100-fold less than without it, this suggests that most of the clear spots formed in the absence of streptomycin are produced by bacteria which synthesize colicine on the plate, but that there are a few cells in the culture each of which at the time of plating already contains enough colicine to produce a clearing.

Clear spots were produced, either in the presence or absence of streptomycin, even when the colicinogenic cells had been grown in broth containing trypsin, provided the trypsin was removed by washing, or neutralized by soy-bean trypsin inhibitor, at the time of plating. As all free colicine in the inoculum culture was destroyed by the trypsin, the colicine causing a clear spot cannot have been adsorbed from solution by a cell of the inoculum culture, and released later, a hypothesis proposed by Frédéricq⁵ to explain the small plaque-like clearings

he observed when dilutions of a colicinogenic culture killed with chloroform were plated with a colicine sensitive indicator strain, it now seems probable that these clearings, like those here reported, resulted from production of colicine by single bacteria.

In certain colicinogenic strains, colicine production is inducible by ultra-violet irradiation¹. The number of clear spots produced by a strain colicinogenic for E2 was much increased by irradiation before plating, if cells irradiated for a time which reduced the viable count by about 70 per cent were plated in a streptomycin soft-agar layer 90 min later, the number of clear spots which appeared was half or more of the total number of colicinogenic bacteria inoculated, determined in a counting chamber.

We propose the term 'lacuna' for the clear spots produced by the colicine released by a single bacterium, in distinction from a phage 'plaque'. The soft agar of an area 0.8 mm in diameter contains about 6,500 colicine-sensitive bacteria at the time of inoculation, the presence of lacunae of this size indicates that some colicinogenic bacteria liberate at least 6,500 bactericidal particles of colicine E2.

The production of colicine by individual bacteria has also been demonstrated by micromanipulative isolation. Cells of the colicine-sensitive indicator strain grew as non-motile filaments, easily distinguishable from the short motile cells of *Salmonella typhimurium*. Cells of the indicator strain inoculated into droplets of broth containing colicine E2 failed to multiply, and became abnormal in appearance, showing alternate bright and dim segments when examined by low-power dark-ground microscopy, cells of a colicine-E2-resistant mutant of the indicator strain multiplied normally in such droplets. To test the production of colicine by individual bacteria, a strain of *S. typhimurium* colicinogenic for colicine E2 was 'induced' by ultra-violet light and incubated for 30 min. at 37° in broth, containing trypsin (500 $\mu\text{g}/\text{ml}$) to inactivate extra-cellular colicine. The irradiated cell suspension was then introduced into a micromanipulation chamber, and each of a series of droplets of broth with trypsin inhibitor 2 mg/ml was inoculated with a single bacterium from the suspension, volumes of the suspension not containing any cells were added to control droplets. 2 hr later the colicinogenic bacterium had multiplied in about 20 per cent of the droplets, in the remainder it had not multiplied but was still visible. The proportion of single bacteria able to multiply in the micro-drops agreed well with the survival-rate of the irradiated suspension inferred from the ratio of viable and total counts. Three to twenty cells of the indicator strain were then added to each droplet. In about 60 per cent of the droplets in which the colicinogenic bacterium had failed to multiply the indicator bacteria added later did not multiply and instead developed the characteristic abnormal appearance. In the remaining 40 per cent the indicator bacteria multiplied normally, as they did also in the control droplets which had received medium, but no bacterium, from the suspension of irradiated colicinogenic bacteria. In droplets in which the colicinogenic bacterium had multiplied, the indicator bacteria at first multiplied, showing absence of colicine, but later ceased to grow, presumably as a result of colicine being released by one or more of the large population of colicinogenic bacteria then present. About 50 per cent of the individual bacteria tested were shown by this method to release colicine, in platings from the same irradiated suspension the

ratio of the number of clear spots to the total number of bacteria was about 6/10.

The micromanipulation experiments described above indicated that all or nearly all the cells of an irradiated culture which release colicine E2 are non-viable. To see whether this was also so for the spontaneous production of colicine E2, about 1,000 cells of a chloramphenicol sensitive colicinogenic strain were plated in a soft agar layer of a defined medium containing chloramphenicol, together with a chloramphenicol resistant indicator strain, the latter was nutritionally exacting, so that it could multiply to only a small extent in the defined medium provided. After 5 hr incubation, twelve lacunae were visible in the thin confluent growth of the indicator. After overnight incubation about 1,000 small colonies of the nutritionally less exacting colicinogenic strain appeared, the chloramphenicol concentration having fallen by diffusion into the base layer of agar, below the level required to inhibit its growth. No colonies developed at the centres of the twelve lacunae marked earlier. It is concluded that the bacteria which produced these clearings by releasing colicine were unable to multiply.

The production of lacunae has been used for a number of other investigations which will be reported in detail elsewhere. *Salmonella typhimurium* strains producing colicines I, B, K and E1 produce lacunae, of sizes about the same as with colicine E2. When overnight broth cultures were tested in soft agar containing streptomycin the numbers of lacunae produced per million bacteria plated were approximately: colicine E2, 1,000; I, 0.2; B, 200; K, 300; and E1, 1,000. The ratio varied in cultures of different ages, for example it increased 10 fold when an overnight culture of a strain producing colicine E2 was diluted in broth and incubated for 1 hr at 37°. After ultra-violet irradiation the fraction of bacteria producing lacunae increased to about 0.5 in strains producing colicines E1 and E2; no increase was detected in a strain producing colicine I.

We thank Prof P. Frédérlec for the provision of colicinogenic strains.

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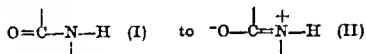
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PERMANENT SET, SUPERCONTRACTION, AND UREA-BISULPHITE SOLUBILITY—THE PROTON-TRANSFER NATURE OF SOME CHANGES IN KERATIN AND THE ANALOGY WITH MUSCLE CONTRACTION

By DR. P. T. SPEAKMAN

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DURING the reaction of cystine residues in keratin with OH⁻ ions sodium bisulphite, etc. the proportion of



contributing to the resonance hybrid of the peptide groups hydrogen bonded to each other in the protein network and eventually to a carbonyl oxygen atom of the cystine residue, can alter. An increase in the proportion of II (that is, an increase in the negative charge on the oxygen atom) will affect the strength of the hydrogen bonds between peptide groups electrostatically, also it can be shown that an increase in the strength of the individual hydrogen bonds will follow as more peptide groups are attracted into the co-operating, hydrogen bonded system. The stability of permanently set keratin, and of keratin treated with alkali with a decreased solubility in urea bisulphite solutions, seems likely to be caused by an increase in the strength of the hydrogen bonds between protein chains, caused in this way. The analogy between muscle contraction and supercontraction of keratin suggests a mechanism of contraction of muscles containing sulphur in which disorientation and contraction of the muscle follows a weakening of the hydrogen bonds between peptide groups by reagents which react with sulphhydryl groups. Re-orientation of the muscle would follow an increase in the charge on the oxygen atoms of the peptide groups during the reverse reaction.

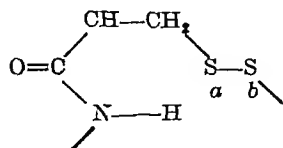
In some early experiments on permanent set¹ a keratin fibre was extended in water and treated under tension with, for example steam boiling buffer solutions, or sodium sulphite solution. The treated fibre was immersed without tension for an arbitrary period (1 hr) in boiling water, and if the fibre was to some extent stabilized in its extended form and its length remained greater than the initial length then it was said to be permanently set. If it was less supercontraction had occurred. Cross linkages between the keratin chains are broken by the treatments, thus allowing the chains to rearrange in the stretched fibres. If no new cross linkages are formed then a change in the arrangement of the uncross-linked protein chains after immersion in boiling water causes supercontraction. If new cross linkages are formed in the treatments, then the chains are to some extent held in their positions in the extended fibre thus causing permanent set. A chemical treatment which decreases the solubility of keratin in urea bisulphite solutions² is similarly most plausibly explained by new resistant linkages between protein chains.

Breaking of cystine disulphide bonds is an essential preliminary to permanent set in wool but work in Australia on fibres containing reduced and alkylated cystine residues³, and on the hurefringence and contraction in lithium bromide solutions of set fibres⁴ shows that it is an over-simplification to suggest that permanent set is entirely due to new covalent cross linkages formed after reduction or hydrolysis of the cystine residues. Two cross linkages which have been

extended fibres are set, the X-ray diffraction photograph of set β -keratin, compared with unset β -keratin¹⁵, shows a sharpening of the backbone reflexion, confirming the orientation of more protein chains into the strict β configuration. Davies, Evans and Lumley Jones¹⁶, using methyl acetamide in carbon tetrachloride, have shown that the shift in the hydrogen-bonded NH vibration infra-red absorption frequency away from the non-hydrogen-bonded NH vibration frequency is increased from approximately 120 cm⁻¹ to 190 cm⁻¹ as the concentration of amide is increased. The shift can be attributed to an increase in the number of amide groups hydrogen-bonded together in each linear aggregate. The difference between the absorption frequencies of the NH vibration in non-bonded and hydrogen-bonded amide groups is proportional to the energy of the hydrogen bond, and therefore in the experiments of Davies, Evans and Lumley Jones the energy has been increased 60 per cent by increasing the number of co-operating hydrogen-bonded amide groups in each linear aggregate. Thus the stability of a hydrogen-bonded protein structure can be increased by bringing more peptide groups into the co-operating hydrogen-bonded system. If it becomes possible to examine the infra-red spectrum of unset β -keratin the NH vibration frequency should show a smaller shift from the non-hydrogen-bonded NH frequency than the NH vibration frequency in set β -keratin where, according to the present theory, the protein chains are oriented so that there are more co-operating peptide groups in each hydrogen-bonded series.

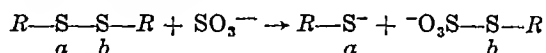
If the hydrolysis of cystine in steam, like the hydrolysis by OH⁻ ions, involves ionization of a proton at the α -carbon atom, then the observed facts of steam setting are readily explained. At first, in the extended fibre, the hydrogen bonds are weakened by the increased polarization of the peptide groups. Immersion of the fibre without tension in boiling water after up to 15 minutes in steam causes supercontraction. Longer treatment in steam allows further orientation of the protein chains, and more co-operating peptide groups increase the strength of the individual hydrogen bonds, thus causing permanent set¹⁵. Treatment of extended keratin fibres in boiling borate buffer solutions¹ (pH 9.2) for 30 min causes permanent set, orientation strengthening the individual hydrogen bonds. Less drastic treatment with phosphate buffers from pH 8 to 10 for 1 hr at 50° C¹⁷ or 20 per cent potassium hydroxide solution at 28.5° C for 3 min¹⁸ causes weakening of the hydrogen bonds by increased polarization of the peptide groups, without sufficient subsequent orientation to strengthen the hydrogen bonds, and thus supercontraction occurs under these conditions.

Swan⁶ has shown that the hydrogen atom attached to the α -carbon of cystine is not involved in the reduction of cystine by sodium sulphite. However, sulphur can take part in hydrogen bonding¹⁹, and the most plausible hydrogen bond in cystine residues would seem to be



The approach of a negative ion, SO₃²⁻ or HSO₃⁻, to sulphur atom *b* would induce a positive charge on *b* and a negative charge on *a*. In turn, the polarity

of the peptide group would be increased. The negative charge on *a* will be further increased if the cysteine residue formed in the reduction is ionized, and in fact the setting reaction does appear to be catalysed by alkali¹⁷.



The changes in the polarization of the peptide group and other peptide groups hydrogen-bonded to it will cause immediate weakening and eventual strengthening of the hydrogen bonds as in steam setting and setting in alkaline solutions.

During the synaeresis of actomyosin after adding adenosine triphosphate, the X-ray diffraction pattern shows in certain conditions the appearance of a faint 'cross- β ' reflexion which is typical of supercontracted keratin²⁰. This suggests that there may be some similarity between the contraction of components of muscle containing sulphur and keratin supercontraction. Reaction with sulphhydryl groups of muscle protein could alter the stability of the hydrogen-bonded network so that the chemical energy from a reversible, high standard free energy transphosphorylation, for example, liberated as kinetic energy, would cause disorientation of the protein structure and contraction. Then the reverse phosphorylation might induce negative charges on the peptide carbonyl oxygen atom and thus re-orient the muscle component into its original α -helical form.

This theory of permanent set, supercontraction, and urea-bisulphite solubility of keratin is put forward to explain those experimental facts²⁻⁵ not fully explained by the early theories of permanent set^{1,15}. There is no doubt, however, that all the chemical forces—covalent, electrovalent, van der Waals, and not merely hydrogen bonding—are involved in the three experimental phenomena considered.

I am grateful to Prof W. T. Astbury for many suggestions during helpful discussions of this work.

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INACTIVATION OF SOME ANIMAL VIRUSES BY HYDROXYLAMINE AND THE STRUCTURE OF RIBONUCLEIC ACID

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IN the course of some studies on factors which might stabilize infectious ribonucleic acid isolated with phenol from animal viruses, it was found that hydroxylamine inactivates the infectious ribonucleic acid extracted from mouse encephalomyelitis virus (Table 1). In addition, several animal viruses, all of which contain ribonucleic acid, proved to be sensitive to hydroxylamine (Table 1).

Hydroxylamine may act on animal viruses by affecting (1) viral protein, (2) viral ribonucleic acid, or (3) both viral components. Several types of experiment were performed in order to locate the site of action of hydroxylamine. In the first type of experiment, mouse encephalomyelitis virus was treated with hydroxylamine and then ribonucleic acid was extracted. If hydroxylamine had reacted with the ribonucleic acid of the virus, then the extracted ribonucleic acid should be non-infectious. This type of experiment must be distinguished from that described in Table 1 where infectious nucleic acid is first extracted from virus particles and then treated with hydroxylamine. The experiments were carried out as follows. Mouse encephalomyelitis virus was incubated in 1 M hydroxylamine at 22° C and pH 7. A control preparation containing no hydroxylamine, was incubated under the same conditions. The virus preparations were treated for various periods of time in the individual experiments. After dialysis of both samples, aliquots were assayed for virus infectivity to determine the virus survival ratio. The same samples were treated with phenol at 42° C to extract ribonucleic acid.¹ Infectivity of ribonucleic acid was titrated by intracerebral inoculation in mice. The ratio of the infectivities of ribonucleic acid extracted from treated virus to that extracted from control virus should be the same as the virus survival ratio if hydroxylamine inactivates the virus only by alteration of viral ribonucleic acid. Highly variable results were obtained, but the average virus survival ratio was only four times higher than the average survival ratio of the extracted ribonucleic acid. Considering the many manipulations involved in these experiments, the results indicate that hydroxylamine acts on mouse encephalomyelitis virus by altering the viral ribonucleic acid. This conclusion is also supported by the fact that mouse encephalomyelitis virus is inactivated at a rate comparable to that of infectious ribonucleic acid isolated from the virus (Table 1).

The second type of experiment to locate the site of action of hydroxylamine tested the effect of this compound on several activities of viral protein. A mouse encephalomyelitis virus preparation inactivated by treatment with 1 M hydroxylamine at 22° C for 24 hr and then dialysed for 24 hr had the same complement fixing activity against a rabbit antiserum to mouse encephalomyelitis virus

Table 1 THE INACTIVATION OF SOME ANIMAL VIRUSES AND ANIMAL VIRUS RIBONUCLEIC ACID BY HYDROXYLAMINE

1.4 M solution of hydroxylamine hydrochloride is adjusted to neutral pH by mixing with an equal part of 24 per cent sodium hydroxide. This solution is mixed with an equal part of infectious material and incubated for 15 min at 22° C. For the inactivation of viruses the reaction is stopped by 1:5 dilution in phosphate buffered saline (ref. 16) at 4° C and excess hydroxylamine is removed by dialysis against phosphate buffered saline for 24 hr. For inactivation of infectious ribonucleic acid the reaction is stopped and hydroxylamine removed by precipitation of the ribonucleic acid with alcohol. The virus infectivity was measured by plaque test (ref. 17) and the infectivity of ribonucleic acid from mouse encephalomyelitis virus was titrated by intracerebral inoculation in mice (ref. 1).

| Infectious material | Survival ratio* |
|--|--|
| Infectious ribonucleic acid from mouse encephalomyelitis virus | 2.6×10^{-1} 1.8×10^{-2} |
| Mouse encephalomyelitis virus | 2×10^{-1} |
| Fowl plague virus | 2×10^{-1} |
| Swine influenza | 2×10^{-4} |
| Western equine encephalomyelitis virus | 3×10^{-1} |

* Title of treated/litre of control

as a control preparation. Thus treatment of mouse encephalomyelitis virus with hydroxylamine results in an alteration of the infectivity of the ribonucleic acid without major alterations in the serological properties of the protein. In order to study the effect of hydroxylamine on other proteins of animal viruses, a fowl plague virus concentrate was treated with 1 M hydroxylamine for 24 hr resulting in complete inactivation. After 24 hr dialysis, the haemagglutinating activity was the same as that of a control. Further, the enzymatic activity of the virus, measured by elution from red blood cells at 37° C, was identical in treated and control preparations. The complement fixing ability of the treated preparations was the same as that of the control when measured with anti fowl plague serum. Hence, as in the case of mouse encephalomyelitis virus, hydroxylamine had not caused any detectable changes in the viral protein, at least in the peripheral protein.

Hydroxylamine also inactivates certain bacterial viruses, but the action in this case is on a protein component, probably resulting in the rupture of thiol ester bonds in the protein of the tail fibres.² The activation energy of this process³ is approximately 10 kcal/mole. To contrast this with the inactivation by hydroxylamine of animal viruses the activation energy for the inactivation of western equine encephalomyelitis virus was determined over the temperature range 20–44° C. A value of approximately 4 kcal/mole was found. The difference observed in the activation energies for the inactivation of bacterial viruses and western equine encephalomyelitis virus indicates that different chemical processes may be involved in the two cases.

(Note added in proof The activation energy for inactivation of mouse encephalomyelitis virus is 15.6 kcal/mole. Since mouse encephalomyelitis virus and mouse encephalomyelitis ribonucleic acid are inactivated at the same rate, this must be the energy associated with the reaction of ribonucleic acid with hydroxylamine. This is similar to the energy for splitting thiol-ester bonds and may further suggest that an ester bond is split from ribonucleic acid by hydroxylamine. The previously determined activation energy for inactivation of western equine encephalomyelitis virus may then represent a secondary reaction, perhaps an alteration of viral lipid.)

A direct attack on the nature of the reaction of hydroxylamine with ribonucleic acid gave little positive information. 'Model' ribonucleic acid was prepared from rat liver and calf liver by extraction with phenol at 4° C, using phosphate-citrate buffer at pH 5 in order to prevent the simultaneous extraction of deoxyribonucleic acid. After alcohol precipitation, followed by precipitation with 1 M sodium chloride, the nucleic acid obtained consists of a two-component system with molecular weights $\sim 2 \times 10^6$ and $\sim 6 \times 10^5$, respectively (cf ref 4). This ribonucleic acid was treated with hydroxylamine for 24 hr or 48 hr and excess hydroxylamine was removed by repeated alcohol precipitation of the ribonucleic acid. There was no degradation of ribonucleic acid, as revealed by analytical ultracentrifugation. Further, paper chromatographic and paper electrophoretic studies of the products of alkaline and acid hydrolysis showed no differences from those of untreated ribonucleic acid. Thus hydroxylamine does not seem to split the phosphate-sugar backbone of ribonucleic acid or alter any of the bases. If one of these processes was responsible for the inactivation of infectious ribonucleic acid, which has a $1/e$ value of 3.7 min, meaning that an average of one such inactivating event has occurred in each molecule in 3.7 min, then approximately 400 such inactivating events would occur per molecule in 24 hr. The failure to detect any changes after 24-48 hr with the methods used is strong evidence that inactivation did not occur by either of the above-mentioned processes. As a comparative example, the oxidative deamination of adenine, guanine and cytosine in ribonucleic acid by nitrous acid can be demonstrated chromatographically after a reaction time of about 20 hr.⁵

Recent studies on the chemistry of protein synthesis have shown that amino acids are bound to a ribonucleic acid of low molecular weight (soluble-ribonucleic acid) before being coupled together in a polypeptide chain.^{6,7} The amino-acid is bonded to soluble ribonucleic acid at a 2' or 3' hydroxy-position of the terminal ribose and this amino acyl ester bond can be split by hydroxylamine.⁸ It could be that a similar structure exists in some forms of high molecular weight ribonucleic acid and that such a structure is essential for the biological activity of ribonucleic acid in those cases. It would be difficult, however, to demonstrate the existence of an amino acyl ester in nucleic acid of molecular weight $\sim 2 \times 10^6$ since, by weight, the amino-acid represents ~ 1 part in 10^4 of nucleic acid. Therefore, this hypothesis must be investigated by some indirect approach.

One such approach is a comparison of the stability of the amino acyl-soluble-ribonucleic acid bond with that of the infectivity of ribonucleic acid from mouse encephalomyelitis virus (Table 2). The stability of infectious ribonucleic acid in the pH range 5-7 and the

instability at pH 8.6 correspond to the pH stability of an amino acyl ester bond. Control experiments on the degradation at pH 8.6 of 'model' ribonucleic acid from calf liver, measured by alteration of viscosity during a 48-hr period, showed that inactivation of infectious ribonucleic acid at pH 8.6 could not be due to alkaline hydrolysis of the phosphate-sugar backbone. Hydroxylamine inactivation of ribonucleic acid from mouse encephalomyelitis virus proceeds more rapidly at pH 7 than at pH 5.5 and this is also true for hydroxylamine splitting of the amino acyl ester bond to soluble-ribonucleic acid.⁸ In contrast, the reaction of hydroxylamine with activated amino-acids (mixed anhydrides in which the carboxyl group of the amino-acid is phosphorylated)⁹ occurs equally well⁸ at pH 5.5 and pH 7.0. Therefore, if an amino-acid or related compound is linked to the ribonucleic acid of certain viruses, as suggested by these experiments, then the bond should be similar to that between amino-acids and soluble ribonucleic acid (ester) rather than to that in activated amino-acids (mixed anhydride).

Table 2. A COMPARISON OF THE STABILITY OF AN INFECTIOUS RIBONUCLEIC ACID FROM MOUSE ENCEPHALOMYELITIS VIRUS AND THE AMINO ACYL ESTER BOND TO SOLUBLE RIBONUCLEIC ACID

| Infectious ribonucleic acid | Amino acyl ester soluble ribonucleic acid bond |
|---|---|
| Stable at pH 5 60° for at least 10 min 22° for at least 15 min | Reported to be stable in 0.15 HCl, as well as in the pH range 3-6 (ref 18) |
| Stable at pH 7 60° for at least 10 min 22° and 37° for at least 30 min | Unstable at pH 8.6, 37° Extrapolation of the data to 30 min $n/n_0 = 0.025$ (ref 18) |
| Unstable at pH 8.6 37° for 30 min $n/n_0 = 0.03$ | Reacts with 1 M NH_4OH at pH 7 to a greater degree than at pH 5.5 (ref 8) |
| 1 M NH_4OH , 22° $1^{\circ} = 0.25 \text{ min}^{-1}$ at pH 6.8 and 0.10 min^{-1} at pH 5.5 | |

* Assuming a first-order reaction, $dn/dt = -kn$, where n is the remaining activity at time t .

Not all animal viruses can be inactivated with hydroxylamine under the conditions described here. For example, Newcastle disease and mumps viruses, which are in one distinct sub-group of the myxoviruses¹⁰, are resistant to 1 M hydroxylamine at 22° C. Fowl plague virus and swine influenza virus, which belong to another sub-group¹⁰, proved to be highly sensitive (Table 1). These results suggest that there are differences in the nucleic acids of these two groups of myxoviruses, although all myxoviruses which have been chemically analysed, including Newcastle disease¹¹, fowl plague¹², and influenza¹³ viruses, contain ribonucleic acid. Herpes simplex, which may contain deoxyribonucleic acid¹⁴, also proved resistant to hydroxylamine. The resistance of some viruses to hydroxylamine inactivation may be further evidence that hydroxylamine attacks a special configuration in the nucleic acid component of certain viruses, since it appears that all nucleic acids have certain chemical properties, such as a phosphate-sugar backbone, in common. Thus it must be concluded that hydroxylamine does not alter any of the chemical bonds common to all nucleic acids.

The biological significance of this hypothetical ester bonded to infectious ribonucleic acid is not clear. One suggestion is that an amino acyl ester or some other acyl group in an ester linkage located at a terminal position on a ribonucleic acid chain would serve to limit the chain-length by providing the

information that the end of the chain had been reached. In any event, such a structure could serve to give the chain a direction in a more striking manner than that provided by the presence or absence of a terminal phosphate¹⁵. Moreover such a terminal ester group may serve as a pruning agent for certain biosynthetic reactions.

The theoretical and practical aspects of the phenomena described here are being investigated further and will be published in full detail elsewhere.

We gratefully acknowledge the many stimulating discussions with Profs G C Mueller, W Schäfer, G Schramm and R Dulbecco. This work was supported by the Deutsche Forschungsgemeinschaft.

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AUXIN AND THE BULBING OF ONIONS

By DR. J. E. CLARK and PROF. O. V. S. HEATH

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DETAILED studies of those changes in the internal morphology and histology of onion plants which are characteristic of the process of bulb development in response to the combined stimuli of long days and high temperature led to the formulation of a speculative hypothesis in terms of a supposed 'bulbing substance' or hormone¹. We are now engaged in a study of the changes in growth-substance content of onion plants during bulbing, using modifications of the methods of paper partition chromatography combined with bioassay of growth substances first developed by Bonnet Clark *et al.*^{2,3} we are also studying the effects of externally applied auxin on bulb development.

When testing for an unknown chemical growth factor supposed to produce a specific effect on a certain organ of an intact plant it is desirable if possible to develop an assay method depending on the production under standard conditions of such an effect in the same or similar tissue. Thus one should, ideally, test a fractionated tissue extract for the presence of a 'flowering hormone' by its capacity to cause flower initiation in growing points, preferably kept under otherwise non-inductive conditions; the appropriate test for growth promoting hormones is one in which increase of growth is measured, rather than inhibition of growth or abscission of organs, for a bulbing substance the assay method should involve bulb development again preferably under non-inductive conditions. If this principle is ignored as is frequently the case irrelevant or misleading information may be obtained. For the comparison of amounts of known compounds in tissue extracts from plants in different treatments, the use of assay methods depending on irrelevant plant responses would however, seem to be justifiable if suitable precautions are taken to confirm that the compound concerned is in fact the one supposed.

For bioassay we have therefore used a modification of the wheat coleoptile cylinder test⁴ in an attempt to compare changes in the 3 indolylacetic acid content of onion plants during bulbing in long days with that of plants remaining in short days, but we have also

developed a method in which onion seedlings constitute the test material and show an increase in bulbing ratio (the ratio of the greatest diameter to the least) when supplied with a suitable growth substance in darkness. The onion seedlings as used for this bioassay have been found not only to give a marked bulbing response to long days but also to externally applied 3 indolylacetic acid in darkness. Seedlings at the 2 leaf stage of development, with roots and leaf blades removed ('seedling sections') rotated horizontally in darkness in a 1 per cent sucrose solution, show from 1 to 8 days an increasing bulbing ratio in the presence of added 3 indolylacetic acid (sodium salt, pH 7.0, at 1×10^{-4} M concentration or approximately 20 p.p.m.), whereas in sucrose alone there are no marked or consistent changes. Such a response is rapid at 25° C, much slower at 20° C and almost non-existent at 15° C, this resembles the effect of temperature on rate of bulbing in response to the stimulus of long days⁵. We have also found with intact seedlings growing in water culture in short days, a small but statistically significant ($P < 0.02$) increase in bulbing ratio due to the addition of 1×10^{-4} M 3 indolylacetic acid to the solution, as compared with seedlings not given 3 indolylacetic acid.

We have made a preliminary survey of the changes, caused by various periods in long days at different stages of development, in the growth substance content of onion plants. For this purpose plants of variety Ebenezer were grown from sets in sand culture in short days (less than 12 hr.) and transferred to long days (17 hr.) at the time of expansion of the tenth, fourteenth, eighteenth and twenty-fourth leaf. Samples were taken from long-day and short-day plants of the same age according to the plan shown in Table 1. Roots and leaf blades were removed and an ethanol extract made of the remaining tissue. The method of fractionation was that of Bonnet Clark *et al.*² and Larsen⁶ except that the pH was brought to 2.5 with 20 per cent orthophosphoric acid. Only the ether soluble, acidic fraction has so far been investigated in detail. Extracts were chromat-

Table 2 DISTRIBUTION OF INHIBITORY ACTIVITY IN ROOT HOMOGENATES

| Addition (0.5 ml) to reaction mixture | Glutamylhydroxamate (μ moles) | |
|--|------------------------------------|---------|
| | Clone 1 | Clone 2 |
| Water | 4.26 | 3.75 |
| Supernatant | 3.83 | 0.84 |
| Arsenate extract of residue | 0 | 3.58 |
| Tissue residue | 0 | 0 |
| Residue after ten extractions with arsenate solution | 3.94 | |

activity of the primary supernatant (clone 2) or of the arsenate extract (clone 1) was thermolabile (Table 3). These solutions did not decrease in activity when dialysed against distilled water for 48 hr and were free from detectable proteolytic and adenosine triphosphatase activity.

Table 3 THERMOLABILITY OF THE SOLUBLE GLUTAMYLTRANSFERASE INHIBITOR OF CLONE 2 ROOTS

| Time (min) of exposure of inhibitor solution to 100° C | Glutamylhydroxamate (μ moles) |
|--|------------------------------------|
| 0 | 0 |
| 5 | 0.8 |
| 10 | 1.2 |
| 15 | 2.5 |
| 30 | 3.7 |
| 45 | 4.5 |
| 60 | 4.5 |
| Water control | 4.65 |

A purified preparation of the glutamyl-transferase enzyme was at this point obtained from 2 kgm dried pea meal (*Pisum sativum* var Meteor) by the method of Elliott⁷, dissolved in the *tris* buffer, and the sensitivity of both the transferase and the synthetase activities of the enzyme to the tomato root inhibitor tested. The standard reaction mixture (3.3 ml) used in assaying glutamine synthetase activity contained 0.5 ml 0.1 M *tris* buffer (pH 7.2), 1 ml enzyme solution, 0.5 ml sodium-adenosine triphosphate (0.05 M), 0.5 ml sodium glutamate (0.5 M), 0.1 ml manganese sulphate (M), 0.1 ml hydroxylamine (M) and adjusted to pH 7.2, and 0.1 ml cysteine (M). In these tests a partially purified preparation of the inhibitor was used. This was prepared from a clone 2 root homogenate (100 gm fresh wt roots to 200 ml water) as follows: the supernatant was treated with 300 ml acetone and the precipitate collected by centrifuging, washed with acetone and reduced to a dry powder in a vacuum desiccator. Half the acetone powder dissolved in 50 ml water was treated with an equal volume of saturated ammonium sulphate solution and the precipitate collected by centrifuging and dissolved in water. This solution was dialysed at 2–5° C for 48 hr and then adjusted to 50 ml. The preparation of an active acetone powder ensured inactivation of any glutaminase⁸ or adenosine triphosphatase⁹ contamination. The inhibition, by the purified inhibitor, of the transferase activity of the pea meal enzyme is shown in Table 4.

Inhibition of the transferase activity by the purified inhibitor was not reduced by addition of 0.05 M

Table 4 ATTEMPTED PURIFICATION OF THE GLUTAMYLTRANSFERASE INHIBITOR PRESENT IN EXTRACTED TOMATO ROOTS

| Inhibitor fraction | Dry wt inhibitor required to cause 50 per cent inhibition of transferase activity (μ gm) |
|--|---|
| 1 Original supernatant | 1,200 |
| 2 Acetone powder | 450 |
| 3 Dialysed ammonium sulphate precipitate | 76 |

cysteine or glutathione. Its inhibitory activity was maximal if incubated with the pea enzyme for 10 min before adding substrates and cofactors. Prolongation of this preincubation for 60 min, using an inhibitor addition causing about 50 per cent inhibition, did not lead to any further decrease in enzyme activity. The inhibition was only slightly reduced by increasing the concentrations of glutamine or adenosine triphosphate in the reaction mixture (Table 5). There was no evidence that the inhibitor reduced the effective concentrations of Mn^{++} , arsenate or hydroxylamine.

Table 5 EFFECTS OF L-GLUTAMINE AND ADENOSINE TRIPHOSPHATE CONCENTRATIONS UPON THE PERCENTAGE INHIBITION OF GLUTAMYLTRANSFERASE ACTIVITY BY THE PARTIALLY PURIFIED TOMATO ROOT INHIBITOR

| L-Glutamine (mM) | Glutamylhydroxamate formed (μ moles) | | Percentage inhibition |
|--------------------|---|-------------------|-----------------------|
| | Inhibitor omitted | Inhibitor present | |
| 4 | 2.4 | 1.14 | 53 |
| 8 | 4.0 | 2.2 | 45 |
| 12 | 5.7 | 3.4 | 41 |
| 20 | 8.1 | 4.95 | 39 |
| ATP (M) | | | |
| 10^{-3} | 0.0 | 0.24 | 60 |
| 4×10^{-3} | 2.1 | 0.90 | 57 |
| 10^{-4} | 3.4 | 1.5 | 55 |
| 4×10^{-4} | 3.8 | 1.0 | 50 |
| 10^{-5} | 3.0 | 1.0 | 47 |

The inhibitor was active against both the transferase and the synthetase activity of the pea meal enzyme (Table 6).

Table 6 ACTIVITY OF THE PARTIALLY PURIFIED INHIBITOR AGAINST THE TRANSFERASE AND SYNTHETASE ACTIVITIES OF THE PEA MEAL ENZYME

| Enzyme activity | Glutamylhydroxamate formed (μ moles) | | Percentage inhibition |
|-----------------------|---|-------------------|-----------------------|
| | Inhibitor omitted | Inhibitor present | |
| Glutamate-transferase | 4.70 | 1.03 | 78 |
| Glutamine synthetase | 0.31 | 2.77 | 56 |

Homogenates of seedling roots of pea (*Pisum sativum* var Meteor) also showed inhibitory activity, but it could not be detected in red clover roots (*Trifolium pratense* var Dorset Marigrass), and seedling roots of *Avena* (var Victory) showed high glutamate-transferase activity.

Acknowledgment is made to the University College of Swansea for a research fellowship and to the Indian Institute of Science for the leave of absence which enabled one of us (C. S. V.) to undertake this work, to Prof. H. Walsch of Columbia University for a pure sample of glutamylhydroxamic acid and to Imperial Chemical Industries, Ltd., for a grant towards the purchase of the Unicam spectrophotometer (SP 500) used in the estimation of the hydroxamic acid.

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FORTHCOMING EVENTS

Monday, September 21

INSTITUTE OF METAL FINISHING (at the Northampton Polytechnic St John Street, London, E.C.1) at 6.15 p.m.—Mr A. O. N. Freund and Mr A. H. Barber: "The Use of Titanium in Electrolytic Processes for Metal Finishing"

Thursday, September 24

OIL AND COLOUR CHEMISTS ASSOCIATION (at Manson House 26 Portland Place, London, W.1) at 7 p.m.—Mr J. A. L. Hawley: "A Technologist's View of the Fourth Epoch"

Friday September 25

HOSPITAL PHYSICIANS ASSOCIATION (in the Lecture Theatre, Main Medical School, King's College Hospital, Denmark Hill, London, S.E.5) at 8.30 p.m.—Prof. D. G. Catchside, F.R.S.: "The Influence of Nutrition on Mutation Induced by Radication" (Sixth Douglas Lea Memorial Lecture)

Wednesday, September 30

BRITISH INSTITUTE OF RADIO ENGINEERS (at the London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C.1) at 8.30 p.m.—Mr W. E. Williams: "Modern Microwave Valves—a Survey of Evolution Principles of Operation and Basic Characteristics"

Thursday October 1—Friday October 2

INSTITUTE OF BIOLOGY (in the Lecture Hall, Royal Geographical Society Kensington Gore, London, S.W.7) at 10 a.m. daily—Symposium on "Biological Problems Arising from the Control of Pests and Diseases"

SOCIETY OF CHEMICAL INDUSTRY FOOD GROUP (at the Royal Society of Medicine, 1 Wimpole Street, London, W.1)—Symposium on "Enzymes in the Manufacture, Storage and Distribution of Food"

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

RESEARCH ASSISTANT (preferably graduate in mathematics and physics) to assist in the design of digital computers in the Computing Laboratory to assemble and run programmes using the Interpretative schemes in the Deuce Computer—The Secretary of University Court, The University, Glasgow (September 28)

ASSISTANT LECTURER IN BOTANY—The Registrar, The University, Manchester 13 (September 30)

TECHNICAL ASSISTANT (qualified to maintain and supervise the use of X-ray apparatus and the electron microscope) in the HOLDSWORTH SCHOOL OF APPLIED SCIENCE—The Registrar, The University, Leeds (September 30)

LECTURER IN PHYSIOLOGY—The Secretary, The University, 38 North Bailey, Durham (October 1)

LECTURER IN THE HISTORY OF SCIENCE—The Registrar, The University, Leicester (October 1)

RESEARCH ASSISTANT (graduate) in the DEPARTMENT OF AGRICULTURE to carry out investigation into the efficiency of farm buildings by the application of work study methods—The Secretary and Registrar, University College of North Wales, Bangor, North Wales (October 1)

LECTURER OR SENIOR LECTURER IN PHYSICS AND/OR CHEMISTRY to take subject to First Degree standard—The Principal, Biele College, Durham (October 3)

READER OR SENIOR LECTURER (with experience in experimental physics and preferably experience in some aspects of applied physics) in the DEPARTMENT OF PHYSICS in the School of Science—The Registrar, The University, Manchester 13 (October 5)

LECTURER (with special qualifications in hydrography) in **OGROGRAPHY**—The Registrar (Room 22, O.H.N.), The University, Reading (October 10)

CHAIR OF PHYSICS, CHAIR OF CHEMISTRY, AND CHAIR OF BIOLOGY in the University of Malia—The Secretary, Inter University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (October 15)

LECTURER OR ASSISTANT LECTURER IN BACTERIOLOGY at the University of Malia (Singapore Division)—The Secretary, Inter University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (October 15)

LECTURER (with a qualification in biochemistry and preferably with a medical qualification) in **CHEMICAL PATHOLOGY**—The Dean, St Thomas' Hospital Medical School, London, S.E.1 (October 16)

LECTURER OR ASSISTANT LECTURER IN PHYSICS at **SIKARENE COLLEGE** (University College of East Africa)—The Secretary, Inter University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (October 20)

LECTURER IN MICROBIOLOGY in the Faculty of Rural Science, University of New Zealand, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, October 23)

LECTURER IN NUTRITION in the Faculty of Rural Science, University of New Zealand, Australia, to undertake teaching and research in livestock nutrition in the Department of Nutrition and Chemical Pathology—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, October 23)

LECTURER, SENIOR LECTURER OR ASSOCIATE PROFESSOR IN APPLIED CHEMISTRY at the University of New England, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, October 23)

SENIOR LECTURER (preferably with research experience in the field of neurophysiology) in **PATHOLOGY** at the University of Sydney, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, October 24)

CHAIR OF BOTANY—The Secretary, The Queen's University Belfast (October 31)

CHAIR OF INORGANIC AND PHYSICAL CHEMISTRY in the University of Tasmania—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, October 31)

DEMONSTRATORS IN BIOCHEMISTRY, ANIMAL OR PLANT PHYSIOLOGY, SOILS, PARASITOLOGY, LIVESTOCK ANATOMY AND HISTOLOGY, VETERINARY AGRICULTURE, LIVESTOCK HYGIENE AND PATHOLOGY—The Registrar, University of New England, Armidale, N.S.W. Australia (October 31)

SENIOR RESEARCH FELLOW OR RESEARCH FELLOW IN THE DEPARTMENT OF THEORETICAL PHYSICS, Research School of Physical Sciences, Australian National University—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, November 2)

LECTURER (with qualifications in either pure or applied mathematics) in **MATHEMATICS** at the University of Canterbury, Christchurch, New Zealand—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (New Zealand, November 30)

ASSISTANT OR ASSOCIATE PROFESSOR OF PATHOLOGY at Queen's University, Kingston, Canada—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1

LECTURER IN MATHEMATICS—The Secretary, Royal College of Science and Technology, Glasgow

RESEARCH ASSISTANTS (graduates) in ELECTRICAL ENGINEERING for work in the fields of transistor applications or the properties of dielectric materials—Head of the Electrical Engineering Department, Northampton College of Advanced Technology, St John Street, London, E.C.1

RESEARCH ASSISTANTS (2) IN PHYSICS one for theoretical and/or experimental work connected with the theory of liquids and the other for meteorological or solid state physics—The Secretary, Sir John Cass College, Jewry Street, London, E.C.3

SENIOR TECHNICAL OFFICER (with a degree or diploma in agriculture or agricultural botany) in the CEREALS SECTION of the Seed Production Branch—The Secretary, National Institute of Agricultural Botany, Huntingford Road, Cambridge

REPORTS AND OTHER PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

Committee of the Privy Council for Agricultural Research. Report of the Agricultural Research Council for the year 1950-1958. Pp. vi+173. (Comm. 750.) (London: H.M.S. Stationery Office, 1958) 8s. 6d.

Report of a Conference on Herbage Seed Production organized by the N.I.A.B. in conjunction with the British Seeds Council (Cambridge Guildhall 16th and 17th November 1958). Pp. 481-576. (Reprinted from the *Journal of the National Institute of Agricultural Botany*, No. 3, 1958). Pp. 1-3. 1s. 6d.

Report of the National Institute of Agricultural Botany, 1959. Pp. 6. (Cambridge: National Institute of Agricultural Botany, 1959) 1s. 6d.

Sir John Cass College. Prospectus Session 1959-60. Pp. 25. (London: Sir John Cass College, 1959) 1s. 6d.

British Electricity Future. Pp. 4. (London: The Gas Council, 1959) 1s. 6d.

Department of Scientific and Industrial Research. Research for Industry 1958. A Report on Work done by the Industrial Research Associations in the Government Scheme. Pp. iv+135. (London: H.M.S. Stationery Office, 1959) 7s. 6d. net.

Report of the National Institute of Research in Rural and District Branch. Annual Report May 1959. Pp. 28. (Sheffield: Council for the Preservation of Rural England, Sheffield and Peak District Branch, 1959) 1s. 6d.

The Hannah Dalry Research Institute. Report for the three years ended 31st March 1959. Pp. 62+12 plates. (Airliehill, Ayr: Hannah Dalry Research Institute, 1959) 1s. 6d.

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LETTERS TO THE EDITORS

ASTROPHYSICS

Magnetic Field Associated with a Great Solar Flare

An unusually large solar flare of intensity 3+ was observed at Mount Wilson on July 16 1959. The flare was in an active region centered on the spot group at approximately 18°N 20°W. It showed a predominantly S-shaped or double spiral configuration, with marked variations of relative intensity in its various parts. Visual observations of the spectrum showed that the flare commenced abruptly between 21 19 and 21 24 UT, maximum was between 22 01 and 22 13 UT. Lines of Ca II, Na I_o and H were observed to be in emission for more than 1 hr; the width of the H α emission was greater than 6 Å. Emission persisted in the lines of Ca II and of H until after observations were terminated at 01 00 UT on July 17.

Beginning at 21 37 UT observations were made at intervals of a few minutes with the solar magnetograph modified for fine scanning, and with the spectroheliograph 14 fine scan magnetograms of hydrogen spectroheliograms and 49 spectroheliograms of the flare region were obtained during the 3½ hr of observation.

To require data on the detailed variations of the photospheric magnetic field during the progress of flares, the solar magnetograph¹ had been extensively modified, making it possible to scan a limited region of the Sun's disk 4.5 min of arc square, with a resolution of 5 sec. The scanning is carried out automatically with conformal recording on a cathode ray tube fitted with a camera. The recording spot is drawn out into a short line which is made to slant either to the right or to the left to indicate the magnetic polarity. Intensity of the component of the field in the line of sight is indicated by means of intensity modulation of the trace, changing abruptly at levels corresponding to 5, 10, 20 and 40 gauss. Thus, each magnetogram is a magnetic map showing the location, polarity and intensity of the detailed magnetic field. With the fine scan equipment sequences of such magnetograms can be produced at the rate of four per hour in order to show changes. Although at the time of these observations the apparatus had not been fully perfected in all technical details, it provided valuable data.

A comparison of the 14 fine scan magnetograms shows no definite change in the magnetic pattern. Thus these observations provide no evidence that the occurrence of the flare led to the destruction or radical redistribution of the magnetic field. This is not surprising, since the flare is a chromospheric phenomenon occurring at a higher level than the photosphere, to which the magnetic observations pertain. Large variations in the magnetic field pattern of the photosphere in a few hours would entail material velocities much greater than those normally observed in the photosphere. High velocities in the chromosphere are of course not excluded.

Four small flares have been observed since the large flare of July 16. For all these there are fine scan magnetic observations before, during and after the flares. In no instance was a change in the field apparent.

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July 30

¹ Barcock H. W. *Astrophys. J.* 118 347 (1953)

Solar Effects in the Motion of Vanguard

A NEW analysis which I have carried out of the complicated period changes of Satellite 1958 g₂ (*Vanguard*) shows a correlation with three solar effects: (1) the hour angle of the Sun as reckoned from the perigee point of the orbit, (2) the 27 day variations in solar activity discovered by Jacek¹, (3) the total daily solar insolation at the latitude of perigee.

The major atmospheric drag is well known to occur at or very near the perigee point of the elliptical orbit of a satellite, and the observed rate of decrease of period is proportional to the Satellite's area/mass ratio, the air density at perigee and the square root of the atmospheric scale height at perigee. Data on the period changes of *Vanguard* are very precise, but nevertheless they show a highly complex periodic variation with time. The dominant variation of the drag of *Vanguard* correlates with the hour angle of the Sun as measured from perigee. A diurnal effect appears to have been first noticed by Jacek¹. In the early days of *Vanguard* in the spring of 1958 the local solar time at perigee was 7 00 or 8 00 a.m. and the average weekly decrease in orbital was only about 0.002 min. Because the perigee advances 4.4 deg per day and the node regresses 3.0 deg per day, the right ascension of perigee on the average advances 1.4 deg per day as compared with 1.0 deg per day for the Sun. Thus the length of the 'day' at *Vanguard*'s perigee is 360°/0.4° days or 2.5 years. During August, September and early October of 1958 the weekly period change increased markedly as the local time at perigee increased from 10 30 a.m. to 1 30 p.m., reaching a peak in October of about 0.007 min. Since then the average change has decreased slowly but steadily to a minimum of only 0.001 min in July 1959, when the local solar time at perigee was 8 00 p.m. Table I gives values of the average weekly period decrease as a function of the solar hour angle at perigee. Entries are the ratios of observed period decreases to the average weekly period decrease over the history of the orbit through July, 1959 (-0.0032 min/week).

Table 1 RELATIVE RATE OF PERIOD DECREASE AS A FUNCTION OF THE HOUR ANGLE OF THE SUN RECKONED FROM PERIGEE

| Hour angle (deg) | 300 | 320 | 340 | 0 | 20 | 40 | 60 | 80 | 100 | 120 |
|---------------------|------|------|------|------|------|------|------|------|------|------|
| Period decrease | 0.65 | 0.58 | 0.67 | 1.31 | 1.93 | 1.57 | 1.36 | 1.13 | 0.70 | 0.32 |

It appears that this correlation of drag with time of day at perigee passage can be accounted for either by a daily expansion and contraction of the exosphere or by a daily variation of ionization in the exosphere. The latter effect will, in accordance with the ideas of Jastrow and Pearce³, result in charged drag, in which the effective cross-sectional area of the satellite is increased. If, however, the maximum admissible electron density in the exosphere is $2 \times 10^5 \text{ cm}^{-3}$, as pointed out by Spitzer⁴, then charged drag is negligible as compared with neutral drag. In my own view the interpretation of this effect as oscillations of the exosphere is to be preferred. If the outer atmosphere pulsates daily, the observed minimum drag of *Vanguard* is consistent with locating the base of the exosphere at 600 km and ascribing to it a scale-height of 100 km and density $9 \times 10^{-13} \text{ gm/cm}^3$, whereas the observed maximum at local time about 130 p.m., suggests that the base has moved up to about 800 km with scale-height 120 km and density $8 \times 10^{-13} \text{ gm/cm}^3$. These figures imply typical vertical winds of some 30 km/hr at the level of *Vanguard's* perigee and greater speeds farther aloft. The time of maximum drag, and hence maximum density and temperature, corresponds roughly with the hour of maximum heat at the Earth's surface and also with the hour of maximum ionisation in the ionosphere.

Superposed on this effect are the 27-day variations in drag due to solar activity, found by Jacchia¹. The decrements in weekly period fluctuate strikingly in phase with the sunspot number, the amplitude of the fluctuations averages 25 or 30 per cent of the mean rate of period decrease.

The third periodic effect is a seasonal one. Since the perigee of *Vanguard* advances at the rate of 4.4 deg per day, it migrates between latitudes 34° N and 34° S , completing a full cycle every 82 days. The total daily insolation at the latitude of perigee stands normally at a high tropical level. In terms of the insolation at the equator on the equinoxes at Earth's mean distance, the equatorial insolation ranges between 0.89 and 1.01, while at latitude 34° it never exceeds 1.18. However at the winter solstices at latitude 34° it dips to 0.46 in the northern hemisphere and 0.43 in the southern. When the hour-angle and solar-activity effects are removed, the residual weekly period decrease is less than normal on the several occasions when perigee has reached maximum latitude on or near the time of the winter solstice. The effect is rather weak in the northern hemisphere, but well marked in the southern. When perigee reached latitude 34° S on July 9, 1958 and again on June 9, 1959, the period decrease was reduced for a couple of weeks to about 50 per cent of neighbouring values, and on September 29, 1958, to about 60 per cent. Although still uncertain, the correlation of this third effect with seasonal insolation is somewhat improved when compared with the insolation some six weeks before the date in question, implying that the exospheric seasons lag in more or less the same way as the surface seasons.

Although the data are not so precise, *Satellite 1958 α (Explorer I)* seems to behave in the same fashion as *Vanguard* with respect to these three effects.

This work was supported by the National Science Foundation under Grant Y32 40/266, with Prof G W Swenson, jun, as principal investigator.

STANLEY P WYATT

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Aug 14

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PHYSICS

Propagation of Ultrasonic Waves in Liquids

PREVIOUS measurements of the heat produced by ultrasonic waves in a trap vessel¹ gave results that differed from those obtained by other methods² for the absorption coefficients in carbon disulphide, xylene and kerosene, the last two appear to have abnormally high values, particularly from measurements with narrow trap vessels. The results were confirmed with trap vessels made of plaster of Paris, with windows of thin paper or 'Cellophane' in place of mica. The abnormal behaviour cannot, therefore, be attributed to any electrical effect in the metallic core of the trap, or to the mica windows.

With the view of elucidating these observations, the steady heat developed in a trap vessel, placed 15 cm from a quartz crystal oscillator, was measured with extra partitions in front. With single partitions at 2 cm or 12 cm, or with partitions at both 2 cm and 12 cm, the heat dissipated in kerosene was reduced by 15, 40 and 80 per cent respectively. Insertion of a diaphragm close to the quartz might be expected to reduce the measured energy by a large amount, due to scattering or reflexion. The results obtained are, therefore, not easily explicable.

It was considered necessary to measure the energy behind one or more partitions directly. For this purpose, the deflexions of a double 'Cellophane' disk and of a single 'Cellophane' disk respectively, suspended in an ultrasonic beam, were measured with a travelling microscope. The disks were suspended from a supporting rod, in a closed glass chamber, by unspun silk threads 50 cm long. The rod could be moved longitudinally and transversely by screws. The deflexion of the single disk measured the flow energy, with a limiting value of about 15 per cent of the total energy due to the frame size. The double 'Cellophane' disk measured the total energy.

Measurements of deflexions of the two disks, suspended in benzene or kerosene, were made at two distances from the quartz crystal, and the absorption coefficients were calculated. The value obtained for benzene was in good agreement with those obtained by other methods. The absorption coefficient of kerosene was also measured at positions near the quartz crystal, and immediately behind the mica window. The values were much higher than those normally obtained (Table 1). This explains the large absorption in a narrow trap vessel placed near the quartz, observed earlier¹.

Table 1 RADIATION AND FLOW PRESSURE AT 3 Mc/s

| Liquid | Disk position (cm from quartz) | No of partitions before disk | Displacement (cm) Double Cellophane disk (D) | Displacement (cm) Single Cellophane disk (S) | Radiation D-S | $a_1^{1/2} \times 10^{11}$ | $S/(D-S)$ Flow (per cent) Limit 15 per cent |
|----------|--------------------------------|------------------------------|---|---|---------------|----------------------------|---|
| Benzene | 8 | None | 0.183 | 0.770 | 1.110 | 945 | 69.4 |
| | 15 | None | 0.63 | 0.225 | 0.345 | — | 68.0 |
| | 15 | 1 | 0.307 | 0.085 | 0.220 | — | 38.8 |
| | 15 | 2 | 0.215 | 0.046 | 0.169 | — | 36.7 |
| | 15 | 3 | 0.185 | 0.035 | 0.150 | — | 33.3 |
| | 15 | 4 | 0.180 | 0.030 | 0.150 | — | 20.0 |
| | 11.5 | None | 0.363 | 0.107 | 0.250 | 240 | 41.9 |
| | 10.5 | None | 0.270 | 0.061 | 0.209 | — | 29.2 |
| | 5* | None | 0.250 | 0.080 | 0.170 | 720 | 47.0 |
| | 0 | None | 0.210 | 0.063 | 0.148 | — | 46.0 |
| Kerosene | 12.5 | 1 at 12 cm | 0.275 | 0.052 | 0.223 | 1,200 | 33.3 |
| | 13.5 | — | 0.210 | 0.036 | 0.174 | — | 29.7 |
| | 14.5 | — | 0.194 | 0.031 | 0.163 | 600 | 20.0 |
| | 7 | None | 1.115 | 0.370 | 0.745 | — | 49.6 |
| | 7 | 1 | 0.830 | 0.250 | 0.580 | — | 40.0 |
| | 7 | 2 | 0.760 | 0.210 | 0.550 | — | 33.2 |
| | 7 | 3 | 0.610 | 0.160 | 0.450 | — | 35.5 |
| | 7 | 4 | 0.610 | 0.169 | 0.450 | — | 35.5 |
| | 17 | 4 at 17 cm | 0.145 | 0.045 | 0.100 | — | 45.0 |
| | 17 | +1 | 0.112 | 0.030 | 0.082 | — | 36.0 |
| | 17 | +2 | 0.070 | 0.017 | 0.053 | — | 32.1 |
| | 17 | +3 | 0.069 | 0.016 | 0.053 | — | 30.0 |

* Power adjusted for different sets

Deflexion measurements were also made with a varying number of partitions in front of the disk (Table 1). The constant intensity of a fairly high percentage, obtained by the insertion of three or four partitions indicates that the ultrasonic radiation passing through three partitions is not affected by the fourth one. The gradually decreasing reductions in energy intensity produced by the first three partitions, together with full transmission by the fourth suggest that vibrations propagated in the liquid are affected differently by the partitions. Some are easily dissipated, whereas others forming a homogeneous group are not affected by the partitions.

From the results in Table 1 benzene appears to absorb a larger percentage of easily dissipated energy. A larger reduction, obtained at higher frequencies (not tabulated) shows that the inhomogeneous group increases with frequency. Observations with two sets of mica partitions, one near the quartz crystal and the other in front of the disk, farther from the quartz, indicate since it has the same effect as the first set, that the inhomogeneity is created in the liquid. The previous observations on heat measurements with a trap vessel and extra partitions are now understandable. The values have also been confirmed by deflexion measurements with a similar arrangement of the partitions.

The nature of the inhomogeneity of the group of rays was ascertained from a study of the number and character of diffraction spectral lines. The spectrum produced by an inhomogeneous ultrasonic beam was noted both when it was unobstructed and when it was reduced by three mica partitions to a homogeneous group with 50 per cent of the former strength. The spectrum for the unobstructed source reduced to 50 per cent of the former strength by a reduction of the input wattage was also noted. The observed numbers of fringes were seven and five respectively determined only by the ultrasonic intensity irrespective of the group character. The

homogeneous group however gave sharp fringes. The comparative numbers of the fringes for the two intensities agree well with Sander's¹ relation $n^2 \propto$ wattage. Apparently the homogeneous and the inhomogeneous groups of rays have only a small variation in wave length, and thus contribute equally to the formation of any spectral order with a small spread. Large variations give rise to dissipation. Such a mechanism had been suggested previously by one of us (A. K. D.)²

The measurements throw some light on the origin of flow energy for which various mechanisms have been suggested.³ Table 1 shows some significant comparative values of the flow energy percentage. (1) The flow energy percentage falls rapidly as the number of partitions is increased. (2) The percentage of flow energy is comparatively large in the following cases: (a) in benzene compared to kerosene, (b) close to, as compared to far from the quartz (c) immediately behind, as compared to far from, a mica partition. All these observations suggest that the flow associated with the vibratory energy is directly related to the associated inhomogeneous group of rays present after strong absorption and that it appears only when there is a superposition of these wave groups. This is in agreement with the requirement deduced by Nyborg.⁴

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April 24

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The Flow of Blood through Narrow Tubes

IN a recent letter, one of us¹ has shown that the flow of the blood of several species in a single capillary tube of radius R and length L follows an equation recently proposed by Casson² for varnishes and inks

$$\left(\frac{PR}{2L}\right)^{1/2} = k_0 + k_1 \left(\frac{4V}{\pi R^3}\right)^{1/2} \quad (1)$$

where P is pressure, V is volume flow/sec, k_0 and k_1 are constants. When k_0 becomes zero, this equation reduces to the well-known equation of Poiseuille, since the terms in parenthesis represent the stress and shear rate respectively, at the wall of the tube. When k_0 has finite values, however, it is a measure of a yield-value or critical shearing stress which, as pressure is raised, will be first reached at the capillary wall. As pressure still further increases, the critical distance (r_0) from the centre at which this occurs, will steadily diminish. A similar phenomenon was studied many years ago for the Bingham equation, which differs from Casson's equation only in the absence of square roots, when Buckingham³ and, independently, Reiner⁴ evaluated the correct equation of flow for such a system

$$V = \frac{\pi R^4}{8k_1^2 L} \left(P - \frac{4}{3}p + \frac{p^3}{P^2} \right) \quad (2)$$

where p is the pressure corresponding to the yield-value given by $p = 2Lk_0^2/R$.

In the present communication a similar treatment is applied to Casson's equation since, like Bingham's equation, a correction to allow for the changing value of r_0 with increasing pressure must be made if a linear relation is to be obtained.

Re-writing equation (1)

$$k_1 D^{1/2} = \tau^{1/2} - k_0 \quad (3)$$

where τ is the shear stress (absolute value). Integration gives

$$k_1^2 v = \frac{r\tau}{2} - \frac{4}{3}r^{-1/2} k_0 + r k_0^2 + C$$

where v is the velocity of flow at distance r from the centre of the tube. If the material adheres to the wall, $v = 0$ when $r = R$, from which the integration constant C can be calculated

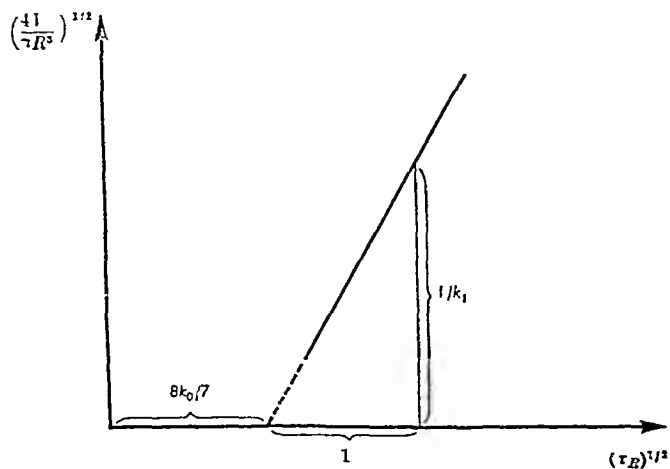


Fig. 1

Introducing τ_R for the shear stress at the wall

$$V = \int_0^R r^2 dv = \frac{\pi R^3}{4} \tau_R \left[1 - \frac{16}{7} \frac{k_0}{\tau_R^{1/2}} + \frac{4}{3} \frac{k_0^2}{\tau_R} - \frac{1}{21} \frac{k_0^4}{\tau_R^3} \right] \quad (4)$$

This replaces the original Buckingham equation (2). $k_0/\tau_R^{1/2}$ is small this approximates to

$$V = \frac{\pi R^3}{4} \tau_R \left[1 - \frac{8}{7} \frac{k_0}{\tau_R^{1/2}} \right]^2$$

or

$$\left(\frac{4V}{\pi R^3}\right)^{1/2} = \frac{1}{k_1} \left(\tau_R^{1/2} - \frac{8}{7} k_0 \right)$$

Thus if $\left(\frac{4V}{\pi R^3}\right)^{1/2}$ is plotted against $\tau_R^{1/2}$, a straight line is obtained, from which k_1 and k_0 can be determined as shown in Fig. 1

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† Scott Blair G W *Nature* 183 613 (1959)

‡ Casson, N., Chap. 5 of *The Rheology of Disperse Systems*, ed C C Mill (Pergamon Press London 1959)

§ Buckingham E *Proc Amer Soc Test Mater*, 21, 1154 (1921)

¶ Reiner, M, *Kolloidzeitschr*, 39, 80 (1926)

Substrate Damage in Film Thickness Measurement by Beam Interferometry

IN the Tolansky method for the measurement of the thickness of thin films by multiple beam interference we have used a narrow channel in the film rather than a sharp step¹. The channel can be formed by gently drawing a needle across the film before the deposition of the reflecting over-layer. The technique is easily applied and has several advantages especially when the substrate is not optically flat as in the case of microscope slides.

Weaver and Benjamin² have recently directed attention to a possible source of error in the technique.

They report that in order to form clear channels through films, deformations of the glass substrate by the needle can occur. For chromium films they measured deformations amounting to several hundred angstroms. Unfortunately no indication was given as to the nature and shape of the deformation.

We have found that while it is certainly possible to mar the glass with a steel needle, any damage can be detected by the irregularities in the shape of the fringe. Hence appreciable errors in thickness arising from damage to the substrate can be avoided.

Dr Weaver kindly sent us some of the gramophone needles which they use, and we have compared the scratches made by these needles with the scratches made by the sewing needles which we often employ. The results are shown in Fig. 1, which illustrates fringes at a low order of interference³. Fringes (a) are from scratches through a film made with a sewing needle held at about 45° to the direction of motion. From (i) to (iv) the loads increase in the range 5–200 gm. Fringes (b i–iv) are from scratches made with a steel gramophone needle. It is evident that

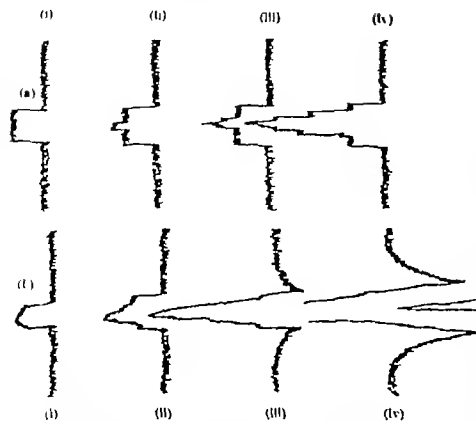


Fig. 1 Multiple interference fringes of scratches made by steel needles through a thin metal film on a glass substrate: (a) with a sewing needle; (b) with a gramophone needle. Loads on the needle increase from (i) to (iv) in each case.

the gramophone needle is considerably harder than the sewing needle. The effect of a plastic deformation is clearly seen in the smooth build up on either side of the channel fringes (b ii) and (b iv). The deformation seen in Fig. (b iv) is very similar to the furrow given by a glass cutting diamond. With the sewing needle the damage is often irregular along the length of the scratch and appears to represent a removal of the glass. Since the substrate on either side of the channel remains plane even at high loads as at (a, iv) it is concluded that there is no plastic deformation of the glass.

Measurement of the hardness of the two kinds of needles showed that the gramophone needles are indeed considerably harder. The sewing needles always show a slight flattening at the point after having been drawn across the glass whereas the gramophone needles do not show any significant deformation. It is our opinion that the softer sewing needles produce a clear channel through a film because the point yields and flattens before marring the glass. No difficulty has been experienced in producing clear channels without substrate damage even in the case of the more strongly adhering films of copper or chromium. On the other hand the gramophone needle probably makes only irregular small area contact and even at light loads will damage the glass before voiding.

Because the multiple beam interference method especially at low orders is capable of detecting distances of one or two angstrom units and because the shape of the fringe is an excellent guide to possible substrate damage, the problem of deformation of the substrate does not introduce any significant error in the measurement of film thickness.

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Some Semiconductive Properties of Dilute Binary Solid Solutions of Bismuth in Tellurium and Tellurium in Bismuth

IN connexion with my previous remarks on the bismuth-tellurium photo-voltaic sandwich layer¹ it has been of interest to investigate the presence of semiconductive properties of bismuth and tellurium alone, as well as of the binary solid solutions of bismuth in tellurium and tellurium in bismuth.

Bismuth and tellurium obtained from the American Smelting and Refining Co. of New Jersey will be designated in this communication as pure with a star, thus pure*. The spectroscopic analysis indicated the following information regarding the purity of these materials:

Bismuth contained 99.999 per cent bismuth, 0.0002 per cent silver, 0.0002 per cent lead, 0.0002 per cent copper, 0.0001 per cent iron and 0.0003 per cent unidentified impurities.

Tellurium contained 99.999 per cent tellurium and very faint traces of iron and copper.

Samples of bismuth-tellurium dilute binary solutions were obtained by melting and mixing the desired amounts of bismuth and tellurium pure* *in vacuo* at about 10^{-3} mm. mercury, and rapidly cooling down the envelope containing the melt. The container was then broken and the material tested with a hot probe for the type of conductivity. A few mgm. of the above material were then crushed into powder introduced into a Vacor tube and sealed to a vacuum system. After evacuating the tube to the pressure of 10^{-3} mm. mercury the powder was condensed on to the surface of a glass plate. The thickness of the layer amounted to about 1μ .

The type of conductivity was determined with a hot probe. It was then determined whether the film possesses the photo-voltaic property. A beam of radiation originating either from a tungsten lamp or from a soldering iron chopped at a frequency of 800 cycles/sec. and incident on the film produced electrical impulses which were amplified with a narrow band amplifier. The magnitude of the impulses was measured either by an oscilloscope or a vacuum tube voltmeter.

Bismuth. Bismuth is a semiconductor with bands which can be separated into slightly overlapping valence and conduction bands*. According to Aubrey and Chambers² the overlap between bands of holes and electrons is 0.018 eV and there are 0.86×10^{-3} electrons and holes in bismuth at 4°K . According to Heino³ there are 1.5×10^3 electrons and holes in bismuth. If donor atoms (tellurium) are added to bismuth the extra electrons go to fill up the band of holes. At concentrations of donors greater than 0.0015 per cent per atom there are no holes left and all further electrons go into the electron band. Is bismuth a photoconductive material? The work of Weber and Friederich⁴ does not prove that it possesses the property of photoconductivity in the modern meaning of the word. The abstract of Drummond⁵ which I came across during the preparation of this manuscript, does not give any information as to the purity of the material and due to its brevity it can only be assumed that the author deals with photoconductivity.

* Scott G. D., McLaughlin T. A. and Bennett R. S. *J. Appl. Phys.* 21, 843 (1950).

* Weaver C. and Benjamin P. *Nature* 182, 1149 (1958).

* Scott G. D. *J. Opt. Soc. Amer.* 48, 843 (1958).

I have performed some experiments on bismuth samples prepared by methods described here. The results are given in Table 1.

Table 1

| Bulk | | | | |
|--|-----------|-----------------------|---------------------|----------------------|
| | Bi pure* | Bi pure* + 0 1% Te | Bi pure* + 1% Te | Bi pure* + 10% Te |
| Thermo electric power in micro- volts per deg C | 50 ± 10 % | 30 ± 10 % | 25 ± 10 % | 20 ± 10 % |
| Type of con- ductivity | " | " | " | " |
| Conductivity in (ohm cm) ⁻¹ | | From 250 to 300 | | |
| Film | | | | |
| | Bi pure* | Bi pure* + 0 1% Te | Bi pure* + 1% Te | Bi pure* + 10% Te |
| Thermo-electric power in micro- volts per deg C | | From 10 to 50 | | |
| Type of con- ductivity | " | " | " | " |
| Conductivity in (ohm cm) ⁻¹ | | From 0.74 to 5 | | |
| Photo E M F in microvolts per 8 × 10 ⁻⁴ watt per mm square of incident radiation | | From 10 to 2 | | |

It is worth while mentioning that a few films of pure* bismuth were evaporated in an atmosphere of air at pressures 75, 15 and 1 μ mercury. Only the last one was found to be sensitive, its output being several microvolts E M F when illuminated.

Tellurium Tellurium is a semiconductor.² According to Loferski³ the optical band gaps are 0.32 eV and 0.37 eV for lights polarized normally to and in parallel with the c axis respectively.

Kronmüller, Jaumann and Seiler⁴ obtained very pure tellurium by distillation and sublimation, and then doped it with arsenic, antimony, bromine and iodine. In all cases the extrinsic tellurium was p type. Moss⁵ prepared a film about 10⁻⁴ cm thick which had considerable photoconductive sensitivity to infra-red at 90° K.

Table 2

| Bulk | | | |
|--|--|---------------------------|----------------------------|
| | Te pure* + | Te pure* + 1% Bi (atomic) | Te pure* + 10% Bi (atomic) |
| Thermo-electric power in microvolts per deg C | 360 ± 10% | 110 ± 10% | 50 ± 10% |
| Type of conductivity | p | p | p |
| Conductivity in (ohm cm) ⁻¹ | 20 ± 10% | 500 ± 10% | 750 ± 10% |
| Film | | | |
| | Te pure* | Te pure* + 1% Bi (atomic) | Te pure* + 10% Te (atomic) |
| Conductivity in (ohm cm) ⁻¹ | About 1 000 times smaller than for bulk material | | |
| Photo E M F in microvolts per 8 × 10 ⁻⁴ watts per mm square of incident radiation | From 30 to 10 | | |

I have prepared a number of samples by the method described above, and carried out some measurements, the results of which are shown in Table 2.

On the basis of the information just presented it seems reasonable to assume that the dilute binary solutions of bismuth-tellurium are semiconductors.

One can also expect that bismuth-tellurium solutions in all other proportions are semiconductive materials.

It was shown by Vasenin¹⁰ and by Haken¹¹ that both the sign and the magnitude of the thermo electric power of bismuth-tellurium solutions depend on the ratio of bismuth to tellurium. The thermo electric power changes sign with respect to copper five times over the range of composition, assuming three maxima and three minima.

It seems thus worth trying to evaporate on to the surface of a glass or quartz plate first a layer of a certain composition of bismuth-tellurium and on the top of it another layer of selected composition with a view of obtaining the best possible characteristic of a p-n junction. Another possibility is to try to realize a p-n-p or n-p-n layer and look for a transistor effect.

As a unit cell of Bi₂Te₃ consists of alternate layers of bismuth and tellurium it is possible that thin-film techniques could be used to investigate the properties of bismuth-telluride.

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- ¹ Piwkowski T. R., *Nature*, 182, 1793 (1958). Note that in this reference in the discussion of the mechanism of carrier production it had been erroneously stated that the polarity of the majority carriers relative to the electrodes is the same for both of the proposed models. In fact, stated polarity is correct for the second model while the opposite polarity holds for the first model.
- ² Callaway, J., "Solid State Physics", 7 (Seltz and Turnbull)
- ³ Aubrey, J. E., and Chambers, R. C., *J. Phys. Chem. Sol.*, 3, 123 (1957)
- ⁴ Holne, V., *Proc. Phys. Soc. A*, 69 (1950)
- ⁵ Weber, A. H., and Friederich, L. M., *Phys. Rev.*, 63, 217 (1943), 68, 248 (1944)
- ⁶ Drummond, Carl E., *ASTIA*, AD 154,280, Div. 25 (April 1, 1959)
- ⁷ Loferski, J. J., *Phys. Rev.*, 93, 707 (1954)
- ⁸ Kronmüller, H., Jaumann, J., and Seiler, K., *Z. Naturforschung*, 11a, 243 (1956)
- ⁹ Moss, T. S., *Proc. Phys. Soc. A*, 62, 264 (1949)
- ¹⁰ Vasenin F. L., *Zurnal Techn. Phys.*, 25, 307, 23 (1955)
- ¹¹ Haken, T., *Ann. Phys. (Leipzig)*, 32, 310, 17 (1910)

METALLURGY

Dislocation Arrangements in Molybdenum

RECENTLY, several studies of dislocations in face centred cubic metals by the method of transmission electron microscopy have been reported. Of the body-centred cubic metals, however, only iron has so far received attention^{1,2}. In this letter we give a preliminary account of some experiments on dislocation movements during deformation and recovery processes in molybdenum.

The starting material was a 0.0005 in thick cross rolled molybdenum foil of 99.90 per cent purity supplied by Messrs Metro-Cutani. Further thinning was achieved by electrolytic polishing in a solution of 25 per cent sulphuric acid in methanol using a technique similar to that described by Bollmann³ but with a cylindrical nickel sheath replacing the stainless steel point cathodes. An applied potential of 2 volts with a current density of about 20 mA cm⁻² were found to be satisfactory and required a polishing time of about 15 min. The specimens were examined in a Siemens Elmiskop 1 microscope operated at 80 kV.

Fig 1a shows a sub grain boundary in a specimen prepared from the as rolled foil. The dislocation density within the sub grains is surprisingly low and it is not yet clear whether this is due to low temperature recovery processes or whether the electrolytic thinning technique is selecting regions of the specimen that are not typical of the whole. So far neither dislocation loops nor dislocation pile ups have been observed.

Specimens which were annealed at a high temperature before electrolytic thinning have also been studied. Fig 1b shows a specimen which was annealed for 1 hr at 1,400°C in vacuum. The dislocations have formed up into a tangled network similar to those already observed in iron. An intermediate stage in the formation of networks is shown in Fig 1c which shows a specimen annealed for 1 hr at 950°C. In this case some of the dislocations have a characteristic zig zag shape suggesting that they have started to move but have been pinned down at various points along their lengths presumably by impurity atoms.

This work is being extended to include a study of deformation processes in fully annealed specimens and also the effects of neutron irradiation damage.

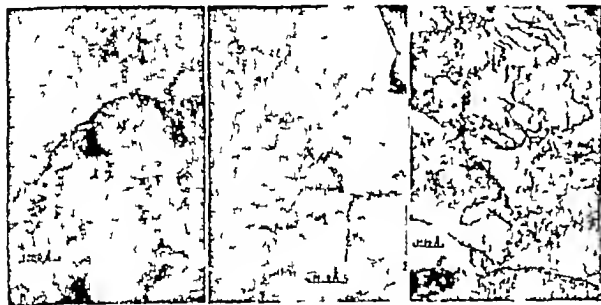


Fig 1. a. A sub-boundary in a rolled and electrolytically thinned molybdenum foil ($\times 77,000$). b. Dislocation networks in molybdenum formed by annealing a rolled foil for 1 hr at 1,400°C in vacuum ($\times 67,000$). c. Zig zag dislocations in a specimen which was annealed for 1 hr at 950°C in vacuum after rolling ($\times 60,000$).

We are indebted to Prof J. G. Ball for his advice and encouragement, to the Central Electricity Generating Board for a research bursary (J. F. K.) and the ICI Research Fellowships Committee of the University of London for the award of an ICI Fellowship (A. A. J.).

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CHEMISTRY

'Eddy' Diffusion in Chromatography

Among the various diffusion and kinetic factors which are responsible for smearing chromatographic zones, the effect known as 'eddy' diffusion has been subject to the most controversy. Its contribution to the height equivalent to a theoretical plate (H) is usually assumed to depend only upon the packing of a column and to be independent of the velocity of flow. This assumption may be questioned by virtue of recent experimental work in chromatography.¹⁻³ An equation will be derived here which predicts 'eddy' diffusion to be dependent on velocity. This will be compared to the existing experimental evidence.

The mathematical difficulties connected with a rigorous treatment of flow in porous media make an approximate theory necessary. While the theory outlined is perhaps over-simplified, it is doubtful if significant gain could be made short of a rigorous solution. Beran⁴ has approached the problem rigorously, but did not arrive at my principle result (equation 7).

'Eddy' diffusion is due to the irregularity of stream paths in a porous medium.⁵ The velocity along a given stream line will persist for a distance of the order of d_p (particle diameter), after which a new velocity differing by about v (the average velocity) from the original will be randomly acquired. The process is analogous to a random walk or flight, in which molecules within the stream paths stop back and forward with respect to the average velocity.

In addition to the velocity fluctuations within a stream path, a molecule is able to alter its velocity by diffusing laterally nearby stream paths. Such an effect is found with capillary columns.⁶ The combined influence of velocity fluctuations due to following and due to crossing stream lines will now be established.

The diffusion coefficient due to the above processes assumed as a random walk is:

$$D = \frac{l^2 n}{2} = \frac{v^2}{2n} \quad (1)$$

where the length of step, l , is the average distance travelled in 1 sec divided by the number, n , of steps per sec, $l = v/n$. The number, n , is the sum of the number due to the two independent processes mentioned above. In the first instance we assume that a stream path must proceed a distance $2d_p$ to complete a step.

$$n_1 = \frac{v}{2d_p} \quad (2)$$

In the second instance we assume that diffusion must take a molecule the distance βd_p to complete a step. The values of λ and β are expected to be of the order of unity, while changing slightly with a change in packing.

¹ D. G. Brundage and J. N. Pittling, *Adv. Mol. Sci.*, 7, 101 (1959).

² M. E. Lean, reported by N. P. Allen, *J. Iron and Steel Inst.*, 191 (1959).

³ W. Follman, *Phys. Rev.*, 103, 1588 (1956).

$$n_2 = \frac{2D_I}{\beta^2 d_p^2} \quad (3)$$

The diffusion coefficient of solute molecules in the mobile phase is D_I . Using the expression $n = n_1 + n_2$ in equation (1) we obtain

$$D = \frac{v^2}{v/\lambda d_p + 4D_I/\beta^2 d_p^2} \quad (4)$$

If the molecule is retained by adsorption or desorption during a fraction $(1 - R)$ of the time, D is correspondingly reduced. The value of H in terms of D is $H = 2D/Rv$. The expression for H is consequently found as

$$H = \frac{2\lambda d_p}{1 + 4D_I/\beta^2 d_p^2} \quad (5)$$

This, of course, is the contribution to H due only to these effects. The full expression for H also has a contribution from ordinary molecular diffusion and kinetic effects. In Fig. 1 H is plotted as a function of v . At the velocity $v_{1/2} = 4\lambda D_I/\beta^2 d_p$, H is one-half its maximum value.

At low velocities of flow, H becomes proportional to the velocity. This limiting value of H is identical in form with that obtained by Golay⁶ for capillary columns. It is exactly equal if we let $\beta d_p = r_0/\sqrt{12}$, where r_0 is the radius of the capillary. This fact may be of some use in estimating β . At high velocities $H = 2\lambda d_p$ and is independent of velocity. This expression is identical with that used in the van Deemter equation for 'eddy' diffusion. In gas chromatography, where the greatest refinements have been made, the transition velocity $v_{1/2}$ will be somewhere in the neighbourhood of 10–100 cm/sec. This is assuming $4D_I/\beta^2 = 10$, $D_I = 0.1$ cm²/sec and $d_p = 0.05$ cm. Due to the approximations, the result 10–100 cm/sec must be regarded only as an indication of where to look for the transition. This velocity, of course, is in the range where the performance of most columns is an optimum.

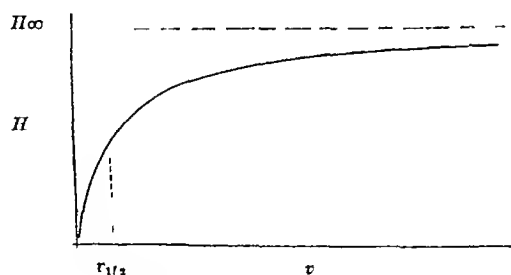


Fig. 1 Variation of theoretical plate height with velocity

Evidence which bears on these effects is indirect and not conclusive. Glueckauf³, assuming $H = 2\lambda d_p$, plotted λ versus velocity of flow for radioactive hydrogen iodide washed by an acidified solution over glass beads of diameter about 0.05 cm. The ordinate and abscissa of his graph vary only by a scale factor from Fig. 1. The two graphs are similar, with a rapid drop at low velocities. The values of $v_{1/2}$ estimated from these curves are of the correct order, assuming $D_I = 10^{-5}$ cm²/sec. In a later experiment⁷, in which krypton-85 was eluted with hydrogen, methane, oxygen and sulphur dioxide, no evidence was found for a variation of 'eddy' diffusion. However, if my equation 5 is substituted for A , curves are obtained which bend slightly away from the $1/v$ axis. The results presented seem to confirm this trend.

An anomalous result concerning 'eddy' diffusion was reported by Bohemen and Purnell.¹ The 'eddy' diffusion term was found to be negative in a number of cases, notably those with small particle size down to about 0.01 cm. This result would be found if one were in the low-velocity domain, and further, one is shifted towards this condition by smaller particle sizes.

In a different experiment performed by Bohemen and Purnell, hydrogen and nitrogen were compared as carrier gases. If 'eddy' diffusion were constant, the difference in plate height, $H_{H_2} - H_{N_2}$, would be described by an equation which allows only for molecular diffusion.

$$\Delta H = H_{H_2} - H_{N_2} = \frac{a}{v} (D_{H_2} - D_{N_2}) \quad (6)$$

plotting experimental values of ΔH against $1/v$ yielded a curved line intercepting the $1/v$ axis rather than a straight line through the origin. If it were assumed that the low-velocity form of equation 5 is valid, the equation for ΔH should read

$$\Delta H = \frac{a}{v} (D_{H_2} - D_{N_2}) + bv \left(\frac{1}{D_{H_2}} - \frac{1}{D_{N_2}} \right) \quad (7)$$

This equation does yield a line curved into the $1/v$ axis. Both a and b are constants that can be identified by use of the appropriate equations.

Further results reported by Littlewood² indicate that H is small or even negative. Similar results have been obtained in this laboratory. However, a number of authors, such as Keulemans and Kwantes⁸, find no indication of abnormally small λ values.

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¹ Bohemen, J., and Purnell, J. H., "Gas Chromatography", 6, edit D. H. Desty, (Butterworth, London, 1958).

² Littlewood, A. B., *ibid.*, 23, 35.

³ Glueckauf, E., "Vapor Phase Chromatography", 20, edit D. H. Desty (Butterworth, London, 1957).

⁴ Beran, M. J., *J. Chem. Phys.*, 27, 270 (1957).

⁵ Giddings, J. C., *J. Chem. Educ.*, 35, 588 (1958).

⁶ Golay, M. J. E., "Gas Chromatography", 36, edit D. H. Desty (Butterworth, London, 1958).

⁷ Glueckauf, E., *ibid.*, 33.

⁸ Keulemans, A. J. M., and Kwantes, A., "Vapor Phase Chromatography", 15, edit D. H. Desty (Butterworth, London).

Atomic Weight of Silver

WHILE trying to improve the thermal ionization efficiency of certain elements evaporated from mass spectrometer solid sources, we have had occasion to measure the ratio silver-107 to silver-109, the accepted value of which is 1.055 ± 0.003 due to White and Cameron¹⁻³. Our results do not agree with this value, but rather with the value of 1.0825 given by Hess, Marshall and Urey⁴, and also with an earlier value given by Paul⁵.

For our experiments, we have used four samples of silver, the first was of analytical reagent grade, the second was from bulk silver hallmarked in 1959, the third was of bulk silver hallmarked in 1899, and the fourth was of bulk silver hallmarked in 1791, and we have detected no differences between the ratio silver-107 to silver-109 found in these samples. We have used two mass-spectrometers in this work, the first is a 6-in. radius, 60° magnetic deflexion

machine, and using this machine and the analytical reagent silver the ratio silver 107 to silver 109 was first found to differ from the accepted value¹⁻³. For greater convenience and accuracy the rest of the work was carried out using a Metropolitan Vickers MS 5 30 cm radius, 90° magnet deflection machine. In no case has more than 20 μ m of silver been applied to the ion source filament, and measurements have been conducted on beams of up to 10⁻¹⁰ amp. We have sought for mass discrimination in the ion emission, and have found that this becomes observable only when more than 90 per cent of the sample has been evaporated, and its effect is negligible on the ratio found early in the life of the sample. In Table 1 our results are compared with previous values together with the calculated atomic weight corresponding to each value.

Table 1 RATIO OF SILVER 107 TO SILVER 109 IN NATURAL SILVER

| Author | Ratio silver-107/silver 109 with standard deviation | Chemical atomic weight* |
|--|---|-------------------------|
| Paul (ref. 5) | 1.090 | 107.871 |
| White and Cameron (ref. 1) | 1.055 \pm 0.003† | 107.883 |
| Hess, Marshall and Urey (ref. 2) (4 samples 619 spectra) | 1.0325 \pm 0.0018* | 107.870 |
| Present work | | |
| First machine (2 samples, 53 spectra) | 1.084 \pm 0.002 | 107.893 |
| Second machine (4 samples 420 spectra) | 1.0840 \pm 0.0007†† | |

* Assuming the ratio physical scale/chemical scale = 1.000275 and atomic masses given by Duckworth (ref. 6).

† White and Cameron do not claim better than 1 per cent accuracy (ref. 1).

* Calculated from the results of four samples given in ref. 4 assuming mean deviation 0.03% and standard deviation 0.01%.

†† Calculated from the combined data on four samples of silver.

Hess, Marshall and Urey concluded that their results must have been inaccurate because they did not agree with those of White and Cameron, whose value was concordant with a chemically determined atomic weight of 107.880. This last figure is, however, still subject to dispute, since it involves a nephelometric end point (ref. 7). Our results are consistent with those of Hess et al. within the errors quoted, and we consider it unlikely that the discrepancy between our value and that of White and Cameron could be accounted for by mass discrimination in our instruments.

We conclude that the atomic weight of silver is 107.898 \pm 0.001 (O = 16.0000) based on the mean of the values found in the present work.

A more detailed account of this work will be published elsewhere.

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BIOCHEMISTRY

Direct Spectroscopic Examination of Electrophoretic Zones in Agar Gel

ELECTROPHORESIS in agar gel as described by Robinson et al.¹, has been found to be a valuable analytical method in the study of haemoglobin variants. We are now able to extend its scope by carrying out spectroscopic examination of the separate zones directly without extraction from the gel. The value of this technique lies, in particular in the fact that agar electrophoresis can be carried out with minute samples, and also that components present in proportions too small to make their isolation feasible can be examined. At the same time, the difficulty of extracting proteins from the gel is circumvented.

Two methods have been employed for the spectroscopic examination of the zones. In the first of these the logarithmic cam spectrograph² is used; this has the great advantage that non-selective background scattering or absorption does not interfere with the location of fine-structure bands. This method was first used in the study of haemoglobin by Jope³ who found a difference between the positions of the tryptophan fine-structure band of the foetal and normal adult pigments. The method has been used for the analysis^{4, 5} of samples containing haemoglobin F.

The procedure used for the examination of a zone in agar is to cut out and transfer it to a strip of quartz with a small spatula. The agar adheres to the quartz, which is mounted in front of the spectrograph slit. The spectrograms so obtained are indistinguishable from those using a haemoglobin solution. In the case of faint zones the effective path length may be increased by folding the strip on itself.

A number of useful results have been obtained in this way. In the first place we have found that zones attributed to haemoglobin F in ion exchange chromatography^{6, 7} of cord blood haemoglobin have invariably been contaminated with haemoglobin A. It is therefore of interest to establish whether the fractionation of haemoglobin F from other haemoglobins in agar is complete. Examination of the leading zone shows a tryptophan band at 280.6-289.7 m μ , which corresponds to pure haemoglobin F. Similarly, the slower moving zone from cord bloods has its tryptophan band at the wavelength (291.0 m μ) corresponding to pure haemoglobin A. It therefore appears that agar gel electrophoresis does indeed give complete separation of haemoglobins F and A. We have also used the same method to examine adult and foetal monkey haemoglobins and the haemoglobins of other species, as well as some other proteins.

The second spectroscopic method which has been developed is the examination of zones directly in a spectrophotometer. The desired zones are removed as before and mounted on strips of quartz which fit in the cell carriage of the instrument. Measurements are carried out against a control consisting of a piece of clear agar taken from the same layer. For measurements in the visible region the exit beam from the monochromator is allowed to fall on the most intense part of the zone, and for the Soret and ultra violet regions the fainter trailing edge is used. Correct positioning is facilitated by opening the slit of the instrument at a wave length setting in the visible when the incident beam can be seen on the agar strip.

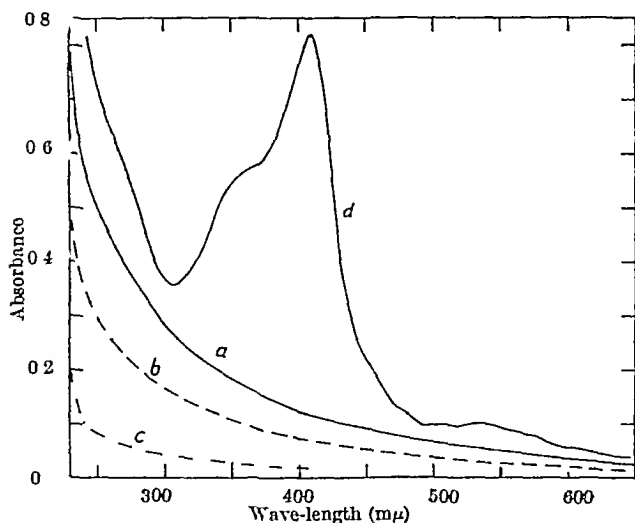


Fig 1 (a) Absorbance (optical density) of 1 mm. layer of 1 per cent agar gel supported on a quartz strip, against a quartz strip as control. The dots indicate the maximum differences in absorbance between pairs of gel samples (see text)

(b) As (a), but with purified agar (see text)

(c) As (a), but dried film

(d) Absorption spectrum, measured in agar gel against an agar control, of a small, very fast-moving brown anodic zone, separated from an old hemoglobin sample. This is presumably identical with a fast-moving anodic component frequently observed in paper electrophoresis of old hemoglobin samples at high pH

The spectrum of a typical sample of agar gel from an electrophoretic layer is shown in Fig 1, curve a. Curve b shows the spectrum of a similar layer prepared from the same agar sample, purified by the procedure described by Bousard and Perrin⁸. Some decrease in background absorption results, but since the matching of agar blanks was not significantly affected, this treatment is unnecessary. Curve c shows the absorption of an agar film which has been allowed to dry down on the quartz strip. It is evident from this that most of the background absorption in the gel above 250 mμ arises from scattering. The absence of specific absorption follows from the known structure of agar.

The matching of two agar strips from the same gel was investigated over the range 250–600 mμ, using 12 pairs of strips from three different batches of agar, as well as a sample purified from one of them as described. The maximum absorbance differences decrease smoothly from ± 0.03 at 250 mμ to ± 0.013 at 600 mμ, the mean differences are about one-half the maximum values.

The loss in accuracy in absorbance readings resulting from background absorption differences between the sample and control strips is not sufficient to vitiate the measurement of adequate spectra (Fig 1), and even absolute measurements, such as those required for the determination of haem-protein ratios⁵, can be made with a fair degree of precision. In a 'Unicam' SP 500 spectrophotometer it was never found necessary to exceed a slit width of 0.4 mm at 250 mμ. Spectroscopy of zones in the dried gel is also possible. If the agar is allowed to dry in the cold, the hemoglobin appears to remain in its native state and good spectra may be obtained, these observations are being further investigated.

The technique described may be capable of extension to other fields. It commends itself in virtue of its simplicity and the very small quantities of material which are required. Many proteins can be characterized, and possibly identified, by the position of their ultra-violet fine-structure bands, which are due to the presence of tryptophan, tyrosine and phenylalanine

residues⁹. The possibility is thus raised of direct characterization of components of such biological fluids, etc., as can be fractionated in agar^{10,11}.

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Failure to Recover Infective 'Ribonucleic Acid' from Myxovirus Preparations

It now seems clear that preparations of infective 'ribonucleic acid' can be obtained from crude preparations of many animal viruses, although Colter *et al.* have reported failure with Bunyamwera virus preparations¹. The technique used in most cases is similar to the treatment introduced by Gierer and Schramm², namely, exposure of the virus preparation to concentrated phenol. Recognition that the infectivity of the product of phenol treatment is due to a component other than intact virus is based on such criteria as susceptibility to ribonucleases, stability in different media and rate of sedimentation in the ultracentrifuge^{1,2}.

There is general agreement that the influenza virus particle contains ribonucleic acid but no deoxyribonucleic acid³, and it has been calculated that the amount of ribonucleic acid per influenza virus particle is about the same as is present in particles of polio virus and in those plant viruses which have been adequately studied⁴. It seemed worth while to try to obtain infective 'ribonucleic acid' from influenza virus preparations although it was realized that the influenza virus particle is more complex, both chemically and structurally, than are particles of other viruses such as tobacco mosaic or poliomyelitis. For this purpose, we used a method of phenol treatment which, when applied to crude preparations of Murray Valley encephalitis virus, yielded high titres of infective 'ribonucleic acid'¹. However, the following experiments with influenza virus preparations yielded negative results.

Preparations of different strains of myxovirus, namely MEL, Neuro WS and WSE (influenza A), LEE (influenza B) and Newcastle disease virus (Victorian strain) were obtained in the form of high titre extracts ($E.I.D. 50 = 10^4$ – 10^5) of infected chick embryo lung or infected mouse brain. Phenol treatment of these extracts did not yield a product infective for mouse brain or, by various routes, for the chick embryo.

Phenol treatment of either purified virus⁵ alone ($E.I.D. 50 = 10^{11}$) or of purified virus added to extracts of chick embryo lungs infected with the same strain did not yield an infective product.

In order to see whether any biological activity less than complete infectivity was present in the extracted ribonucleic acid, attempts were made to show recombination on the chorion allantoic membrane of the chick embryo. Several authors* have shown that virus inactivated by heat or by irradiation with ultra violet can recombine with an appropriate active virus. In the present experiments, ribonucleic acid extracted from *WSE*, a strain pathogenic for the chick embryo, was inoculated on to the chorion allantoic membrane with intact *MEL* or *WIS* virus, strains which are non pathogenic for the chick embryo. Recombination was not observed. In other experiments a preparation of ribonucleic acid derived from mouse brain infected with *Neuro WIS* failed to show interference in the mouse brain when the mice were challenged with active *Neuro WIS* virus.

The phenol treatment applied did not extract all ribonucleic acid from purified virus. Both extracted and unextracted ribonucleic acid were found to have similar base ratios.

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Production of Serum Albumin and of Globulins by Chick Mesenchymal Tissue and by HeLa Tumour Tissue in Culture

A technique has been described for establishing the autonomous production of well-defined soluble proteins by tissue in culture^{1,2}. The tissue is grown in a medium containing a radioactive amino acid. After incubation, the tissue is homogenized with the medium, the homogenate centrifuged, inactive amino acid added as a hold back carrier, and the proteins in the supernatant separated from all compounds of low molecular weight, including the radioactive amino-acid by ultrafiltration under pressure (autogon). The different proteins are then separated, burnt to carbon dioxide and the radioactivity of the carbon is determined with the very sensitive gas Geiger counter^{3,4}. Radioactivity of the carbon dioxide indicates that the amino-acid has been incorporated into the protein, that is, that proteins have been synthesized from the amino acids by the tissue.

We have now shown that both chick mesenchymal tissue (taken from the legs of embryos 8-10 days old) and human cervix HeLa carcinoma tissue make serum albumin. The mesenchymal tissue was grown after trypsinization of the explants, as a monolayer^{5,6} in roller tubes at 37°C in a medium consisting of chicken fibroblasts was observed by Landsteiner and 4 per cent chick embryo extract, 40 per cent human

ascitic fluid and 56 per cent buffered isotonic salt solution (Goy). The initial number of cells was about 6×10^4 per roller tube. On the third day after the preparation of the monolayer, about $0.5 \mu\text{c}$ ($\sim 10^4$ disintegrations per min) of generally labelled L-tyrosine were added to the medium in each tube and incubation continued for two days. After homogenization, ultrafiltration and thorough washing, the serum proteins were separated by precipitation with alcohol in the cold⁷, and the purity of the resulting fractions checked by electrophoresis of a small part in starch gel and staining⁸. Finally, the bulk of the serum albumin, dissolved in physiological saline, was mixed with antiserum against serum albumin (obtained from rabbits), and the precipitate and the supernatant separately burnt and measured for radioactivity.

After precipitation with rabbit antiserum containing antibody against human serum albumin (anti *HSA*), 94 per cent of the total radioactivity of 0,460 d.p.m. was found in the supernatant fluid in another aliquot after precipitation with rabbit antiserum against chick serum albumin (anti *CSA*). 98 per cent of the radioactivity of 0,110 d.p.m. was found in the precipitate. In the former case the addition of a non radioactive carrier was unnecessary, because of the presence of large amounts of human serum albumin from the nutrient medium, but in the latter case non radioactive chick serum albumin was added to obtain optimal precipitation.

In analogous experiments with the human tumour tissue (here the ascitic fluid in the medium was replaced by human cord serum), the bulk (84 per cent) of the radiocarbon (3,620 d.p.m. in all) went into the precipitate with anti *HSA*, while only 8 per cent of the radiocarbon (3,310 d.p.m.) was found in the precipitate with anti *CSA*. Thus the newly formed serum albumin from the chick tissue and from the human tissue are clearly distinguished. In blank experiments nutrient medium alone without tissue was incubated with the radioactive amino acid: in this case no radioactivity at all was found in the soluble proteins after ultrafiltration and thorough washing.

The α -peptidic linkage of the amino acid in the serum albumin was confirmed by the ninhydrin test⁹. Ninhydrin removes carbon dioxide from those carboxyl groups which adjoin free amino groups. After incubation of mesenchymal tissue with medium containing D,L-leucine labelled at its carboxyl group, isolation of the serum albumin and treatment with ninhydrin, only 4 per cent of the total radiocarbon (2,430 d.p.m.) of the serum albumin was found in the carbon dioxide released, however, if the serum albumin was hydrolysed with hydrochloric acid before treatment with ninhydrin, 85 per cent of the radiocarbon (3,700 d.p.m.) was found in the carbon dioxide.

The *HIM* tissue strain derived from human liver (supplied by Dr I Leslie, Belfast) was also shown, by radioimmunochemistry, to produce serum albumin. Further, radioactive leucine was found to be incorporated in the fractions of α globulin and of $(\beta + \gamma)$ globulin of chick embryo mesenchymal tissue and of HeLa tissue. This was established by determination of the radiocarbon in the proteins separated by precipitation with alcohol and checked for purity by electrophoresis, though no immunochemistry was carried out with these samples.

The production of proteins identical with or closely related to, serum proteins in cultures of

Parker¹⁰, but no detailed assignments were possible with the techniques then available. The extra-hepatic synthesis of serum albumin is of especial interest. In the case of HeLa tissue it is likely that the parent epithelial tissue was capable of making serum albumin, and that this capacity was conserved in cancerization. A full report of our experiments will be published elsewhere. The experiments on the γ -globulins are being continued.

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The Behaviour of Haptoglobin during Routine Fractionation

HAPToglobulin is a very interesting plasma protein, because of its specific binding capacity for haemoglobin and the existence of different genetically determined types.

Jayle *et al.*¹ reported the isolation of haptoglobin from the urine of a nephrotic child and from plasma of a haptoglobin-rich individual² by a technique based on precipitation with ammonium sulphate. Laurell³ has recently published a method for preparing haptoglobin from ascitic fluid. Apparently no attempt has been made to prepare haptoglobin during routine fractionation of human plasma. Haptoglobin from ordinary pooled plasma would represent a mixture of the known types of haptoglobin. Mixed haptoglobin would thus be unsuitable for genetic research, but might be used for studies concerning the haemoglobin-binding capacity. But a method allowing the preparation of haptoglobin from pooled plasma would, with slight modifications due to differences in solubility, be suitable for obtaining haptoglobin from a single, well-defined plasma group. However, the additional controls necessary for pooling plasma belonging to a single haptoglobin group would only be acceptable, if a good technique for obtaining haptoglobin was available.

Haptoglobin present in the serum is revealed by paper-electrophoresis after addition of haemoglobin. The complex migrates as an α_2 -globulin. This complex has peroxidase activity. Haptoglobin alone has no such activity, haemoglobin a smaller one than the complex. Haemoglobin migrates as a β -globulin, in the presence of the classical Michaelis-buffer at pH 8.6. Heremans⁴ has proposed a phosphate-buffer of pH 6.8 for the study of haptoglobin-haemoglobin complexes. No migration occurs with haemoglobin alone at pH 6.8, while the complex migrates normally.

This technique permits differentiation between excess haemoglobin and slightly altered haptoglobin-haemoglobin complexes which sometimes have the mobility of a β_1 -globulin. Peroxidase activity is conclusively demonstrated by oxidation of benzidine or anisidine in the presence of hydrogen peroxide.

By both these methods we studied the distribution of haptoglobin in the different fractions resulting from the alcohol fractionation of human plasma (a slightly modified Nitschmann technique⁵).

The only fraction containing haptoglobin in considerable quantities is fraction IV, obtained at pH 5.8 with 33 per cent alcohol. This fraction can be subfractionated by rivanol as recently described⁶. Haptoglobin is still present in the supernatant after the precipitation of ceruloplasmin.

The precipitate obtained from this supernatant by addition of alcohol (35 per cent) at pH 5.9 contains siderophilin (main component), haptoglobin and a small quantity of albumin. The albumin can be removed by rivanol at alkaline pH. Haptoglobin and siderophilin can then be separated by alcohol precipitation at pH 4.4-4.6.

Thus it is possible to prepare haptoglobin together with other plasma proteins during routine fractionation, and pooled plasma obtained from a single haptoglobin group would not be wasted because of the preparation of one minor component of plasma proteins.

Further details will be published elsewhere.

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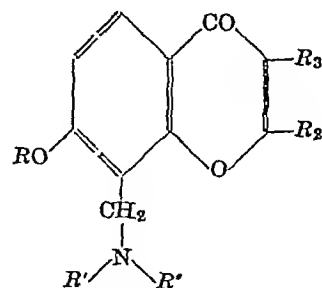
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N-Substituted 7-Methoxy-8-Aminomethylchromones and Flavones: New Brain-Stem Stimulants

THE pharmacological screening of various chromone and flavone derivatives has led to the discovery of a new class of brain-stem stimulants, the N-substituted aminomethyl derivatives of these two nuclei, with the following structure



where $R = \text{H}$ or alkyl radical,
 $R' = R'' = \text{H}$ or alkyl radicals,
 R' and R'' can be a part of a cycle,
 $R_2 = \text{H}$ or alkyl or aryl radical,
 $R_3 = \text{H}$ or alkyl radical

The 3 methyl 7 methoxy 8 dimethylaminomethyl flavone (Rec 7 0267) seems to be the most interesting compound, its brain-stem stimulating activity is even higher than that of picrotoxin, the most potent brain stem excitator so far known.

The respiratory stimulating effect of Rec. 7 0267 in normal animals as well as in animals depressed with morphine, is approximately three times higher than that of picrotoxin, 10-20 times higher than that of bemegride and about 200 times higher than that of metrazol.

The brain stem stimulating activity of the compound as measured in animals poisoned by barbiturates, in which the antidotal action of the drug prevents the animals from death is interesting. By administering 2 mgm/kgm of Rec 7 0267 to mice injected with an LD_{50} of nembutal, 90 per cent of the animals survived, in other words 95 per cent of the animals has been saved by the treatment with the new compound.

The minimal active dose ($P = 0.05$) of Rec 7 0267 is 2-3 times lower than that of picrotoxin, 10 times lower than that of bemegride and 27 times lower than that of metrazol.

The safety index (ratio between LD_{50} s and the minimal active dose) was found to be 1.6 times higher than that of bemegride and 2.0 times higher than that of metrazol.

Notwithstanding the brain-stem stimulating activity at therapeutic doses Rec 7 0267 does not show any particular effects on the brain cortex.

The relationships between the pharmacological activity and the chemical structure are significant: the oxygen function (methoxy or hydroxy groups) seems to play a fundamental part in determining the type of respiratory as well as circulatory analeptic activity.

It has been observed that the methoxy compounds act almost exclusively on the respiratory centre while the corresponding hydroxy compounds display a stimulation also on the vasomotor centre causing besides hyperpnea, a prolonged increase of arterial blood pressure.

The optimum position of the aminomethyl chain seems to be 8. It has already been shown¹ that the 6 aminomethylchromones and flavones N-substituted, devoid of the oxygen function in the 7 position display only very slight analeptic activity while acting as papaverine like antispasmodics.

In the specific case of the flavone derivatives simultaneous displacement of the basic chain and of methoxy group from 8 to 4,3 positions causes a considerable loss of activity. The presence of alkyl groups at the nitrogen seems also to be fundamental since the unsubstituted ones are inactive.

The activity increases in marked degree in the monosubstituted derivatives, the N-methylamino methyl compounds, and reaches a maximum for the compounds with two substituents at the nitrogen (also when the substituents are a part of a cycle).

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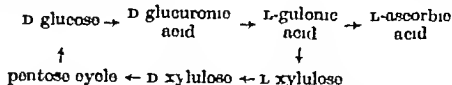
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Stimulatory Effect of Foreign Compounds on Ascorbic Acid Biosynthesis and on Drug-Metabolizing Enzymes

PREVIOUS studies in rats have shown that drugs such as Chloretone¹, barbital, phenobarbital and amino pyrine can stimulate the biosynthesis of L-ascorbic acid from glucose through the glucuronic acid pathway²⁻³ as follows



Evidence for this has come from the observations that these drugs markedly increase the urinary excretion of L-ascorbic acid and that they stimulate the conversion of glucose-1-¹⁴C to labelled D glucuronic acid, L-gulonic acid and L-ascorbic acid²⁻³. In the present study the following compounds were also found to be potent in stimulating the biosynthesis of L-ascorbic acid: the antirheumatic drug phenylbutazone, the muscular relaxant orphenadrine (2-dimethylaminoethyl 2-methyl benzhydryl ether), and the carcinogenic hydrocarbons 3-methylcholanthrene, 1,2,5,6-diben-zanthrone and 3,4-benzpyrene. Phenylbutazone and orphenadrine in doses of 20-50 mgm/day for 4 days to adult rats produced about a 20 fold increase in L-ascorbic acid excretion. The striking effect of a single 10 mgm dose of 3-methylcholanthrene on the urinary excretion of the vitamin is shown in Fig. 1. By 6 days

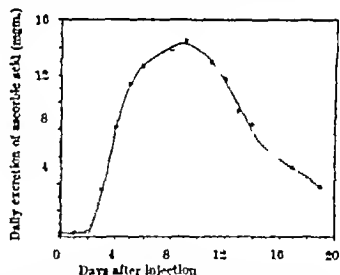


Fig. 1 Stimulation of L-ascorbic acid excretion by 3-methylcholanthrene. A male Wistar rat (250 gm) was injected intraperitoneally with a single 10 mgm dose of 3-methylcholanthrene in 0.5 ml corn oil and the daily urinary excretion of L-ascorbic acid was measured by titration with 2,6-dichlorophenolindophenol dye. A milk diet free of vitamin C was used in this study (ref. 2). Similar doses of 1,2,5,6-diben-zanthrone or 3,4-benzpyrene to rats (250-300 gm.) resulted in a 20- to 100-fold increase in L-ascorbic acid excretion by 5 days.

after administration the urinary excretion was 50-75 times greater than the control value and in fact during the 19-day period about 140 mgm of L-ascorbic acid was excreted. This represents a minimum value for the total L-ascorbic acid synthesized since the vitamin is extensively metabolized in the rat⁴.

The observation that the carcinogenic hydrocarbons are potent stimulators of L-ascorbic acid biosynthesis is of particular interest since these compounds are also known to be extremely potent in inducing the synthesis of several liver microsomal enzymes which metabolize foreign compounds^{5,6}. These biocatalysts are closely related to a variety of drug-metabolizing enzymes in liver microsomes⁷. The marked effect of other compounds which stimulate L-ascorbic acid biosynthesis to increase the activity of one of these

¹ Da Re, P., Verlicchi, L., and Setnikar, I. (in the press)

microsomal enzymes, azo dye demethylase, is shown in Table 1. The striking effectiveness of phenobarbital

Table 1 INCREASED ACTIVITY OF AZO DYE DEMETHYLASE CAUSED BY THE ADMINISTRATION OF VARIOUS FOREIGN COMPOUNDS

| Compound | Dose mgm./day | Demethylase activity |
|-----------------------|------------------|----------------------|
| Control | — | 5 |
| Chloretone | 4.3 | 15 |
| Barbital | 5.0 | 21 |
| Phenobarbital | 1.0 | 25 |
| Thiopental | 2.0 | 17 |
| Aminopyrine | 11.2 | 13 |
| Phenylbutazone | 7.5 | 14 |
| Orphenadrine | 3.8 | 12 |
| 3-Methylcholanthrene* | 0.1 | 15 |

Male Holtzman rats (40–50 gm.) were maintained on a synthetic diet (ref. 7) and were injected twice daily for 4 days. The animals were killed on the fifth day and the demethylation of 3-methyl-4-monomethylaminoazobenzene was determined in fortified whole liver homogenate as previously described (ref. 7). The demethylase activity represents the $\mu\text{gm.}$ of 3-methyl-4-aminoazobenzene formed per 50 mgm. liver per 12 minute incubation. Each enzyme activity represents pooled livers from at least 4 animals. The variation in enzyme activity of controls was less than $\pm 1 \mu\text{gm.}$ in 10 experiments.

* These animals were killed 24 hours after a single injection.

to stimulate the activity of this demethylase is demonstrated in Fig. 2. Further experiments were

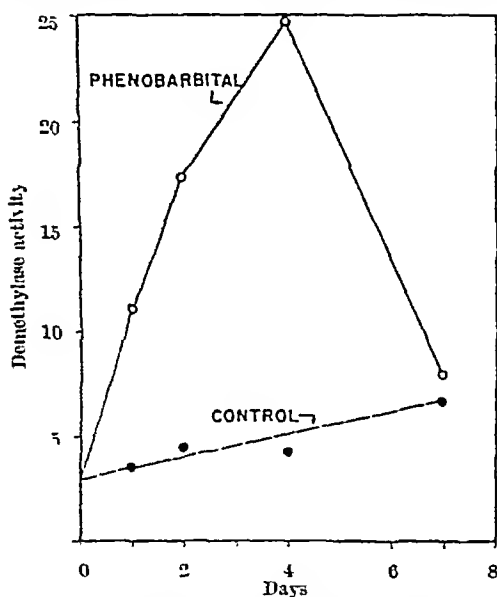


Fig. 2 Effect of phenobarbital on the activity of azo dye demethylase. Male Holtzman rats (40–50 gm.) were fed a synthetic diet (ref. 7) and were injected intraperitoneally with 5 mgm. of phenobarbital. The animals were killed at intervals after drug administration and the demethylation of 3-methyl-4-monomethylaminoazobenzene by fortified whole liver homogenate was determined (ref. 7). The demethylase activity represents $\mu\text{gm.}$ of 3-methyl-4-aminoazobenzene formed per 50 mgm. liver per 12 minutes incubation. Each point represents the values obtained on 4 animals.

carried out to test the activity of barbiturates on other liver microsomal enzymes. The intraperitoneal administration of phenobarbital (3 mgm./day for 4 days) or barbital (7 mgm./day for 6 days) causes appreciable increases in the activities of the enzymes which reduce the azo linkage of aminoazo dyes and which hydroxylate 3,4-benzpyrene and zoxazolamine.

It is likely that phenobarbital and the other active drugs, like the polycyclic hydrocarbons, induce the synthesis of azo dye demethylase. The addition of phenobarbital *in vitro* to liver homogenates did not affect the activity of this enzyme. No evidence was found that activators or inhibitors caused the increased enzyme activity. Furthermore, pretreatment of the rat with ethionine, which has been used to inhibit induced enzyme synthesis, was found to block completely the effect of phenobarbital on demethylase activity and methionine prevents this inhibitory action of ethionine.

The results presented here show that foreign compounds differing widely in chemical structure and pharmacological activity have the dual property of stimulating the biosynthesis of L-ascorbic acid and of increasing the activity of certain drug-metabolizing enzymes in liver microsomes. The finding that the same compounds exert both actions suggests a possible relationship between these two responses. It is of particular interest that one of the most potent compound in each case is barbital, a drug which is not metabolized or conjugated but is excreted unchanged in the urine³. These effects may represent adaptive responses on the part of the body to foreign compounds by a mechanism which does not involve the adrenal gland^{3,7}. Further studies are now under way to elucidate the nature of these biochemical responses.

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Spectrophotofluorometric Assay of Griseofulvin

ALTHOUGH griseofulvin was isolated twenty years ago¹ its value as a systemic anti-fungal agent was not appreciated until 1958, when Gentles² reported that he had eradicated experimental ring-worm in guinea pigs by its use in oral treatment. Clinical reports^{3–5} that have appeared since have evoked considerable interest among dermatologists and seem to have justified Gentles' optimism.

We are currently studying the absorption, distribution and excretion of griseofulvin in laboratory animals and man, to facilitate these studies we have developed a simple and rapid spectrofluorometric assay. We give here the details of the assay and indicate briefly our findings to date.

A 1 per cent ethanolic solution containing 0.5 $\mu\text{gm.}$ griseofulvin/ml was scanned on a Farrand spectro photofluorometer. The spectra obtained are shown in Fig. 1. The activating spectrum contains two well defined peaks, one at 295 m μ and another at 335 m μ (uncorrected values). For assay purposes, an activating wave-length of 295 m μ and an analysing wave-length of 450 m μ were chosen. Choice of slit-widths depends on the characteristics of the photomultiplier tube. A 1 per cent ethanolic solution containing 0.05 $\mu\text{gm.}$ griseofulvin/ml fluoresces twice as strongly as 1 per cent ethanol, a full-scale deflection is obtained on the most sensitive range at a concentration of 0.5 $\mu\text{gm.}/\text{ml}$. The intensity of fluorescence increases linearly over the concentration range 0.05–0.5 $\mu\text{gm.}/\text{ml}$ and is independent of pH over the range 3–10. Below pH 3 the fluorescence decreases sharply. Temperature of the solution is important,

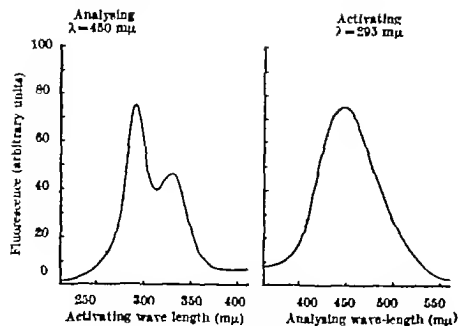


Fig. 1 Fluorescence spectra of griseofulvin

Because the fluorescence decreases with increasing temperature. Over the range 10–25° C the change is linear, and each degree rise results in 2.5 per cent less activity than at the lower temperature.

Before attempting any assay of griseofulvin by the method described, all glassware (syringes, flasks, shake tubes, pipettes, cuvettes, etc.) must be cleaned in chromic acid and rinsed with distilled water and 1 per cent ethanol. Detergents should be avoided. The final 1 per cent ethanol washings are checked on the spectrofluorometer before the apparatus can be considered suitable for use.

A small sample (1 ml or less) of blood, plasma, serum or urine is mixed with 1 ml of 1 per cent ethanol and shaken for 15 sec with 10 ml of other light ml of the other phase (total volume after shaking = 9.7 ml) are removed and evaporated to dryness. The residue is dissolved in 10 ml of 1 per cent ethanol, and the fluorescence of the solution is measured against a griseofulvin standard (0.5 μgm/ml) at the same temperature. Pre-dosage samples of blood, plasma, serum or urine, with and without added griseofulvin, are included in each set of assays. Blood, plasma and serum have similar blank values, which do not vary greatly between either individuals or species (rat, guinea pig, rabbit and man). Griseofulvin added to heparinized blood at concentrations ranging from 1 to 5 μgm/ml gave percentage recoveries averaging 90 ± S.E. 1.4 (25 assays). At 10 μgm/ml the average recovery fell to 84 per cent ± 1.1 (10 assays). Blank urine values differ greatly both between individuals and between samples taken from the same individual at different times. However, it is possible to overcome most difficulties by raising the pH of the urine to approximately 10 before extracting with ether. The mean percentage recovery of griseofulvin added to human urine over the concentration range 1–5 μgm/ml was 90 ± 2.9 (30 assays).

An experiment was conducted to test the agreement between microbiological and spectrofluorometric assay results. Three volunteers were given single oral doses of griseofulvin (0.5 gm), and serum levels were determined at intervals over the next twenty-four hours. The samples were assayed both microbiologically by Dr P. W. Mingleton and his colleagues using a *Microsporum canis* tube assay that they have developed in these laboratories and by the spectrofluorometric method. The results are compared in Fig. 2. The half-life during the decay period is approximately eight hours.

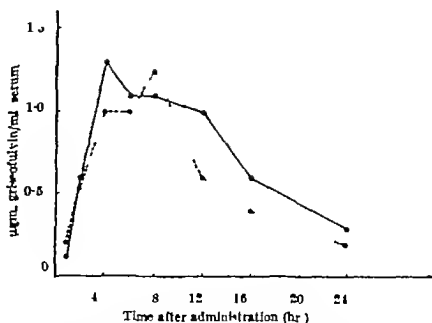


Fig. 2 Serum-levels of griseofulvin in man after single oral dose of 0.5 gm. —●— biological assay; —○— spectrofluorometric assay. Each value represents the group mean for three individuals.

To determine the effect of dosage on serum levels three groups of three volunteers were given single oral doses of 0.25, 1 or 2 gm. The serum levels which were determined spectrofluorometrically at 2, 5 and 9 hr are shown in Fig. 3. During the first

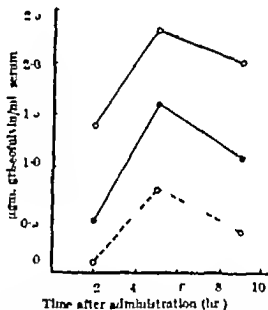


Fig. 3 Serum-levels in man after graded oral doses of griseofulvin. —○— 2 gm. per man; —●— 1 gm. per man; —○— 0.25 gm. per man. Each value is the group mean for three individuals.

8 hr after administration the average amount of griseofulvin found in the urine of the group dosed with 1 gm was 0.5 mgm and the corresponding value for those given 2 gm was 0.6 mgm.

The work described above continues and it is hoped to present further results for publication.

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Calcium Ions and the Permeability of Human Red Cells

It is well known that many tissues when placed in an electrolyte medium are profoundly affected by the presence or absence of calcium ions. This is also true of the red cells of the tortoise¹, of the snapping turtle² and probably of the red cells of certain fishes³⁻⁵, which in a calcium-free electrolyte medium become highly permeable to cations, and hence swell and rupture (haemolysis). The red cells of the frog, chicken and of *Mammalia*, however, are little affected by suspension in calcium-free sodium chloride solution, exchange of cations with the external medium being very slow, and haemolysis correspondingly delayed. Nevertheless dependence on calcium of the human red cell may be demonstrated after suitable treatment of the cells in conformity with earlier work by Maizels⁶ and Wilbrandt⁷. The former showed that human red cells became highly permeable to cations when placed in an electrolyte-free medium (for example, glucose), unless about 10 mM sodium or potassium chloride were present, while Wilbrandt found sodium and potassium chlorides to be less effective than the salts of the alkaline earths, though there was no specificity within this group, the actions of calcium, magnesium, strontium and barium being quantitatively similar.

The treatment of red cells used in the present investigation involves three stages, details of which are shown in Table 1. In stage 1 (depletion stage) red

Table 1 EFFECTS OF THE SALTS OF THE ALKALINE EARTHS ON THE PERMEABILITY OF MODIFIED HUMAN RED CELLS TO MONOVALENT CATIONS

| Additions | mM | Ratio of the cation flux per hour to the concentration difference between cells and the external medium | | |
|-------------------|-----|---|---------------|-------------|
| | | Sodium in | Potassium out | Lithium out |
| None | — | 0.31 | 0.28 | 0.44 |
| MgCl ₂ | 2.5 | 0.28 | 0.31 | 0.41 |
| SrCl ₂ | 2.5 | 0.25 | 0.25 | 0.35 |
| BaCl ₂ | 2.5 | 0.30 | 0.31 | 0.43 |
| CaCl ₂ | 2.5 | 0.04 | 0.06 | 0.07 |

Note. Cells were first incubated for 3 hr. at 37° C in lactose solution (6 per cent w/v), then for 1½ hr. in a solution of potassium and lithium chloride (70 mM of each), and finally transferred to sodium chloride solution (140 mM) for 1 hr. at 37° C. Additions of calcium chloride, magnesium chloride, etc. were made at the beginning of the last stage, during which cation exchanges were measured.

cells are incubated in lactose solution, which increases permeability twenty-fold. Natural sodium and potassium leak from the cells accompanied by water and the cells shrink. In stage 2 (cation replacement stage) the cells are transferred to an electrolyte medium, one containing a mixture of potassium and lithium chloride is suitable. Here, potassium chloride, lithium chloride and water enter the cells, and it would be possible to measure penetration-rates in this stage, were it not for the uncertainty in correcting for the considerable swelling which now occurs. Hence it is necessary to proceed to stage 3 (cation exchange stage) and transfer the cells (now containing potassium and lithium) to a different electrolyte medium, usually sodium chloride solution. In this stage potassium and lithium leave the cells, whilst sodium enters, changes in volume of the cells being slight. If to a series of such suspensions, chlorides of magnesium, strontium, barium or calcium are respectively added, cation penetration is rapid in the case of the first three, and slow in the presence of calcium. This is shown in Table 1 where permeability is expressed as the ratio of the cation flux per hour to the mean difference in concentration between cells and medium.

Maizels' and Wilbrandt's earlier observations suggest that if red cells are suspended in a solution of non-electrolyte and monovalent cations or certain divalent cations are added at once, then normal low cell permeability is maintained, and that in the absence of such cations low permeability is lost. The present observations show that once relative impermeability has been lost in this way, calcium alone can restore it. This may well be true of other cells, including the unfertilised egg of the sea-urchin which in sea-water is only slightly permeable to water, but becomes highly permeable in non-electrolyte media unless either calcium or magnesium chloride is added⁸. It is suggested that some substance is present in the red cell membrane which contributes to low permeability, that loss of this substance is prevented by various cations, but that replacement can only be effected by calcium. It is possible that the substance itself is a calcium compound, if so, it can only be present in trace amounts.

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Splenic Siderosis in Mice Treated with Dithiourethane

In an attempt to elucidate the mode of action of urethane (ethyl carbamate) as a carcinogen for mice, its dithio analogue (NH₂CSSC₂H₅) was prepared^{1,2} and a study was made of its lethal dose and general toxic effects before testing it for carcinogenicity. A report of the latter is in preparation. The short-term tests revealed an action of this compound whose significance is, at the moment, rather obscure.

CBA strain mice of both sexes were injected subcutaneously with 0.15 ml. of a 5 per cent solution of dithiourethane in arachis oil. After three or more weekly injections, a brown pigment in haematoxylin and eosin-stained sections of the spleen was seen in all cases. When, on a few occasions, stock outbred mice were used, the same phenomenon occurred. The pigment also appeared in unstained sections and was found to contain iron by the Prussian blue test. It was distributed in the macrophages of the perfollicular reticulo-endothelial tissue (Fig. 1). The spleens of mice injected with the solvent (arachis oil) alone, of mice treated with 0.2 ml. of a 5 per cent aqueous urethane solution for the same time and of untreated mice, all showed considerably smaller amounts of the pigment scattered throughout the spleen (Fig. 2). A number of other organs of the same mice were examined histologically as a routine in these tests, and no evidence of this pigment was ever found in liver, kidney, lung, axillary lymph node or testis. Nor was any seen in pancreas when, on occasion, a piece was accidentally included in the section with spleen.

In the long-term experiments, weekly injections were carried out for up to three months. The amount of pigment deposited in the spleen was found to be proportional to the number of treatments during that time. When treatment stopped the amount of pigment

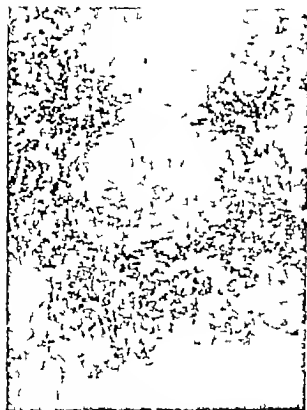


Fig. 1. Spleen of dithiourethane-treated mouse stained for iron (Prussian blue method $\times 55$)

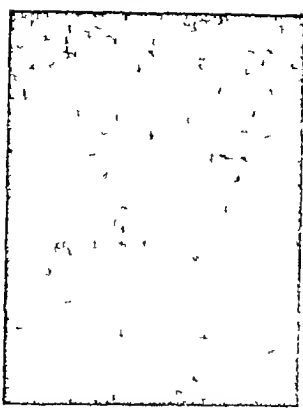


Fig. 2. Spleen of control mouse injected with the solvent (arachis oil) similarly stained ($\times 55$)

decreased slowly over the following three months when detectable amounts were still present. As the amount of siderosis increased with treatment the spleens became noticeably darker in colour when compared to those of untreated mice. While the spleens were not weighed there was never any apparent change in the size of those from treated mice. The mice themselves always appeared perfectly well and healthy and showed no loss of body weight, even when the above mentioned dose was given twice weekly for one month.

A number of possible explanations for this phenomenon were considered. A haemolytic effect of the dithiourethane might have been responsible but neither decreased erythrocyte counts nor increased erythrocyte osmotic fragility was found in the treated mice.

Since the haemoglobin content of the mice was normal and the splenic iron was so markedly increased, the next investigation was to determine the total iron content of the dithiourethane treated mice compared with controls. The iron assay was done by titration of the ferrous to ferric iron with dichromate by the standard method. In order to obtain sufficient iron for a 2 ml titration (error of titration not more than 2 per cent) about 8 mice had to be pooled. In the first instance, 8 *CBA* mice were given eight biweekly injections of dithiourethane (same dose as above). 8 were given injections of the arachis oil solvent and 8 were untreated. Each group of mice was then sacrificed, weighed and incinerated carefully in fused quartz crucibles at 500°–600° C. The ashes were extracted with about 5N hydrochloric acid and the extracts from each group pooled. The results for the experimental mice solvent injected controls and untreated controls were respectively 74, 63 and 61 mgm. of iron per kgm. body weight.

This was repeated on two groups of treated mice (9 and 8 *CBA*) and two groups of solvent treated controls (9 *CBA* mice in each). The figures in this case were 72 and 68 mgm. iron/kgm. for the experimental mice and 53 and 51 mgm. iron/kgm. for the controls. These results suggest that the total iron content of the dithiourethane-treated mice was increased. Consideration was given to the possibility that the normal mechanism of iron absorption through the gastro-

intestinal mucosa was interfered with allowing larger amounts than normal to be absorbed, the excess being taken up by the splenic macrophages. On the other hand dithiourethane may have had a specific effect on the spleen resulting in an increased rate of erythrocyte destruction. The relatively large amounts of pigment deposited would indicate the temporary removal of iron as a readily utilisable source from the animal's store, with resultant increased absorption from the gut as compensation. The erythrocyte destruction being relatively slow the compensation would occur fast enough to prevent any marked anaemia, and the mouse's total iron content would thus increase. This appears to be the most likely explanation of an increased total iron content of the mice showing siderosis only of the spleen.

This work was carried out at the Cancer Research Department of the London Hospital Medical College. Expenses were partly defrayed out of a block grant from the British Empire Cancer Campaign.

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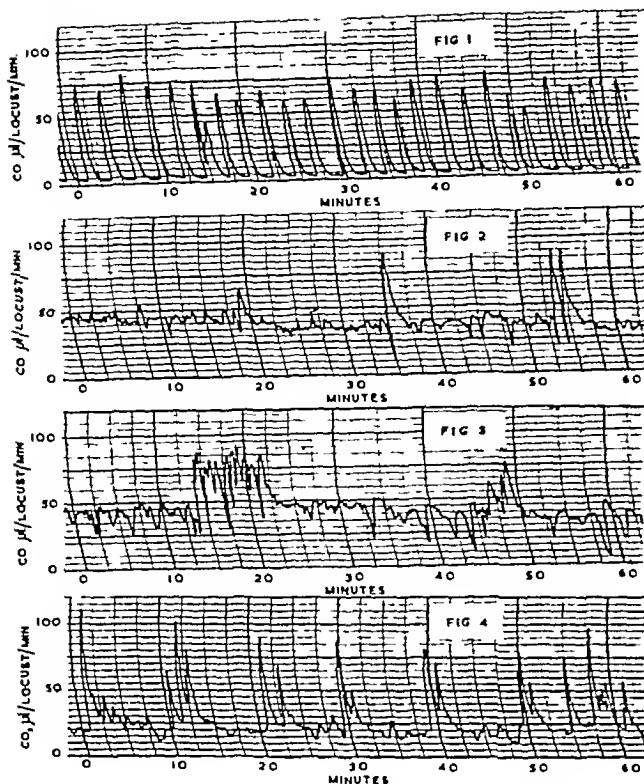
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The Infra-red Gas Analyser as a Means of Measuring the Carbon Dioxide Output of Individual Insects

It has been known for some time that some insects (larvae, pupae and adults) may discharge the carbon dioxide produced during metabolism either as a continuous stream or in bursts¹⁻⁴. Pant using a diaphragmometer, was able to demonstrate changes in the concentration of carbon dioxide but he points out that the sensitivity of his instrument was always adapted to the amount of carbon dioxide produced and was calibrated for this amount. Thus his graphs from different animals cannot be compared with one another, whereas those made using an infra red analyser can be compared.

Using the infra red analyser it is possible to observe and record whether the carbon dioxide is produced in bursts (Fig. 1) or as a continuous stream (Figs. 2, 3 and 4). Also, by using a planimeter on the recording it is possible to calculate the mean output of carbon dioxide per insect per minute. The analyser used by me was specially built by the Infra Red Development Company to suit my requirements. It has three ranges (per cent) 0.0 to 0.02, 0.0 to 0.2 and 0.15 to 1.0 for the complete deflexion of the galvanometer and of the grapho recorder (response time 0.6 sec.) it is possible to switch from one range to another simply by



Figs 1-4 Recordings showing the carbon dioxide output of adult locusts. Fig 1, newly merged. Figs 2 and 3, 5 days after emergence. Fig 4, 70 days after emergence.

a tap and/or altering a switch. All the recordings given here were made on the 0.0 to 0.2 per cent range with the graphic recorder running at 6 in./hr. The rate of flow of air over the insect was so controlled that it was equivalent to 100 ml/min at 0°C. Thus it is possible to give the results as microlitres per insect per minute at 0°C.

All experiments were carried out with the insect (male, *Schistocerca gregaria* Forsk.) in a tube, in the dark, in a constant temperature bath at 32°C, and at a relative humidity between 60 and 70 per cent. Carbon dioxide free air was pumped into the tube and the air leaving the tube passed through the analyser, the cooler and finally through the flow-meter. Each experiment lasted 2-3 hr. The recordings given here are for the second hour of the experiment because, in the majority of the experiments, it was found that the metabolic rate was higher and more erratic during the first 20-40 min. than after this initial period. It is thought that this high metabolic rate at the beginning of the experiment is due to the locust being handled. If, as in all these experiments, the locust is kept in the dark then it settles down more quickly and the output of carbon dioxide remains more constant than if it is in bright light. It should be noted at this stage that by 'constant' is meant for a period of 2-3 hr, but if the recording is continued for 24-48 hr, without the locust feeding, then a drop in output of carbon dioxide does occur. At first the analyser was kept at laboratory temperature and its temperature was controlled by a heater and thermostat. This was soon found to be insufficient control for an analyser as sensitive as mine, so the thermostat and heater of the analyser were removed and the whole apparatus placed in a constant-temperature cabinet at 26°C. The actual temperature of the cabinet is of little importance provided it remains constant once the analyser has been zeroed and standardized against a gas of known concentration.

As a full account of this work will be published elsewhere, I propose to give here only a few typical

recordings of the output of carbon dioxide of male *Schistocerca gregaria* adults to show the advantages of this method of measuring the carbon dioxide output. Fig 1 is a recording of an adult 3 hr after shedding the last hopper skin. At this age, carbon dioxide is produced in bursts at the rate of 24 bursts an hour, but there is considerable individual variation in the number of bursts an hour. After the locust was removed from the analysing apparatus it was placed in a tube under the binocular microscope in order to investigate the opening and closing of the spiracles. It was still in the dark except for small peep holes through which the spiracles could be observed. Also a stream of air was passed through the tube so conditions were very similar to those in the analysing apparatus. It was observed that the bursts of carbon dioxide were produced by the locust stopping all respiratory movement and closing all spiracles for 1½ min (average). At the end of this period respiratory movements would start and the spiracles would start to open and close at the rate of one opening per second (average) for 15-30 sec. This was generally followed by a short period (5-1 sec) when the spiracles opened once every 5 sec. Then the spiracles would remain closed and the cycle would be repeated. These times are by no means constant, indeed, it can be seen from this recording that all bursts are not identical. It should be noted that there is a small amount of carbon dioxide produced between the bursts. As all respiratory movements ceased, and all spiracles appeared closed during this period, the small amount of carbon dioxide produced must be the result of a slight leakage through the closed spiracles or diffusion through the general surface of the locust. At this age the cuticle of the locust is still fairly soft, so that it is just possible for diffusion to take place. As adult locusts seldom start feeding until at least 12 hr after moulting, they must, at this age, be utilizing the reserve food (fat) stored in the body and the burst method of breathing is obviously the best for the conservation of water. The mean output of carbon dioxide for Fig 1 is 20.12 μl/locust/min, which agrees fairly well with the results obtained chemically⁶ and it is well within the range observed in these experiments. By the time the locust has been in the adult stage for one day and has started to feed, the bursts of carbon dioxide have been replaced by a continuous stream of the gas, which varies in amount from time to time.

Fig 2 is a recording of an adult 5 days after shedding the last hopper skin. The carbon dioxide is no longer produced in bursts but as a continuous stream. The small changes in the amount of carbon dioxide are the result of changes in the rate of the respiratory movements and in the rate of opening of the spiracles. At this age the rate of opening of the spiracles varies from 25 to 55 per min but they never remain closed for more than 3 sec at a time. The peaks on this recording (a single at 35 min and a double one between 53 and 55 min) are, I think, the result of a sudden change in the respiratory rate due to some very slight movement of an antenna or a leg. If the locust does try to move along the tube, then a rapid increase in the respiratory rate occurs and is continued for some minutes, as for example, between 14 and 24 min on the recording in Fig 3. At this age locusts are heavy feeders and are utilizing fresh food, so the necessity for conserving water by discharging the carbon dioxide in bursts does not arise. Also they tend to be more active. The mean output of carbon dioxide for Fig 2 is 40.77 μl/locust/min and for Fig 3 it is 44.72 μl/locust/min.

Fig 4 is a recording of an adult 70 days after hatching the last hopper skin. This is old for a locust kept at 32° C and a relative humidity of approximately 55 per cent. At this age the results are very variable but this recording is of the average type. It shows that the main output is around the 20 μ l mark with very distinct and fairly regular bursts superimposed upon it. The mean for the whole recording is 27.80 μ l/pocust/min.

Recordings made less than 24 hr prior to death (from natural causes) of the locust show the burst type of respiration similar to that for newly emerged adults except that the intervals between the bursts, when the spiracles are closed, are much longer.

Although the recordings given here were made over short periods, it is possible, with this analyser, to make continuous recordings extending over 24, 48 hr or longer.

I am indebted to the Central Research Fund of the University of London for a grant which made this work possible.

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Anticoagulant Activity of Human Arterial Mucopolysaccharides

THE isolation of acid mucopolysaccharide material from human aortic tissue was reported in a previous publication¹ from this laboratory. Analysis of the isolated material² and of components separated by paper electrophoresis³ indicated that the major part of the material consisted of chondroitin sulphate. The presence in the material of a fraction susceptible to the action of staphylococcal hyaluronidase⁴ and of a sulphated component containing both galactosamine and glucosamine⁵ was also observed. The isolation of heparin sulphate from human aortic tissue has recently been reported by Linker, Hoffman and Meyer.⁶

Of the sulphated mucopolysaccharides present in various connective tissues three possess anticoagulant activity, namely α heparin chondroitin sulphate B (β heparin), and heparin sulphate. Although α heparin has been isolated from the aorta of cattle⁷, this sulphated mucopolysaccharide has not been identified in the acid mucopolysaccharide material extracted from the intima media layers of human aortic tissue. The present study was undertaken with the purpose of determining the anticoagulant activity of acid aortic mucopolysaccharide samples from subjects of various ages.

Extraction of mucopolysaccharide material was made from the intima media layers of 27 samples of the descending thoracic aorta by the procedure of Dyrby and Kirk.¹ Since the average yield of sulphated mucopolysaccharides obtained by this procedure is about 60 per cent of the acid hydrolyzable sulphate present in the arterial tissue the samples may be considered as being fairly representative of the tissue content of these compounds. The age of the subjects from whom the samples were obtained ranged from 3

to 76 years. The average percentage composition of the samples was sulphate (SO₄), 12.5, hexosamine, 24.2, uronic acid, 33.5, 80 per cent of the hexosamine was galactosamine and 20 per cent glucosamine. No significant change with age was found in the sulphate content of the samples.

The anticoagulant activity of the mucopolysaccharide material was determined by the procedure of Freeman, Engolberg, and Dudley.⁷ Each of the 27 samples was tested at four different levels by addition of 100, 200, 400, and 800 μ g of the material, dissolved in 0.9 per cent sodium chloride solution, to aliquots of the plasma. After 5 min incubation the calcium chloride reagent was added and the coagulation time recorded. A high reproducibility of the results was observed when determinations were performed with the same samples on different days. A coagulation time test with heparin sodium (US Pharm) added in quantities of 0.4, 0.8, 1.2, 1.6, 2.0 and 2.4 μ g was run with each set of experiments. For comparative purposes the anticoagulant activity of a commercial chondroitin sulphate A preparation from the cartilage of cattle was likewise determined.

The results of the investigation are presented in Fig. 1. It will be seen from the reported values that the arterial mucopolysaccharide material was found to possess a definite, but low anticoagulant activity. When compared on a weight by weight basis, the anticoagulant activity of the material was less than 1 per cent of that exhibited by heparin sodium (α heparin), but was considerably greater than the activity observed for the commercial chondroitin sulphate A preparation. The anticoagulant activity of mucopolysaccharide samples from children was moderately higher than that recorded for samples from adults, but the number of samples obtainable from children was too small to permit definite conclusions with regard to this point.

The observed anticoagulant activity of human arterial mucopolysaccharides may constitute a factor

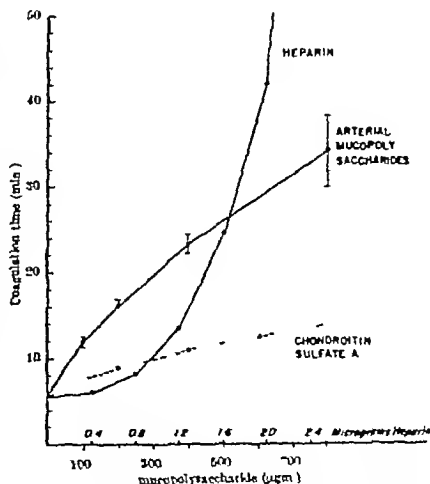


Fig. 1. Comparison of anticoagulant activities of human arterial acid mucopolysaccharide material, heparin sodium (US Pharm) and chondroitin sulphate A.

of significance in connexion with Duguid's⁸ theory concerning the etiology of atherosclerosis

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Urethane as a Carcinogen and as an Anaesthetic for Fishes

PROBABLY the most important factor which determines the carcinogenic properties of a substance is the species (and sometimes the strain) of the animals which are being treated with it. This makes it very difficult to deal with such substances from the public health point of view since results from animal experiments in the field of cancer research cannot always be related to what may happen in man. In practice, substances with known marked carcinogenic activity for man or animals, and which are liable to constitute an occupational hazard, are usually recognized and treated with the respect due to them.

There is one possible exception which we feel warrants more publicity than it has received in the past. Urethane (ethyl carbamate) was found to induce tumours of the lung in mice¹ and rats², and since then has been found carcinogenic for other mouse tissues to a lesser extent³. This compound was not found to be carcinogenic for other species so far tried (rabbits⁴, chickens and guinea-pigs⁵), but nevertheless, the possibility of such an action in man cannot be ignored. Furthermore, evidence was presented that urethane was absorbed in carcinogenic doses from mouse skin^{6,7} and warning was given⁶ to those who handle the compound not only of its possible carcinogenicity, but of its known leucopenic effects on man⁸. Since then, absorption from human skin has also been noted⁹.

A common way of anaesthetising fishes and aquatic invertebrates is to immerse the animals in an aqueous solution of urethane. Wood¹⁰, in a journal of comparatively limited circulation, stressed the risks to the operator in this process, but it appears that even now an appreciable number of people who deal with this substance are unaware of its possible effects. We would suggest, first, that when its use cannot be avoided, reasonable precautions should always be taken to prevent contact of urethane with the skin and secondly that its use as a fish anaesthetic should be discontinued. As a substitute, we recommend tricaine methane sulphonate (*M.S. 222* Sandoz), in the light of the fact that no deleterious effects, as with urethane, have been reported following its use so far.

M.S. 222 has given excellent results in anaesthesia with a wide range of fishes and amphibians^{11,12}. The optimal solution strength to be employed is known to vary with species, individual size and temperature^{11,12}, and suitable concentrations must be determined

empirically for every species and in different situations. A 1 in 2,000 solution has been used successfully in operations on goldfish^{13,14}, brown trout, *Mollenes latipinna* and axolotls¹⁴. Pickford¹⁵ used a 1 in 3,500 solution for *Fundulus heteroclitus*, and a 1 in 5,000 solution is suitable for eels (*Anguilla anguilla*). Various concentrations have been employed by many different workers on amphibian embryos, larvae and adults, and at least one worker has used *M.S. 222* to anaesthetise planarians¹². Apart from its use in the laboratory, this substance is excellent as an anaesthetic to immobilize hatchery and wild fishes during tag and fin-clipping and measuring operations, or to 'traquillize' various game, pet and ornamental fish during transport¹², and Gilbert and Wood¹⁷ report that the palatability of sharks and rays anaesthetized with *M.S. 222* was not affected, and that no deleterious effect was observed in people who ate these fishes.

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Composition of the Hæmolymph of *Petrobius maritimus* Leach

A CONSIDERABLE amount of information concerning the hæmolymph composition of pterygote insects is available, but nothing has been known about hæmolymph composition of any apterygote insect.

Specimens of *Petrobius maritimus* Leach (Aptergota, Thysanura) were collected from under stones just above high-tide line of the Firth of Forth. The dorsal thoracic intersegmental membrane was punctured to obtain hæmolymph. In most cases, hæmolymph from several individuals was pooled. Osmotic pressure, sodium, potassium and chloride concentrations were determined as previously described¹. So far as possible a determination was carried out in duplicate or triplicate on any one sample; many cases the osmotic pressure and several values were determined on the same sample.

The mean values and standard errors are given in Table 1. The numbers in brackets are the number of different samples on which determinations were carried out.

Table 1

| | |
|-------------------------|---------------|
| Osmotic pressure, mM/l. | 232 ± 3 (9) |
| Sodium, mE/l. | 208 ± 4 (7) |
| Potassium, mE/l. | 5.8 ± 0.3 (8) |
| Chloride, mE/l. | 194 ± 5 (9) |

The osmotic pressure of *Petrobius* haemolymph, although high, is very much less than that of sea water end of *Ligia*¹ which lives in the same habitat. This suggests that *Petrobius* is not a relic of a group that might have colonized the shore from a true marine environment.

In *Petrobius* the bulk of the haemolymph osmotic pressure is accounted for by sodium chloride. This is similar to the aquatic Crustacea, the isopod *Ligia*², the spider *Tegenaria*³ and Diplopoda⁴, but is different from the Pterygota. In the Pterygota the chloride concentration is usually low compared to the total cation concentration, and it appears probable that a high concentration of organic anions is present. Also the cations considered to be present as ionized salts account for only a fairly small proportion of the osmotic pressure. These characteristic features of the haemolymph of pterygote insects presumably could be regarded as specializations that have appeared subsequent to the apterygote level of organization. But *Petrobius* is eating seaweed detritus that would be expected to have a high concentration of potassium chloride⁵, and a high concentration of this chloride in the diet markedly decreases the chloride organic anion ratio in the haemolymph of *Drosophila* larvae⁶. It would thus be of interest to compare the haemolymph of some non littoral apterygote insect with *P. maritimus*.

In Pterygota the haemolymph sodium:potassium ratio appears to be associated with the diet, and in phytophagous insects is low, but in *Petrobius* the sodium:potassium ratio is very high. Although seaweed detritus probably has a high potassium concentration, the sodium concentration is also likely to be high, and, if we regard a low sodium:potassium ratio as an adaptation primarily to low sodium availability, the *Petrobius* ratio is as would be expected.

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Disappearance of the Erythropoietic Factor from Plasma of Anemic Dogs after Nephrectomy

In previous communications it was shown that bilateral nephrectomy abolished erythropoiesis in the dog^{1,2} whereas ureter ligation did not impair erythropoiesis despite a similar state of intoxication and malnutrition³. From these observations as well as the demonstration by Jacobson *et al.*⁴ that an elevated erythropoietin level was not obtained in hypoxic rats after nephrectomy, it was suggested that the kidney may be the site of production of one erythropoietic stimulating substance.

In a recent paper erythropoietin response was demonstrated in plasma and urine of the dog when severe anemia was produced⁵. The present study discloses the failure of erythropoietin production by dogs similarly anemic after bilateral nephrectomy. Additionally, the rapid disappearance of the erythropoietic factor after ablation of the kidneys was demonstrated.

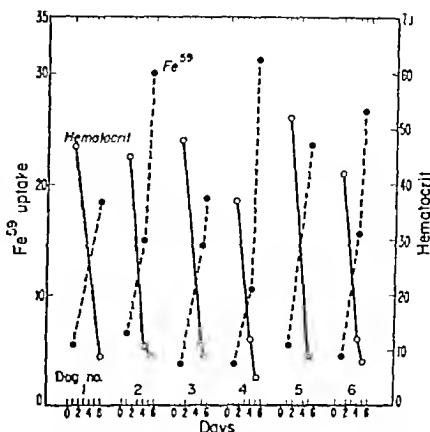


Fig. 1. Erythropoietic activity of plasma from bled dogs with regard to corresponding hematocrit.

Twelve mongrel dogs weighing between 12 and 20 kgm were used. Six dogs were bled once or twice daily to hematocrit values from 5 to 11 per cent. Blood volume was maintained by administration of 6 per cent dextran in saline. In another group six dogs were nephrectomized after one or several venaectomies and still bled after the operation. The bleeding schedule was the same in both groups except in dog No. 37. The erythropoietic activity of the plasma was measured by iron ⁵⁹ red cell incorporation assay⁶ using starved female rats of the Long Evans strain. 6-10 rats were used for each determination. Different amounts of plasma were injected. Each rat received 2 cc of plasma from normal bled dogs subcutaneously daily for 2 successive days, and 6 cc daily when nephrectomized dog plasma was assayed. This larger quantity of plasma was used in order to rule out the presence of small quantities of erythropoietic factor. It has been shown⁷ that no erythropoietic activity could be demonstrated in plasma of anemic dogs by daily injection of 2 cc of plasma when hematocrit was higher than 12 per cent and erythropoietic factor level relatively low.

In Figs. 1 and 2 the relation is shown between hematocrit measurement of bled dogs and effect of corresponding plasma on red cell iron ⁵⁹ uptake of

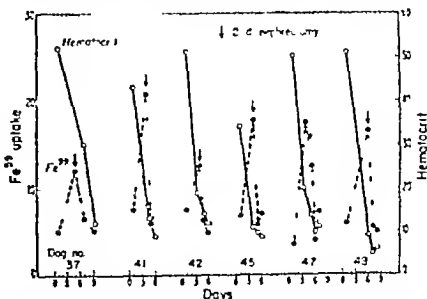


Fig. 2. Values of erythropoietic activity of plasma from bled dogs before and after nephrectomy with regard to corresponding hematocrit.

Table 1 EFFECT OF ANÆMIC DOG PLASMA BEFORE AND AFTER NEPHRECTOMY ON RED CELL IRON 59 UPTAKE OF THE STARVED RAT

| Dog No | Hematocrit % before nephrectomy | Quantity injected plasma daily (c.c.) | Control* | Before nephrectomy | After nephrectomy | | | |
|--------|---------------------------------|---------------------------------------|------------|--------------------|-------------------------|------------|------------|-----------|
| | | | | | 3 hr | 6 hr | 11 hr | 24 hr |
| | | | | | per cent iron 59 uptake | | | |
| 47 | 14 | 6 | 35 ± 0.08† | 12.9 ± 6.9 | 9.5 ± 6 | 5.5 ± 1.8 | 5.1 ± 2.6 | 4.1 ± 1.4 |
| 48 | 9 | 6 | 6.1 ± 3.8 | 16.4 ± 8.8 | 16.5 ± 5.2 | 13.8 ± 8.7 | 11.0 ± 6.2 | 5.5 ± 2.9 |

*Control normal plasma injected before bleeding and before nephrectomy

†Standard deviation

starved rats Fig 1 illustrates the increased iron-59 uptake when severely anæmic dog plasma was injected into the rat. When nephrectomy was carried out no further erythropoietic activity could be demonstrated in the plasma 24 hours later in spite of increased anæmia (Fig 2). Plasma from 2 dogs (47 and 48) assayed 3, 6, and 11 hours after nephrectomy (Table 1) show the very rapid plasma disappearance of the erythropoietic stimulating factor. These results suggest that suppression of erythropoiesis in nephrectomized dogs results from a lack of erythropoietic factor and supports the evidence that the kidney is the source of this factor. It seems unlikely that after nephrectomy intoxication of another site of erythropoietic factor production occurs when erythropoietic stimulating activity disappears in such a short time as 6–24 hours after nephrectomy. Normal erythropoiesis in ureter-ligated dogs with comparable azolæmia also supports this view.

Another hypothesis compatible with these data is that the kidney normally destroys an erythropoietic factor inhibitor. To date removal of organs other than the kidney has not been shown to reduce the erythropoietic response to hypoxia.

This study is based on work performed under contracts with the United States Atomic Energy Commission.

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A New Method for Studying the Functioning of the Lungs

In 1953 a gas in an aqueous solution, injected intravenously was used for the first time in studying the functioning of the lungs¹. It was later shown that all acetylene so injected was eliminated rapidly through the lungs. About 40 per cent was eliminated in the first minute by a healthy person. If the concentration of acetylene in the expired air was registered continuously by means of a special infra-red spectrophotometric method a direct determination of the interval between the commencement of the injection and the initial appearance of acetylene in the expired air could be made. This is probably the most accurate method for measuring the time of circulation from the site of the injection to the lungs. The acetylene elimination capacity was specially low in the presence of extensive pulmonary fibrosis, elimination of the gas was also retarded during an asthmatic attack.

Acetylene is, like carbon dioxide, very soluble in water. For respiratory studies it is, however, also of interest to study the elimination rate of gases with low solubility in water, especially if one wishes to investigate the rate of diffusion of the gases from the lung capillaries to the alveolae. Noble gases are especially good as radioactive tracers for this purpose as they are completely eliminated from the body in a short time. The diffusion of a gas through the lung membranes according to well-known physical laws, is directly proportional to the solubility of the gas in water and inversely proportional to the square root of its molecular weight. The diffusion rate for argon is accordingly about 40 times less than that for acetylene. The corresponding figure for xenon is about 20. The diffusion rates for argon and xenon are about the same as that of oxygen.

If acetylene and argon-41 are injected intravenously together, and the concentrations of the gases are continuously registered in the expired air, one would expect to find a retardation of the elimination of argon compared with that of acetylene, especially if difficulties of diffusion exist. The conveyance in the blood and the mixing of the gases in the alveolar-bronchial system will be equal in both gases.

Since September 1958 about 30 experiments have been performed with combined injections of acetylene and radioactive argon or xenon in a saline solution. Noble gases in small quartz bulbs were irradiated in a pile. The injections were performed in the cubital vein. 30 ml were injected in 2 seconds with an automatic syringe driven by compressed air. The radioactivity in the syringe was measured just before the injection. As the half life for argon is short, it is necessary to make a correction for this. The concentrations of gases, both acetylene and argon, were measured simultaneously in the same cuvette of an infra-red spectro-photometer. A sodium iodide scintillator is placed close to the cuvette. The spectrometer is supplied with a pulse-height analyser. The concentrations of the gases are registered on a kymograph of the mingograph type. After passing the cuvette the expired air is collected in rubber bulbs.

Figs 1 and 2 show the gas elimination in 2 persons, one with normal lungs and one with sarcoidosis in the lungs. The latter patient had only slight breathing difficulties during exercise.

From Fig 1A we can see that the greatest intensity of both acetylene and argon is reached after about 10 seconds. In Fig 1B the greatest intensity for acetylene is reached after about 11 seconds but that for argon is not reached until after 16 seconds.

The amounts of the gases eliminated, expressed as percentages of the amounts injected, were determined by collecting expired air for different periods of time in bags and analysing it. The values obtained for the two persons mentioned are shown in Fig 2. It shows that the person with normal lungs eliminates both gases at the same rate (Fig 2A). The person with sarcoidosis in the lungs, however, eliminated argon

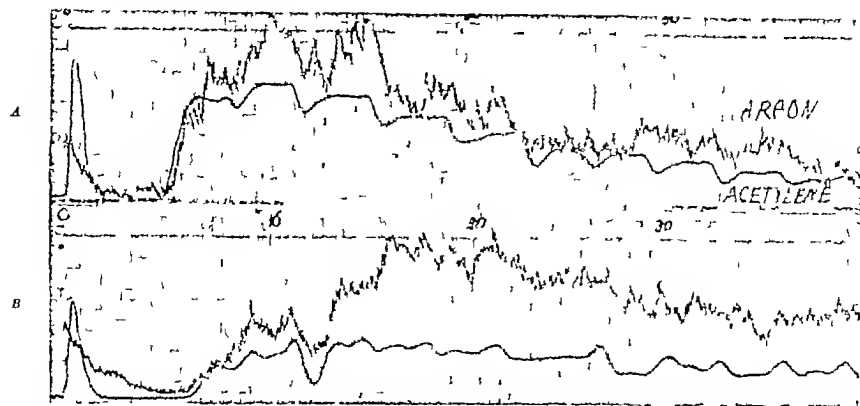


Fig. 1 (A) Person with normal lungs. (B) Person with lung sarcoidosis. Abscissa, Time in seconds. Ordinate, acetylene concentration (on a logarithmic scale) and the counting rate for argon (on a linear scale). The top intensity for acetylene corresponds to an acetylene concentration of 0.15 per cent, the top intensity for argon to a counting rate of 1,500 c.p.m. (The initial curve deflections at time 0 depend on electric signals from the apparatus and are independent of gas concentrations.)

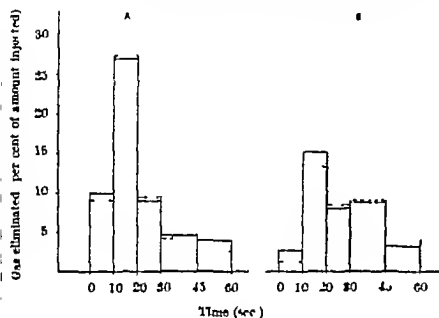


Fig. 2 (A) Person with normal lungs. (B) Person with lung sarcoidosis. — Acetylene — — — argon

RADIOBIOLOGY

Fate of Injected Dextran Labelled with Tritium in Mice

THE metabolism of the blood plasma substitute dextran has been widely studied during the last decade. It was early shown that starch-splitting enzymes do not break down dextran but Grunwall found evidence that dextran is altered in the tissues to make it stainable with leuco fuchsin without previous treatment with periodio acid. Cargill and Brunner² showed that dextran labelled with carbon 14 is metabolized in mice since $^{14}\text{CO}_2$ could be recovered from the expired air and labelled carbonates isolated from the urine.

Several authors²⁻⁵ have found by using histochemical methods that part of intravenously administered dextran is stored in various organs and chiefly in the reticulo-endothelial system. Engstrand and Åberg⁶ showed that dextran is eliminated at least to a certain extent via the gastro-intestinal tract. This was later confirmed in a report by Troell and Åberg⁷. On the other hand, Burson and Bloom⁸ found no evidence of gastro-intestinal excretion of dextran.

Due to the controversies in the literature, we decided to tritiate dextran and to follow its distribution in mice autoradiographically after intravenous administration of the labelled product.

The following dextran preparations were used (kindly placed at our disposal by Pharmacia Ltd, Uppsala, Sweden):

- (1) Clinical dextran (mean mol. wt., 78,000 minimum mol. wt., 39,000)
- (2) Mean mol. wt., 197,000 minimum mol. wt., 133,000,
- (3) Mean mol. wt., 457,000 minimum mol. wt., 177,000

The tritiation was performed according to Wilzbach's method⁹. 100 mgm of dextran was exposed to 1 μ of tritium gas in a glass ampoule for 3 weeks. After tritiation the dextran was repeatedly dissolved

more slowly than acetylene in the first two periods of 10 seconds (Fig. 2B).

We believe that this difference can be used as a measure of impaired diffusion between capillaries and alveoli. The transport in the blood and the mixing of the gases in the alveolar bronchial system will be equal for both gases. Experiments are being continued on and different lung diseases are being investigated on these lines.

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in 100 ml of distilled water and precipitated with ethanol

The specific activity of the tritiated dextran was 15.2–5.1 mc per gm dextran

The tritiated dextran was dissolved in water to give a final concentration of 6 per cent. Of this solution 0.3 ml was injected intravenously into a tail vein of white mice weighing about 25 gm. The animals were killed after 5, 30, 60 and 90 min and after 6, 24 and 48 hr. Autoradiography was performed according to Ullberg's method¹⁰. This method gives sections of the whole animal and dextran is not lost from the sections.

In order to check the stability of the tritium label, the following experiment was performed. A mouse was given tritiated dextran intravenously, the urine was collected during the following 4 hr and the urinary dextran precipitated with ethanol. After centrifugation, the radioactivity of the supernatant and the precipitate was measured. It was found that 96 per cent of the activity was present in the precipitate.

Thirty minutes after the injection of dextran, the autoradiograms show an accumulation of radioactivity in liver and spleen and an excretion into the gastrointestinal tract and via the kidneys. The radioactivity in the blood decreases fairly rapidly. In the spleen the dextran is localized to the marginal zone of the white pulp (Fig 1). In the liver the dextran seems to be confined to the reticulo-endothelial cells. No radioactivity is visible in the bile. The kidneys show high radioactivity especially during the first hour after the administration.

In Fig 2 the distribution of dextran is shown autoradiographically 24 hr after administration. The greatest part of the activity is contained in the liver. Radioactivity is also found in the intestines and the spleen (not shown in Fig 2) but the activity is considerably less than that of the liver.



Fig 1 Autoradiogram showing the distribution of tritiated dextran in a mouse 90 min after intravenous injection. White areas correspond to high dextran content. Note high activity in stomach, liver and spleen.

When the various fractions (1–3) are compared, it appears that the excretion, especially into the gastrointestinal tract, is higher for fraction 1 having the lowest mol weight. The different fractions however,

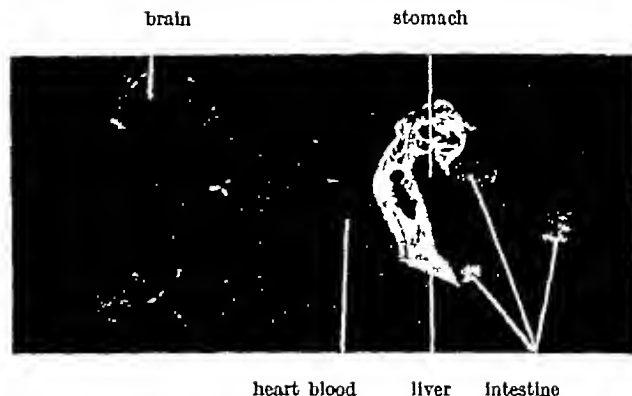


Fig 2 Autoradiogram showing the distribution of tritiated dextran 24 hr after intravenous injection. White areas correspond to high dextran content. Note high activity in liver and intestines.

show about the same accumulation in the liver and spleen. A detailed report will be published later.

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Removal of Strontium and Cesium from Milk

THE appearance of radioactive isotopes of strontium in the food chain has caused considerable concern. There is complete agreement that these isotopes constitute a hazard to health, but controversy about the quantitative aspects of this hazard.

Milk is one of the most important dietary sources of the strontium isotopes. Reduction or elimination of these isotopes from milk may be a means of resolving the hazard.

It has been repeatedly observed by investigators studying bone metabolism that isotopes of calcium and strontium are removed from blood very quickly and appear in the skeleton^{1,2}. The heteroionic exchange with skeletal calcium accounts in large part for this rapid removal and does not result in a change in the net calcium concentration of the blood³.

With this exchange process in mind it was decided to try to remove strontium from milk by means of a cation exchange resin in a calcium form.

In 1954, Nervik, Kalkstein and Libby⁴ used a cation exchange resin in a sodium form which removed both calcium and strontium from the milk. This method would necessitate replacement of the calcium content. After the present work was started, a report by Glueckauf, Cosslet and Watts⁵ came to my attention. They employed an anion exchange resin in the chloride form to remove iodide, and suggested that radiostrontium could be removed by passing the milk through a cation exchanger bed,

which is regenerated with a mixture of calcium and sodium chloride

In the present investigation, 'Dowex 50H-A12 was employed. Experiments were conducted on commercial milk to which strontium 89 was added and on guinea pig milk containing strontium 89 diluted with cow's milk. The resin was treated with a solution of 18.0 per cent calcium chloride, 15.5 per cent potassium chloride, 6.5 per cent sodium chloride. The ratio of the cations in this solution is the same as that which exists in milk. 50 gm of the resin was stirred for 30 min with five successive 200 ml portions of the salt solution. Table 1 shows the efficiency of this resin for removing strontium from milk.

Table 1. EFFECT OF CALCIUM-POTASSIUM-SODIUM RESIN TREATMENT ON REMOVAL OF STRONTIUM 89 AND CATION COMPOSITION OF MILK

| Amount resin per 20 ml milk (gm) | Calcium (per cent) | Sodium (per cent) | Potassium (per cent) | Strontium-89 removed (per cent) |
|----------------------------------|--------------------|-------------------|----------------------|---------------------------------|
| 0 | 0.120 | 0.018 | 0.105 | |
| 0.25 | 0.127 | 0.031 | 0.105 | 63.5 |
| 0.50 | 0.126 | 0.019 | 0.101 | 76.8 |
| 1.00 | 0.128 | 0.050 | 0.101 | 80.7 |

Note—Strontium-89 content of milk was 6.75 µg./100 ml

Table 2. EFFECT OF CALCIUM-POTASSIUM-SODIUM RESIN TREATMENT ON REMOVAL OF CESIUM FROM MILK

| Amount of resin per 20 ml milk (gm) | Cesium removed (per cent) |
|-------------------------------------|---------------------------|
| 0.25 | 50.1 |
| 0.50 | 56.6 |
| 0.75 | 60.6 |
| 1.00 | 75.8 |

The analyses of milk before and after treatment are also shown in Table 1. The results indicate that no change is produced in the calcium, potassium or sodium content of the milk and 80.0 per cent of the strontium has been removed by one treatment with resin. A taste panel could not detect any change in flavour of the milk as a result of the resin treatment.

Milk obtained from guinea pigs previously injected with strontium 89 and diluted with cow's milk was also treated in the same manner. The percentage of strontium removed was the same.

An experiment was carried out with milk to which cesium 137 was added. The results shown in Table 2 indicate that cesium 137 is removable by means of the same resin which removes strontium.

The indications are that removal of strontium and cesium from milk is feasible without altering the milk. The question remains whether the process could be placed on a commercial basis if it ever became necessary; the answer can best be obtained by co-operative effort among the organizations concerned with this matter.

I thank Mr F. Pheasant for his assistance and Dr D. F. Coffin and Mr S. M. Skinner for analyses of the cations in the milk.

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In Vitro Labelling of Antibody Globulin by Tritium Exchange

CRAWFORD L. Hawkins and Smyth¹ have reported the preparation of tritiated antibody by biosynthesis. The report of successful labelling of lysozyme and ribonuclease by *in vitro* tritium exchange² suggested that antibodies might also be amenable to tritiation by the latter method which has the advantages of simplicity, larger yields and usually results in products of sufficiently high specific activity to permit their use as reagents in radioautographic studies.

We have found it possible to label γ_2 globulin prepared from antisera against the Ehrlich mouse ascites carcinoma in this manner. Specific activities varied between 1 and 10 mc/gm of protein depending on the time of exposure to tritium gas (one to two weeks). Labelling was carried out both in the dry state at room temperature and in solution at 5°C, degradation products were formed to the approximate extent of 5 per cent of the original protein in the case of the first method and 15 per cent in the case of the second. Subfractionation of the labelled globulin by chromatography on DEAE cellulose revealed some changes in the distribution of combining activity between peaks; the combining activity of the whole labelled globulin however was unchanged as estimated by the quantitative complement fixation test. Ultracentrifugal studies showed a tendency toward separation of the original major peak of the unlabelled material into two peaks after labelling. Observation of the fate of the labelled material in the bloodstream of the rabbit yielded no evidence of change in the direction of antigenicity and there was no increase of any consequence in the rate of elimination.

It is concluded that labelled antibody globulin may be prepared by *in vitro* exchange with tritium gas without loss in titre and without major changes in physical properties. It is therefore possible that tritiated antibodies may find application in localisation studies using the radioautographic technique.

A detailed report of this study will appear elsewhere.³ This research was supported by a grant from the Michigan Memorial Phoenix Project.

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BIOLOGY

An Embedding Resin Miscible with Water for Electron Microscopy

THERE are three embedding media commonly used at present to prepare biological specimens for thin sectioning and electron microscopy: methacrylate esters,¹ Vestopal polyester resin² and 'Araldite' epoxy resin.³ These although excellent for many purposes all have the limitation that they are not miscible with water and so require the specimen to be

dehydrated before it can be infiltrated with the medium. This dehydration, for which ethanol is most often used, frequently causes undesirable leaching of tissue components. The introduction of a water-miscible resin of low solvent power therefore appears desirable.

Several commercial epoxy resins approach these requirements but none is completely miscible. A suitable resin ('Aquon') has therefore been prepared by extracting the completely miscible fraction of a partially miscible commercial resin, 'Epon 812' (Shell Chemical Corp., 380 Madison Ave., New York 17). A solution of 'Aquon' was obtained by extracting 'Epon 812' with two volumes of water. The resin was crudely separated from this solution by salting it out with sodium sulphate. Residual water was removed by drying in a vacuum desiccator. The yield obtained was about 30 per cent. The resin, kept dry, has proved stable over a period of six months.

Prepared in this way, 'Aquon' resin is a colourless hygroscopic liquid of fairly low viscosity ($\eta \sim 100$ centipoises at 25°C). It is completely miscible with water at temperatures below about 15°C , at slightly higher temperatures it is only partially miscible.

When treated with a suitable hardener and accelerator 'Aquon' cures, without appreciably shrinking, to a solid resin that can easily be thin sectioned by conventional methods. A suitable mixture is 10 ml 'Aquon' resin, 25 ml dodecyl succinic anhydride (National Aniline Division, Allied Chemical and Dye Corp., 40 Rector St., New York 6), 0.35 ml benzyl dimethylamine (Sumner Chemical Corp., 6 East 45th St., New York 17). Heating the mixture to 60°C for four days provides an adequate cure.

The following procedure has been used for embedding. The fixed and washed specimens were slowly dehydrated by passing them through a series of increasingly concentrated cold (4°C) solutions of plain 'Aquon' resin in water. When they had been completely dehydrated by soaking in dry 'Aquon' resin the specimens were transferred to the complete embedding mixture given above. After about four hours for soaking, they were transferred to fresh embedding mixture in dry gelatin capsules and placed in the oven to cure.

Thin sections were prepared with a Porter-Blum ultra-microtome fitted with a glass knife and a trough of distilled water, those showing a silver interference colour were easily obtained. The sections were slightly softened, but not dissolved, by the water in the trough. Suitable staining for either light or electron microscopy was readily accomplished without removing the embedding medium.⁴

In trials 'Aquon' resin has been used to dehydrate and embed osmium tetroxide fixed specimens of pancreas, retina, and testis, bacteria (*E. coli*), and plant root tips. Comparison specimens have been prepared firstly by dehydration in ethanol and embedding in 'Aquon' resin and secondly by dehydration in ethanol and embedding in 'Araldite' epoxy resin. In most cases the general quality of preservation in the test specimens dehydrated in 'Aquon' appeared very good and equal to that in the control preparations. The characteristic organization of the centrioles, granular and agranular cytoplasmic membranes, mitochondria, nuclei, and retinal rod cells appeared substantially the same in all cases, further work is required to decide whether any significant differences occur.

It is considered that an embedding resin miscible with water will be valuable in cases where it is

desired to avoid subjecting specimens to conventional dehydrating agents with their strong solvent power. The range of applications in which practical benefits will be obtained from this technique remains to be determined. Preliminary experiments have indicated that specimens fixed with formaldehyde show substantially improved preservation.

Epoxy compounds in aqueous solution are known to react readily with proteins and nucleic acids^{5,6}. Poly-epoxides, such as 'Aquon' resin, introduce intermolecular cross-linkages, they will therefore tend to act as fixatives and aid in the preservation of structure. This fixative action, although probably insufficient by itself for adequate preservation of the tissue as a whole, may be important in preserving structures rich in nucleic acids, with which other common fixatives do not react.

Full experimental details of this work will be reported elsewhere. The greater part of the work was carried out at the Johnson Research Foundation of the University of Pennsylvania and was supported by a grant from the National Science Foundation to Dr T. F. Anderson, to whom I am grateful for his interest and encouragement.

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8-Azaguanine Inhibition of Hæmoglobin Synthesis in De-embryonated Chick Blastoderm

THAT an important relationship exists between nucleic acid metabolism and protein synthesis is well known. The addition of some analogues of nucleic acid components to developing systems has been shown to result in abnormal growth, differentiation or cell division, which it is assumed are due to an interference with normal protein synthesis. Investigations concerned with the effect of nucleic acid analogues on the formation of a specific protein have been restricted mostly to micro-organisms^{1,2}.

The following report summarizes the development *in vitro* of a simple vertebrate histogenic system in which the appearance of a specific protein, hæmoglobin, is studied in the presence of the nucleic acid base analogue 8-azaguanine and of the normal component guanine.

The chick blastoderm at approximately 20-hours incubation is removed from the egg and transferred to a watch glass containing fluid albumen³ where it undergoes further development. At the stage required the embryo proper is excised from the middle of the blastoderm and the remainder of the blastoderm is washed and transferred to an agar gel. This step serves to block cell migration entirely and growth very considerably in the ectodermal and endodermal layers, leaving the mesodermal blood islands unaffected in respect to both cell division and differentiation. The primitive erythroblasts multiply, synthesize hæmoglobin and ultimately form primitive erythrocytes contained within ill-defined tubular endothelium.

The development of hemoglobin is observed microscopically both directly as a red colouration in the blood islands and indirectly with the more sensitive and stable haemoglobin peroxidase reaction with o-dianisidine. Within the system described this peroxidase reaction is specific for cells of the blood islands and, as indicated by colorimetric and electrophoretic tests specific for hemoglobin.

nucleic acid associated reactions are involved in this particular protein synthesis, they are much more responsive to analogue inhibition before, than after stage 9 by which time the synthetic pathway has become established.

Of further interest is a series of experiments which locate the end point of this period in a relatively narrow zone on the developmental time scale. In this

series there are two categories: (1) the de-embryonated blastoderm is first incubated on $N + Az$ gel for a certain time then transferred to A (Fig. 1, $Az \rightarrow N$); (2) the de-embryonated blastoderm initially incubated on A gel then transferred to $Z + Az$ gel (Fig. 1, $N \rightarrow Az$).

In all cases where hemoglobin appears there is some inhibition though the time of appearance is much the same as in the earlier series. Prior to stage 8 no hemoglobin develops if de-embryonated blastoderm are first placed on $N + Az$ gel (minimum period in these experiments 1 hour). If however they are first placed on N gel for a period such that they reach the equivalent (in time) of developmental stage 9 before contact

with azaguanine hemoglobin will develop.

This effect is most apparent when blastoderms de-embryonated at stage 8 are studied in more detail: (1) One hour exposure to azaguanine in only system prior to stage 8 blocks hemoglobin synthesis but not at stage 8 or beyond; (2) Two hours exposure at stage 8 will delay while (3) three hours will block the appearance of hemoglobin although some nuclei now show a positive peroxidase reaction. If a stage 8 blastoderm is first incubated on A gel and then transferred to $N + Az$ gel then (a) two hours on the former is insufficient for hemoglobin development; (b) three hours results in the system producing some hemoglobin; (c) four hours results in almost normal hemoglobin synthesis.

Comparing (1) and (2) with (a) and (3) with (b) and (c) these experiments suggest that there is a period of only a few hours prior to stage 9 that is critical to the final synthesis and production of hemoglobin when that synthesis is being blocked by 8 azaguanine. It is about this time that the peroxidase reaction becomes positive in the nuclei of single erythroblasts and in small groups of nuclei scattered within the blood islands.

This study of hemoglobin synthesis during the simple *in vitro* histogenesis described above leads to three conclusions:

(1) The nucleic acid base analogue 8 azaguanine (10 mgm/100 ml) will block hemoglobin formation before but not after a period during which some part of the synthetic pathway or perhaps some ribonucleic acid associated structure is forming.

(2) This period is of two to three hours duration and occurs just before developmental stage 9 on the Hamburger and Hamilton scale.

(3) The erythroblast nuclei rather than the cytoplasm show the first evidence of haemoglobin synthesis.

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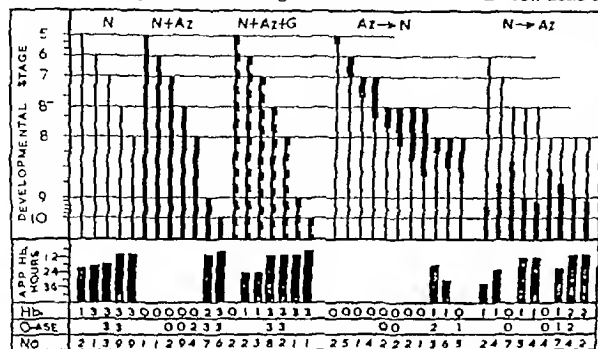


Fig. 1. Columnal indicate the developmental stage of transfer to gel medium. (1) Head region; (2) Head fold; (3) Somite; (4) (5), (6) and (10) 2×4 and 10- μ (Hamburger and Hamilton). Areas subdivided into hours. Each set represents a particular treatment. $N + Az$ represents the transfer to a buffered saline glucose-azur gel. $N + Az$ gel contains 8-azaguanine (10 mgm/100 ml.) in addition to the constituents of the N gel. $N + Az + G$ contains guanine (10 mgm/100 ml.) as well as 8-azaguanine (10 mgm/100 ml.) ($N \rightarrow Az$). In this set the de-embryonated blastoderm is first placed in a gel containing 8-azaguanine. After a certain time it is transferred to an A gel ($Az \rightarrow A$) the preceding treatment reversed.

Matograms show the time of appearance of hemoglobin in hours from plating in the gel in the first three sets and from the transfer to the second set in the last two sets. Row (Ib) indicates the extent of hemoglobin development at 48 hours and row (0-48) the hemoglobin peroxidase activity at 12 hours, after transfer to the final gel. The values to be interpreted as follows: (a) No visible pigment or reaction in cell groups, cytotelomeres or nucleus; (1) A few scattered, small isolated faintly pigmented blood islands or isolated single nuclei and small groups of nuclei peroxidase positive; (2) blood islands interconnecting some interconnected but pigmentation still faint; peroxidase reaction more intense and reticular appearance well defined; (3) Deep red pigmentation clearly visible to naked eye. Intense and extensive peroxidase reaction in both cytotelomeres and nucleus. Blank space indicates no reaction. Row (No) refers to the number of embryos used in row (Ib). In row (0-48) two embryos were used in each case.

Fig. 1, A demonstrates the synthetic *in vitro* of hemoglobin by the blastoderms de-embryonated at developmental stages 5 to 8 (Hamburger and Hamilton scale) transferred to agar and incubated at 37.5°C for 48 hours. Blastoderms incubated for 12 hours were used for peroxidase reactions. At this time hemoglobin was only just microscopically visible (level 1 Fig. 1) in isolated small groups of cells.

The presence of 8 azaguanine (10 mgm/100 ml.) effectively blocked the appearance of hemoglobin (Fig. 1, $N + Az$) in all systems set up before the entire blastoderm had developed to stage 9. Stage 8 systems gave a faint positive peroxidase reaction but did not develop visible hemoglobin.

Guanine at the same concentration and in the presence of 8-azaguanine (Fig. 1, $N + Az + G$) relieved the block completely except in stage 5 where inhibition still remains. In systems set up at stage 9 and beyond, haemoglobin synthesis was unaffected by azaguanine in concentrations of 10 mgm and 20 mgm per 100 ml and histological examination showed normal erythrocytes to be present in the blood vascular spaces.

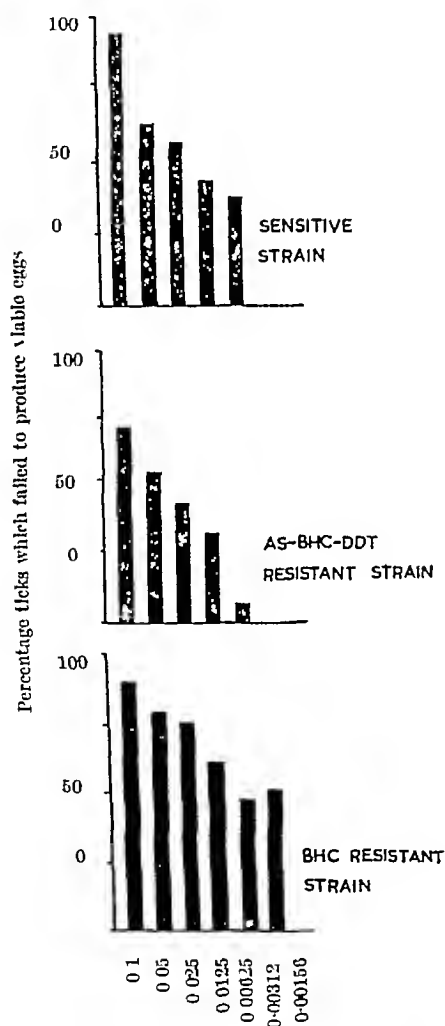
These results demonstrate that whatever ribo-

Pyrethrum Resistance conferred by Resistance to DDT in the Blue Tick

IN a general investigation of the effectiveness of pyrethrum formulations for the control of a variety of species of cattle ticks in South Africa, a laboratory study of the effect of pyrethrum on the blue tick, *Boophilus decoloratus* Koch, was undertaken.

The blue tick from some localities of South Africa has developed resistance to a number of insecticides. A study of the pattern of cross resistance using a number of insecticides has shown that resistance in the blue tick is of three distinct types (a) to sodium arsenite, (b) to γ -BHC and related compounds, and (c) to DDT and its analogues¹. The types of resistance may occur singly or in combination.

Results of an examination of the effect of a pyrethrum formulation applied to three strains of adult blue ticks by an *in vitro* immersion technique¹ are shown in Fig. 1. The formulation concentrate con-



Per cent concentration of pyrethrum ($\times 10^{-4}$)

Fig. 1 The effect of pyrethrum on three strains of the adult female blue tick. The formulation concentrate contained 10 per cent pyrethrin, and was made by diluting pyrethrin extract (25 per cent) with aromatic solvent, adding 10 per cent of a proprietary blend of anionic/nonionic emulsifier to render the formulation dispersible in water. It was used freshly-prepared, obviating the need for stabilising materials.

The results indicated that the arsenic-BHC-DDT resistant strain was more tolerant to pyrethrum than was the sensitive strain or the strain resistant solely to the BHC group of insecticides. Later it was possible

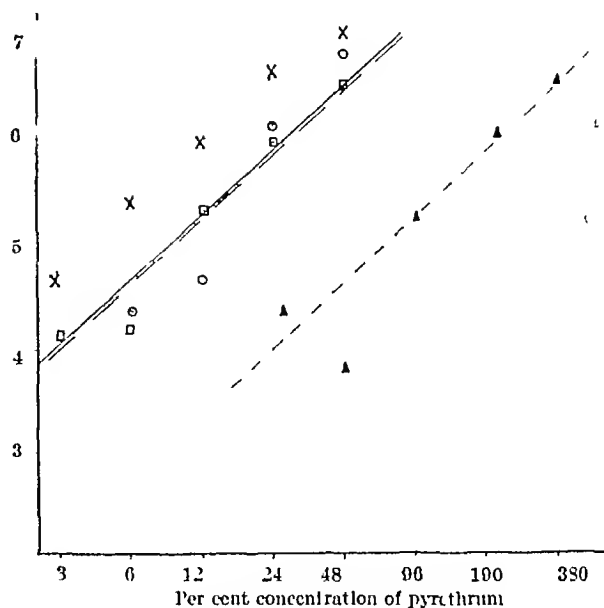


Fig. 2 The effect of pyrethrum on four strains of blue tick larvae. O, BHC resistant; Δ , AS BHC DDT resistant; \square , AS BHC resistant; X, sensitive strain. Probit of per cent mortality.

to examine four different strains of blue tick larvae in a technique designed to detect differences in response to a number of insecticides¹. The results of these tests are shown in the log dose-probit mortality curves in Fig. 2 (see also Table 1).

Table 1 THE DIFFERENCE IN RESPONSE TO PYRETHRUM BY DIFFERENT STRAINS OF BLUE TICK LARVAE

| No. | Strain of blue tick larvae | LC 50 pyrethrum concentration (per cent) | Factor of increased tolerance as compared with the most sensitive strain |
|-----|---|--|--|
| 1 | Resistant only to the BHC group of insecticides | 9.5×10^{-4} | 2.38 |
| 2 | Resistant to sodium arsenite, the BHC group and the DDT group of insecticides | 72.4×10^{-4} | 18.1 |
| 3 | Resistant to sodium arsenite and the BHC group of insecticides | 9.6×10^{-4} | 2.4 |
| 4 | Sensitive to all insecticides | 4.0×10^{-4} | 1.0 |

These results suggest that the blue tick resistant to BHC alone and resistant to BHC and sodium arsenite is slightly more tolerant to pyrethrum than the strain with no record of any insecticidal resistance. However, the increase in pyrethrum concentration required to produce 50 per cent mortality in these two resistant strains is comparatively low and is most probably a result of a difference in vigour.

The 18.1 fold increase in tolerance shown by the arsenic-BHC-DDT-resistant strain of larvae is too high to be accounted for by a general increase in vigour and suggests a definite biochemical resistance.

In houseflies, where the pattern of insecticide resistance is in many respects similar to that in the blue tick, there is no general cross-tolerance to pyrethrum conferred by resistance to DDT², although an Italian strain of flies resistant to DDT showed a clear cross-tolerance to pyrethrum³. It was not stated in this instance whether or not the Italian strain had been in contact with pyrethrum in the field at any time and under these circumstances the independent development of resistance to pyrethrum cannot be excluded. However, in South Africa the treatment of cattle with pyrethrum for the control of ticks on a field scale has never been practised and the only conclusion that can be drawn is that resistance to DDT confers a substantial cross-resistance to pyrethrum.

This work was undertaken in the Research Department of African Explosives and Chemical Industries Ltd with the collaboration of Cooper and Nephews South Africa (Pty) Ltd to which thanks are accorded for permission to publish the result

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Organ Cultures of Total Mammary Glands of the Mouse

In the course of experiments on hormonal influences upon tissue cultures of normal and malignant mammary tissue, a difficulty was encountered that in the common tissue culture and organ culture methods the duct systems are cut or disturbed by other means, resulting in wound healing reactions of the epithelium. These reactions may interfere with the normal functions of the epithelium to hormonal stimuli.

Hardy² described the development of mammary glands from the anlage when culturing parts of the ventral body wall of 10-13 day mouse embryos. Her conclusion was that at this stage of development the differentiation of the mammary gland is not primarily dependent on specific hormonal stimulation. In the case of embryonic tissues independent developmental tendencies may obscure hormonal influences.

A method was therefore devised for cultivating whole mammary glands of mice beyond the embryonic stage. The third mammary glands of such mice are spread out in a flat thin flat pads offering favourable culturing conditions. In these experiments female *C57BL/6J* mice (*J1* hybrids *C57BL/6J* × *DBA/1*) six weeks of age were used.

The mouse is killed by breaking the neck spine. It is then immersed for a moment in 70 per cent alcohol to sterilize the skin. The integument is stripped off taking care not to damage the attached mammary apparatus. After extending it on a cork plate—made uppermost—the tissue overlying the third mammary glands is carefully removed. Next a piece of nylon gauze (nylon filter gauze as used in blood transfusion systems) is spread over each gland and a drop of cockerel plasma and one drop of chick embryo extract are put upon it in order to stick the gland to the gauze. This sticking prevents the gland from shrinking afterwards. The excess of fluid is sucked off. The plasma is allowed to clot during which period the whole is covered with a glass lid to prevent desiccation. Afterwards the gland plus the gauze are prepared loose from the underlying skin using very sharp knives of appropriate shape (Paragon scalpel blade No 17). All is done under normal aseptic precautions. If properly done, the only cut through the duct system of the gland is through the nipple.

Gauze and gland are then placed on the surface of a feeding medium gland tissue upwards. The medium is contained in a little cup formed by a stainless steel ring that has been immersed in melted paraffin wax and placed while still warm on a sterile glass plate; as the paraffin wax solidifies a cup is formed into which culture medium is pipetted. The bordering ring supports the nylon gauze. The whole is covered

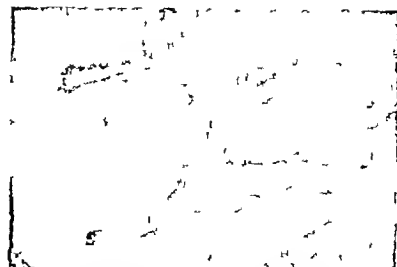


Fig. 1. Part of first mammary gland of a 6-week-old mouse fixed at the first title experiment.

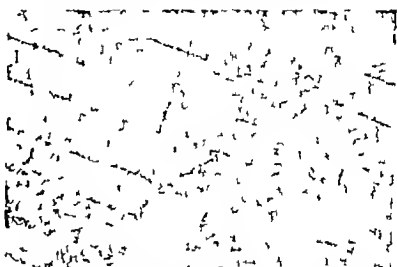


Fig. 2. Part of third mammary gland of the same mouse cultured for 13 days.

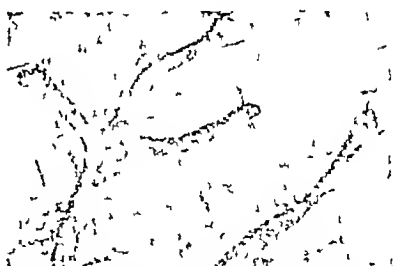


Fig. 3. Part of third mammary gland of the same mouse cultured for five days with the addition of progesterone by half a Petri dish sealed to the glass plate by paraffin wax.

by half a Petri dish sealed to the glass plate by paraffin wax.

The culture medium was a mixture of Tyrode (7 drops), mouse embryo extract (1 drop), human umbilical cord serum (2 drops) and horse serum (2 drops) with ± 500 u/ml penicillin added. This medium was devised for the culture of human mammary carcinoma and gives excellent results with mouse mammary glands although a less complicated medium might suffice for the latter. The quantity of nutrient in the cup (inside diameter 17 mm, height 3 mm) is sufficient for a five day culture period. For long term cultures it is advisable to renew the medium three times a week.

The accompanying illustrations are of a pair of third mammary glands of a mouse, one of these was cultured as described above (control). The other was cultured identically except that about 1 mgm of progesterone had been added. This progesterone had

been dried on to the nylon gauze from a solution of progesterone in acetone, before the gland was stuck to it

The control culture shows a regression in development compared with the first mammary gland that had been fixed at the beginning of the experiment. This is a regression, not merely a degeneration, a number of cells of the tubuli degenerate and die, the remaining cells remain in good condition and may survive for at least three weeks.

The control culture shows collapsed tubules but without signs of regression, there is possibly an increase in nuclear material. The cultures shown were fixed after five days in culture. These effects were found to be reproducible in four series of each one pair of experiments.

Full details of results obtained with several hormones will be published elsewhere.

An additional advantage of the method is that pictures are obtained comparable with the mammary gland preparations as used in hormone and cancer research in intact mice.

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Speciation among Lampreys

Not all lampreys migrate to the sea. Some (the 'landlocked') always remain in fresh water, but after metamorphosis they migrate from the brooks, where they are born, to lakes and rivers. After a long feeding period they go back to the brooks, where they spawn and then die. This is known to happen with *Petromyzon marinus*, the landlocked form of which multiplied abundantly and spread widely in the Great Lakes of North America¹. The same phenomenon was recorded for *Lampetra fluviatilis* of Lakes Ladoga and Onega in the U.S.S.R.²

In other cases more differentiated forms of species have originated. These I would call 'paired forms' or 'paired species'. There are, in fact, related forms of lampreys (usually a couple), which are almost identical morphologically, while their biological features are quite different. One form, in the couple, after metamorphosis, feeds parasitically on other fishes, while the other does not take any food. Moreover, the former reaches sexual maturity after the feeding period, whereas the latter begins its maturation during metamorphosis.

So far, cases of paired species of this kind were known only in the genus *Ichthyomyzon* and *Lampetra*. Recently I have found another one in the Danube waters for the genus *Eudontomyzon*. The relationship among the paired species or paired forms are shown in Table 1.

In every case the non-parasitic forms can be found in the same river basin together with the parasitic forms, but they are confined to the upper zone. Sometimes, however, both forms can be caught spawning at the same time and place³.

The parasitic lamprey in the Danube does not migrate at all, unlike the parasitic forms of other paired species. The former always remains in the same streams where it lived as a larva and underwent metamorphosis, just as the non-parasitic forms of the other cases of paired species. This perhaps explains why the existence of these two forms has remained so far unknown.

The presence of paired lampreys in so many different localities raises the problem of their specific difference and of their origin. The most common opinion to-day is that each of the two paired forms is a 'bona species' and that the non-parasitic species originated from the parasitic one.

Some previous authors thought that the parasitic form had become non-parasitic through having come to live in a habitat where they could not find suitable hosts. Recently Young⁴ and Leach⁵ advanced the suggestion that this phenomenon is similar to that of the neoteny or pedomorphosis: gonads maturation has been anticipated, probably by action of anterior hypophysis⁶, thus inhibiting parasitism after metamorphosis. This fact seems to be confirmed by the recent capture of female ammocoetes with mature eggs and well-developed secondary sexual characters⁶.

The lampreys of the Danube suggest the existence of a gradual stage in this process of transformation. At first, they apparently kept within fresh-water boundaries, which allowed internal migrations. Later, they stopped these migrations in fresh-water also, though retaining their nutrition stage. Finally, either on account of nutrition difficulties or because of anticipated gonads maturity, they become non-parasite, breeding without nutrition after metamorphosis.

From the observations which, so far, have been made on the lampreys of the Danube, it may be concluded that from *E. danfordi* may have arisen a non-parasitic, but morphologically similar form, which I name *E. danfordi vladylori*. This lives in the upper part of the Danube. Perhaps *E. mariae*, with some morphological differences and living in Russian streams flowing into Black Sea as well as in some tributaries of the lower Danube (Prut and some others), has a similar origin, but this hypothesis needs confirmation.

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Table 1 RELATIONSHIPS AMONG THE PAIRED SPECIES OF LAMPREYS

| Genus | Parasitic species | Non parasitic forms | Habitat |
|---------------------|---|--|--|
| <i>Ichthyomyzon</i> | <i>I. uncinatus</i> <i>I. castaneus</i> <i>I. bellum</i> <i>I. fluviatilis</i> | <i>I. fossor</i> <i>I. gageri</i> <i>I. greeleyi</i> and <i>I. hubbsi</i> <i>I. planeri</i> | Great Lakes and northern region of the Mississippi basin Western region of the Mississippi basin Eastern region of the Mississippi basin |
| <i>Lampetra</i> | <i>L. japonica</i> <i>E. danfordi</i> | <i>L. japonica lessleri</i> <i>E. danfordi vladylori</i> | West and southern Europe (Atlantic and Mediterranean tributaries except Adriatic and Black Sea tributaries) North Europe and North Asia (Glacial and Pacific Ocean tributaries) Danube |

BACTERIOLOGY

A Non-Gummy Chromogenic Strain of *Azotobacter vinelandii*

BECAUSE of the widespread use of *Azotobacter vinelandii*: Wisconsin strain O, in biochemical studies recent observations concerning colonial types obtained from transfers of this strain are worthy of more general knowledge. As many investigators have noted (private communications) cultures of this strain at times become more 'gummy' than usual, and their further use for physiological or biochemical studies is difficult. Although we have attempted in the past to isolate a non gummy strain by selection of colonies such efforts have been only temporarily successful.

A *vinelandii* strain O was streaked on modified Burks nitrogen free agar plates¹. Differences in colonial morphology were readily evident within 18 hr of incubation at 30°C, when colonies were examined with the low power of a compound microscope or within 48 hr, when colonies were examined with the unaided eye. Colonies were obtained which differed in size, gumminess or pigment production in proportions that depended on the origin of the culture. The stability of these colonial characteristics was checked by streaking the cells of a well isolated colony on a fresh agar plate: two colony types were chosen for further study.

A gummy colony type that did not elaborate a pigment was easily recognized during microscopic examination of colonies, since at a magnification of 100 individual cells could be seen to be well separated by a clear slime. A non gummy colony type was dense, yellow, and free of slime. Since a colony composed of both bacterial types was easily recognized, the selection of a pure culture of each strain was made only from colonies that were homogeneous by microscopic examination. After a limited number of streakings it was evident that a pure culture of each strain had been obtained. The non gummy variety henceforth to be designated strain OP produced a yellowish green fluorescent pigment that is characteristic of other strains of *A. vinelandii*. Each isolate grew readily in Burks's nitrogen free liquid medium in shake flasks and fixed nitrogen as shown by total nitrogen analyses by the Kjeldahl method. Shake cultures of strain OP did not become gummy, whereas those of the other strain did. Even after numerous transfers in liquid or solid media strain OP remained non gummy, and during frequent examination of isolated colonies no gummy colonies were observed. The two strains had cells with a similar size and form with peritrichous flagella. Both strains would be distinguished from members of the *Azotobacter agilis* group on the basis of cell size and mannitol utilization². A *vinelandii* strain OP, which resembles very closely the first culture of *A. vinelandii* to be isolated³ will be deposited with the American Type Culture Collection.

It is appropriate to mention again the frequent observations (private communications) that cultures of *Azotobacter* spp may carry contaminants which are not detected unless special care is taken to search for them. Winogradsky⁴ observed that cultures of *Azotobacter* spp were impure even with primary isolation from natural material because of the limita-

tions of the standard method of isolation by plating. In nitrogen free media contaminants unable to fix nitrogen remain latent until nitrogenous products are released by the *Azotobacter*. Microscopic examination of colonies on solid nitrogen free media may reveal contaminants as satellite colonies. The use of sugar free peptone media recommended by Burk and Burris⁵ is convenient to detect contaminants since these generally grow well in such media while the *Azotobacter* do not. Accordingly the isolation of a pure culture of *Azotobacter* is best carried out when colonies are selected by microscopic examination.

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N,O-Diacetylneuraminic Acid and N-Acetylneuraminic Acid in *Escherichia coli*

DURING the course of an investigation of the biochemical and biological properties of endotoxins extracted from various Gram negative bacteria, chiefly several *Escherichia coli* strains we found and reported briefly¹ on the presence in some of these endotoxins of a material having the colour reactions of a sialic acid. The bacterial lipoproteins and lipopolysaccharides which yield this material were prepared by the phenol water extraction method of Westphal², separated from accompanying nucleic acid and exhaustively dialysed. The sialic acid is released from this large molecule only upon mild acid hydrolysis and we, therefore, proposed that it forms an integral part of the cell wall of these bacteria. Members of the sialic acid group had been found previously mainly in mammalian tissue. Barry and Goebel³ had reported the elaboration of a sialic acid like material, colominic acid by a specific strain of *E. coli*. Barry⁴ has since reported this to be a simple polymer of N-acetylneuraminic acid.

We now wish to report the isolation and identification of both N-acetylneuraminic acid and N,O-diacetylneuraminic acid in several strains of *E. coli*.

Washed living cells of *E. coli* O15:H15:H15⁺ contain a minimum of 1 per cent neuraminic acid on dry weight basis which is released optimally by hydrolysis in 0.1N sulphuric acid for 30 min at 80°C. Such hydrolysates neutralised with barium hydroxide, were freed of cations by passage over a column of Dowex 50 X 8 resin in the H⁺ cycle. The neuraminic acids were adsorbed from this effluent by passage over a Dowex 2 X 8 acetate resin. After washing with water, the column was gradually eluted with 2 M sodium acetate-acetic acid buffer at pH 4.8 and distilled water in equal volumes so as to yield a first-order relationship of volume to buffer concentration in the eluate⁵. The entire method is a modifica-

cation of that of Svennerholm⁷. The peak of resorcinol and *p* dimethylaminobenzaldehyde reactive material appearing at 0.4–0.5 *M* is composed of 40–60 per cent neuraminic acids with a small portion being the diacetyl compound and the remainder the *N*-acetyl derivative. Two other broad peaks are eluted which contain neuraminic acid in combined forms, probably as saccharic peptides or as nucleosides and nucleotides. These are being examined at present.

The two neuraminic acid derivatives are separable by paper chromatography in a number of systems. When the two components were compared in four different solvent systems with *N*-acetylneuraminic acid⁸ and *N*,*O*-diacetylneuraminic acid⁹ no separation from authentic material was seen. Fig. 1 is repre-

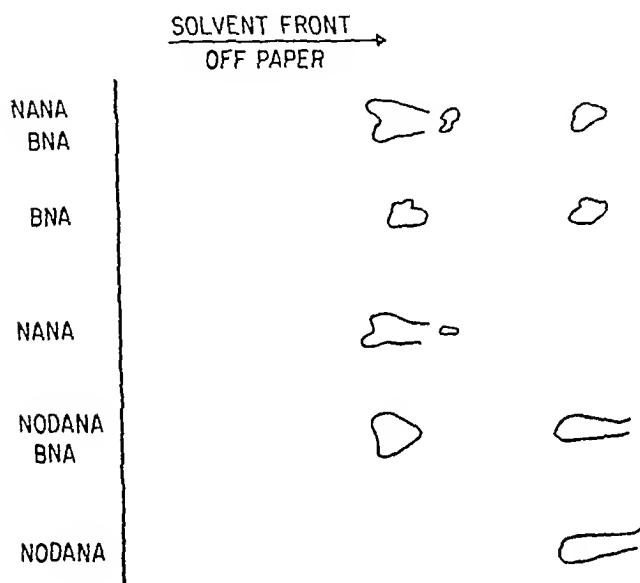


Fig. 1. Paper chromatographic separation of bacterial neuraminic acid (NANA) into *N*-acetylneuraminic acid (NANA) and *N*,*O*-diacetylneuraminic acid (NODANA). System: ethyl acetate-pyridine-acetic acid-water (5.5-1-3). Spray: *p* dimethylaminobenzaldehyde (0.5 gm) and trichloroacetic acid (5 gm) in 20 ml of 50 per cent aqueous ethanol plus 60 ml *n*-butanol.

sentative of these results in one system (ethyl acetate-pyridine-acetic acid-water 5.5-1-3). The solvent front has been run off the paper in order to enhance any subtle differences in mobilities.

The slow-moving component gives positive resorcinol and orcinol reactions, is direct Ehrlich positive, ninhydrin negative and reacts as an α -keto acid and a reducing sugar. The adsorption spectrum of the resorcinol pigment formed from this component is identical to that obtained with authentic *N*-acetylneuraminic acid-resorcinol pigment. Tests for hexosamines, 3-*O*-substituted hexosamines, pentoses, 5-methylpentoses and hexuronic acids are negative. It does not contain any detectable glycolyl substituent by the assay of Klenk and Uhlenbruck¹⁰ nor is it separable from authentic *N*-acetylneuraminic acid on paper chromatography in *n*-butanol-*n*-propanol-0.1 *N* hydrochloric acid (1-2-1)¹¹.

The faster component reacts as *N*-acetylneuraminic acid in all the above reactions and, in addition, contains an *O*-acetyl group which has been isolated as the hydroxamate¹² and found identical with authentic acetylhydroxamate on paper chromatography in water-saturated *n*-butanol. This component is found in varying concentrations after ion-exchange resin purification and is unstable in solution even at low

temperatures. It appears to degrade to the *N*-acetyl derivative.

Treatment of partially purified bacterial neuraminic acid mixtures (~30 per cent as *N*-acetylneuraminic acid) with the bacterial aldolase of Comb and Roseman¹³ causes a loss (50–60 per cent) in resorcinol reactive material which agrees quantitatively with the formation of puuvic acid as determined enzymatically with lactic acid dehydrogenase. An *N*-acetylhexosamine, which cannot be distinguished from *N*-acetylmannosamine by chromatography on borate treated paper¹⁴, is also produced by enzymic action.

As the endotoxins extracted by the phenol water method are lipoproteins and have been shown by Weidel and Primosigh¹⁵ to derive from the exterior, non-rigid portion of the wall, it is probable that no structural significance vital to the integrity of the cell can be assigned to the bacterial neuraminic acids as has been indicated for muicamic acid by Work¹⁶. Other possible functions such as bacteriophage attachment, virulence or *K* antigen specificity are attractive hypotheses only.

Recently, Barry¹⁷ has suggested a correlation of *K*1 antigen and neuraminic acid occurrence in *E. coli*. It should be noted, however, that the two strains found by us to date to have the highest neuraminic acid content are an O₁₁₁B₄ (*K*58) and an O_{2A} (*K* untypable). This point is being examined further.

Although the colominic acid producing *E. coli* reported by Barry^{3,4} has been found by us to yield an endotoxin containing neuraminic acid and thus presumably has neuraminic acids in its cell wall, the level present in its endotoxin is no greater than that found in the lipopolysaccharides extracted from either of the other two strains. We believe that *N*,*O*-diacetylneuraminic, or possibly both this compound and the *N*-acetyl derivative, exists as a structural component in the cell wall of certain bacteria. A survey is in progress to determine the validity of this point.

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NUCLEAR POWER AND ITS DEVELOPMENT

SIR JOHN COCKCROFT is reported to have expressed the opinion on April 26 that in 1966 some 25 per cent of the requirements of the United Kingdom for electricity would be met by nuclear generation, 50 per cent by 1975 and 100 per cent by the end of the century. Questions asked in the House of Commons on June 8 indicate a disposition to allow political and social considerations to over-ride, if not distort, the technical and economic aspects, and there have been other attempts to make the effect on the coal industry the deciding factor in determining the development of nuclear power. The implications of technological change have been ignored, as has the effect of development on the cost of electricity supplied by nuclear power stations, which Sir Christopher Hinton stressed very strongly in his Axel Axelson Johnson Lecture delivered at Stockholm on March 15 1957.

In his reply on behalf of the Government, the Paymaster General was emphatic that the programme for the development of nuclear energy in Britain over the next few years was arranged after careful consideration, and it certainly could not be upset on any temporary considerations. An admirable broadsheet, 'Prospects for Nuclear Power' (No 431, March 1959), issued by Political and Economic Planning is well designed to remove misunderstandings and facilitate an objective approach to this problem, in which it is extremely difficult to separate at all sharply the technical and economic from the political and social elements. Although the broadsheet is particularly concerned with the world position and Britain's export prospects, it includes a lucid discussion of the impact of nuclear power which deserves to be widely read. The brief paragraph on the position in the United Kingdom points out that by 1966, when the dozen or so nuclear power stations required to supply the target capacity of 5 000-6 000 MW are in operation the cost of the electricity generated should be almost competitive with that from other types of power stations wherever sited, this answers the criticism implied in the questions in the House of Commons.

The broadsheet points out that by 1966 the nuclear power stations will be supplying a quarter of the electricity used in Britain and doing the work of 18 million tons of coal a year, and that it is estimated that the cost of generating electricity from the largest of the stations now under construction that at Hinkley Point, will be between 0.58d and 0.66d per kWh, compared with 0.53-0.64d for an up-to-date coal-fired plant. The cost of electricity from the largest station now being built is competitive with that from a high-efficiency coal-fired station built on the same site. Moreover, for the later stages of the present programme when all new generating plant may be nuclear Britain is considering types of reactor that will be cheaper to build and more efficient

to operate, as well as able to accept recycled plutonium to replenish the burnt fuels, and these types should produce electricity more cheaply than conventional plants. Two such reactors are the gas-cooled heavy water moderated reactor and the advanced gas-cooled reactor—an experimental version of the latter is already being built at Windscale.

These facts, which were essentially given by Sir Ian Horobin in moving the second reading of the Electricity (Borrowing Powers) Bill on January 20 sufficiently display the tendentious character of the question to which Sir Ian replied in Parliament on June 8. It should also be remembered that the high temperature gas-cooled reactor is to be studied at Winfrith Heath, and the sodium-cooled fast breeder reactor at Dounreay, both within the subsequent period in mind when reactors will be needed to take over an increasing proportion of the base load. From the Dounreay reactor, to be in operation this year, will come the data necessary to enable fast reactors using plutonium fuel to be integrated with existing thermal reactors. This will improve the burn up of natural uranium to somewhere near the theoretical limit. The reactor programme is also supported by large facilities for research and an extensive research programme while production and fuel processing facilities are also well developed in Britain, and capacities are sufficient to meet the needs of other countries. Lord Mills the Minister of Power, stated explicitly in the House of Lords on March 3 that the nuclear power programme for 1964 onwards had not yet been determined.

This position, however, needs to be set against the general background outlined in the PEP broadsheet which stresses too the dynamic nature of the energy position both nationally and internationally, and the way in which non-economic influences often determine the most economical way of meeting demands for energy. The great promise of nuclear energy is that with ample resources of uranium and thorium, and the high energy content of each ton of raw material which makes transport a negligible factor it will eventually provide all nations with an unlimited and virtually indigenous supply of energy at an economic cost. Although this lies well into the future, nuclear energy should make an immediate though modest contribution particularly in Europe.

The factors which limit this contribution must be carefully noted in an objective assessment of the situation. First for technical reasons nuclear fission reactors are only efficient when employed in large units. The large amounts of electricity produced from each nuclear power station can in the near future be generated at an economic cost only if they can be used to the maximum. This is only possible where electricity systems are fully developed in a grid network such as an industrial area provides.

Accordingly, nuclear energy is as yet unlikely to help under-developed countries, nor will it be suitable for some time for the direct production of heat where small units are normal. In Europe, where fossil fuels are expensive, nuclear energy should be competitive within the next ten years for what is called base-load operation, that is, power-stations operating virtually all around the clock feeding electricity into the grid.

The second factor is that small coal is particularly suitable for power-stations, and the proportion of small-coal production is continually growing as more coal is mined by mechanical methods. This coal can only be burnt efficiently in very large plants and its use is thus almost confined to power-stations. Criticism of Britain's nuclear-power programme arises largely from this fact that nuclear energy is suitable for the production of electricity only in the conditions to which the growing quantity of small coal is also suited.

The third factor is that production of electricity at a price competitive with conventional power only means an additional supply of electricity and not the introduction of a cheap new fuel. Electricity has its own particular advantages, and its use in Britain is continually growing, but it is not, at present costs, an economic substitute for other sources of energy for many purposes. The nuclear-power programme should enable those needs to be met more easily, but it will not obviate the need for other fuels for these purposes. Nevertheless, the development of nuclear energy holds great promise, and Britain's prompt start has given her an early lead in tackling the vast technical problems involved, and only the U.S.S.R. and the United States have programmes at all comparable in size to the British. Moreover, the British power programme, based on the gas-cooled natural-uranium reactor, is the only large-scale programme which is being carried out in a Western country, and the British type of reactor has been proved in operation, having supplied electricity to the grid for some two years.

Nevertheless, the survey in *Planning* of the prospects for British exports of nuclear power-stations and related fuel and equipment leads to the conclusions that the prospects for British firms to export reactors are not so bright as they were once thought to be. Nuclear power is indeed regarded as the most helpful long-term solution of the fuel problem in many European countries, and the principal countries are in a position to exploit nuclear power without too much difficulty. They possess the necessary scientific and technical skills and the capacity to build equipment, and they will therefore want to develop their own nuclear industry as fast as they can. They may buy one or two reactors from other countries, as Italy has done, in order to gain experience of operation and construction, but after that they will probably do more and more of the work themselves. They are unlikely to set up their own fuel-processing plant, partly because of expense and partly because most European countries have no uranium deposits and are unlikely to obtain uranium

without some control against the production of plutonium. France is the one country of Europe which will have a self-contained nuclear industry.

In the Scandinavian countries, and possibly in Spain and Portugal, competition is likely to be fierce, and although the Calder Hall power-station has impressed potential customers with the merits of the British type of reactor, steady and impressive publicity is required. Outside Europe, the first markets—for the next ten years at least—will be in Japan and India, but China is likely to be tied to Russian developments at first. Several countries in Latin America might prove customers for the British type of large power-station reactor.

Whether British or American power reactors are bought—and these are the only countries at present offering to sell power reactors and supporting the offer with a fuel service—the PEP broadsheet suggests that the future of the nuclear reactor export market is closely tied to a successful small reactor. A cheap small reactor similar to that for moderately powered gas-turbine and diesel-powered generating sets could transform areas which are now under developed. Here, since British efforts have been concentrated on the Calder Hall type, Britain is less favourably placed than the United States to design reactors for special conditions. Without the urgency of Britain's fuel problems, the United States has been able to experiment with a wide variety of types of reactor, and this could prove an important advantage in meeting the future export demand for a small and flexible reactor system. Besides this, the United States is at present the only country that can supply enriched uranium for reactors abroad.

Britain is now taking the preliminary steps to enable her to meet the demand for small reactors, but it is possible that the Soviet Union, although it has not yet been active in export competition, could also have an advantage over Britain in the matter of reactor types. Nevertheless, the broadsheet points out, reactors are not the only product that can be exported. The one part of the British power-reactor which is not manufactured by industry is the fuel element. The rest, including ancillary equipment, such as turbines, generators, handling gear, processing equipment and control instruments, are all the products of industrial firms. Lord Mills, it is true, has directed attention to the more limited opportunities in the near future for new consortia of firms with design teams trained by the Atomic Energy Authority and which would be capable of tendering for the construction of complete nuclear power-stations, but at the same time, he emphasized the opportunities for the manufacture of small reactors, including research reactors.

Nuclear energy, as the PEP broadsheet puts it, means that there will be an increased demand for those products which British firms can supply as cheaply as any of their competitors, but the prospects for British exports of nuclear reactors and equipment are not determined solely by the competitive ability of British firms. One dominant factor will be the political agreements that the Government

is able to make Marketing nuclear reactors is not purely a commercial undertaking, for, as the broad sheet duly notes international politics are involved and unless this is clearly understood British chances of building up an export trade will be small.

For this reason alone it is important that Britain should establish close and satisfactory relations both with the International Atomic Energy Agency and the European Organization for Nuclear Research and also with Euratom—the European Atomic Energy Community and its six members. A second factor however to which Planning does not direct attention is that of scientific and technical man power. Although in the stricter sense this lies outside the scope of the broadsheet, it is probably the ultimate factor on which the prospects for British development of nuclear energy depend. Unless the resources of scientific and technical man power in Britain are fully developed and effectively used, Britain is unlikely to be able to seize the opportunities that nuclear energy will bring—even to secure all the advantages which its development in Britain might offer to the economy of the country—still less to hold her own in the keen competition forecast in this broadsheet. Nor is this simply a matter of training sufficient scientists and technologists: it is also a matter of seeing that they are wisely used that our organization and administration of research are adequate and in balance and that the administrators and statesmen called upon to handle the complex and interlocked technical, economic and social problems which the development of nuclear power will bring are competent to give due weight to all the scientific and technical issues no less than to the economic or political aspects of the situation.

For some months Euratom experts have been drafting a new and realistic programme for the six member countries, taking account of changing oil and coal prices. Since the PEP broadsheet was issued, the report on this programme has been finished, but owing to disagreement at the top it has been withheld and is not to be published. This disagreement has jettisoned Euratom's plans for all but the 1,000 megawatt programme being carried out with American aid, and it is obvious from the broadsheet that most of the chances open to British industry of tendering for foreign nuclear power stations have likewise disappeared.

Sir Ian Horobin took a far more confident view in replying in an adjournment debate on the nuclear power programme in Britain in the House of Commons on July 1. He confirmed that latest figures gave the cost of electricity from conventional stations as 0.5-0.65d a unit compared with 0.65-0.7d for electricity from nuclear power stations, but he emphasized that the statement that nuclear energy to day is 40 per cent more expensive than conventional power was based on a comparison of the cheapest possible coal and the dearest existing nuclear energy. Sir Ian suggested that the real difference is probably more like 15-20 per cent and he pointed out that in view of the 70 per cent rise in the price of coal over the past ten years it would have been

unrealistic to base policy on the assumption that coal would not be 5-7s a ton dearer than it is now. He also thought that the price of uranium will fall when the present contracts expire and that this factor with a further slight rise in the price of coal, is likely to decrease the margin of 15-17 per cent against nuclear energy, and that the price of generating electricity by nuclear energy is likely to touch that of generating by coal in the late 'sixties.

Sir Ian Horobin insisted that the British nuclear power programme is a very carefully considered whole and that it is probable that what may be called the Calder Hall type of reactor has several years of valuable development before it. About 1961 the advanced gas-cooled reactor should become critical and if this is successful the first commercial type may be in operation about 1965. The work done with the fast breeder reactor now being developed at Dounreay has been very successful and a period of low power testing at Dounreay is expected to begin this summer. If all goes well we may hope to have this type in operation by about 1970, and its low capital cost and its place in the balanced programme offer exciting possibilities particularly in flexibility. By that time a substantial number of stations of the Calder Hall type would be in operation all producing plutonium. We must bear in mind Sir Ian said, the possibility of a situation arising when it would be possible to build very much larger stations than originally conceived and that perhaps only about half a dozen more stations would come into the programme. He repeated that we cannot afford to run any risk of completely unbalancing the structure of the industry in Britain by interfering with the present programme. When that programme is complete further decisions will be required and although preliminary consideration is being given by the Government to the subject, it is not thought that it is necessary to decide for a further year or two what stations should be built after 1965. It is very important he said that everyone should realize that a nuclear power programme on the scale of that in Great Britain must be a long term, carefully balanced programme and that it cannot be interrupted in response to short term considerations. Britain is now the major civil nuclear power, and the need for thought and care in investment and design are correspondingly great.

DARWIN WITHOUT MODERN SCIENCE

Darwin and the Darwinian Revolution

By Dr Gertrude Himmelfarb Pp ix+422. (London Chatto and Windus Ltd 1959) 42s net

AN adequate study of Darwin his scientific achievements and the result of his work in all the fields of human endeavour which they have affected makes rigorous demands on the competence of whoever attempts to write such a book. Dr Himmelfarb brings to her task a concentration of interest and of effort, the former of which is passed

on to the reader by the sustained vigour and elegance of her style and the skill with which the book is constructed, while the mastery of her technique hides the laboriousness of the work involved.

She has read practically everything there is to read by Darwin and on Darwin, including manuscripts hitherto unpublished, and has subjected the material to lucid analysis in terms of the history of Darwin's life, experiences, contacts with other persons, researches, results, doubts and beliefs. He is situated in his intellectual environment, his home life, his ailments real or imagined, and his place in history. The social, scientific, religious, political and general public climates of his day are vividly portrayed, and there can seldom have been a work of biography undertaken with such bibliographical care.

But while it would be difficult to exaggerate the excellence of this book as a contribution to the history of the events, ideas and arguments as a result of which Darwin produced his theory of evolution by natural selection, the case is altered when it comes to the evaluation of this theory in terms of the present state of scientific knowledge, because Dr Himmelfarb's work is imbued with a relentless aversion to natural selection, pursued by means of a skilful and acute dialectic without reference or regard to the results of scientific research during the past fifty years. Indeed, this is directly implied by the statement (p 366) that "the present status of Darwinism has not altered much since 1860, when Huxley pronounced it to be not an established theory but a tentative hypothesis". When she tries (p 368) to substantiate such a view to-day by quoting William Bateson, she gives herself away at once.

That the author is not familiar with, or prefers to ignore, the growing edge of scientific knowledge by observation and experiment during the past fifty years appears from statements such as the following (p 269) "In the experiments of Mendel and de Vries, new species appeared suddenly in the form of mutations". Mendel neither claimed nor obtained any such results. On the contrary, his genius lay in selecting for his experimental material strains which differed only in one or two characters, differences immeasurably inferior to those of specific rank. As for de Vries's 'mutations', it has long been recognized, thanks primarily to the work of T. H. Morgan and his colleagues A. H. Sturtevant, C. Bridges and H. J. Muller, that they are not mutations at all, but the results of a rare method of 'sporting' by permanently heterozygous strains technically known as the 'crossing-over of balanced lethals'.

When the author attributes to neo-Darwinians the statement (p 270) that "only the smallest mutations could be favourable and that such favourable mutations were in fact so rare a phenomenon that without natural selection not even a fruit-fly, let alone a man, could have developed", and concludes, "Thus it became the very paucity of variations, the very improbability of their concurrence, that was now made to tell in favour of natural selection", she makes the elementary and very outdated mistake of thinking that mutation is the only supply of variation. It has long been known that recombination of genes is enormously greater as a source of supply of variation than mutation itself, and it produces gradual change.

Dr Himmelfarb has not grasped the fundamental significance of the work of Sir Ronald Fisher, whom she calls "the mathematician". He showed, first, that natural selection of genes within the gene-complex

is a universal phenomenon, which explains why the genes gradually become either dominant or recessive. This is how evolution proceeds. Mendelian genetics itself provides evidence of Darwinian selection. He showed, secondly, that selection is so much more powerful than mutation, that no mutation can have the remotest chance of becoming a normal component of a population if there is the slightest degree of adverse selection exerted against it. He showed, thirdly, that as all organisms are tolerably well adapted to the conditions under which they live in their present environment, the vast majority of mutations are bound to be deleterious to the organisms in the conditions under which they arise, and this proves that any attempt to explain evolution by an appeal to causes which might be supposed to impart favourable qualities or directions to mutations through 'inner feelings', '*élan vital*', 'urges', or the transmission of somatic modifications, is killed stone dead at the start. "Every theory of evolution which assumes, as do all the theories alternative to natural selection, that evolutionary changes can be explained by some hypothetical agency capable of controlling the nature of mutations which occur, is involving a cause which demonstrably would not work even if it were known to exist." The fact that wild species in Nature are highly heterozygous shows that mutant genes, subjected to adverse selection when they first arose, remain as recessives in the gene-pool, and function as a reserve which is drawn on when environmental conditions change, and some of these genes then become dominant by selection in the gene-complex, and established in the population. It can also be shown that selection is exerted in favour of the heterozygous state *per se*.

Results such as those should find a place in any modern appraisal of the position of natural selection at the present stage of knowledge, but Dr Himmelfarb has preferred to say (p 276) that "Posing as a massive deduction from the evidence, it (natural selection) ends up as an ingenious argument from ignorance". The word "ignorance" is a double-edged weapon when it is used by an author without any indication of awareness of the experimental results obtained by such distinguished scientists as E. B. Ford, C. D. Darlington, P. M. Sheppard, A. J. Cain, W. H. Dowdeswell, H. B. D. Kettlewell or C. H. Waddington, to mention only those working in Great Britain.

The intercalation of quotations from Darwin, labouring in his unavoidable ignorance of the principles of Mendelian genetics, to disparage arguments which have since been substantiated by the results of modern experimentation in natural selection is regrettable. When Darwin wrote a hundred years ago that "we are far too ignorant, in almost every case, to be enabled to assert that any part or organ is so unimportant for the welfare of a species that modification in its structure could not have been slowly accumulated by natural selection", he was quite correct, and it was merely tendentious for Dr Himmelfarb to say (p 276) that "three negatives do not normally constitute a positive". When Darwin went on to say that "it would be extremely bold to maintain that no serviceable transitions are possible by which these (electric) organs might have been gradually developed", he was prophetic, as Dr Lissman's researches have since proved. The initial stages in the evolution of flight in birds, colour-vision, or the whale's adaptation for avoiding *caisson*-disease, to mention only a few additional striking

cases have all been shown to be capable of conferring survival value from the inception of the improvement.

The statement (p 277) that "The eye is obviously of no use at all except in its final, complete form" completely ignores the comparative anatomy, embryology and physiology of the lower chordates which show how light-sensitive cells in the epidermis have been brought into place, from the surface of the skin into the neural tube and then into the retinal layer of the eye-cup, and are functional at each stage. Dr Himmelfarb (p 279) accuses Darwin of invoking the perfection of the eye at the same time as he quoted Helmholtz on the inadequacy and imperfection of the eye, but in the 'Origin of Species' (World's Classics edition, p 180), Darwin wrote, "his marvellous yet not absolutely perfect charactera". What Darwin claimed was that natural selection confers improvement, and in the case of the vertebrate eye this is undeniable to anybody familiar with the visual organs in *Amphioxus*.

The statement that "the persistence without change of any form over a long period of time is difficult to explain by natural selection" is particularly unfortunate, because so long ago as 1878 T H Huxley pointed out that natural selection is the only mechanism that can account both for change and for stability, and as recently as 1952 E B Ford supplied the genetic explanation of this by showing that the non continuation of genes and the rarity of mutation produced stability, while the power of recombination of genes can produce endless variability, under the control of natural selection in each case.

How can selection, knowing nothing of the end or final process function which the only test is precisely that end or purpose?" asks Dr Himmelfarb (p 277). The experimental results of investigations on the evolution of industrial melanism in moths show how the selective taking by predators of prey ill adapted to their environment can be seen going on, and the intensity of the selection pressure can be measured with mathematical precision. Mimetic resemblances in butterflies are improved and confer survival value in mathematical relation to the prevalence of distasteful models. The method of capture marking release and recapture enables the predations by thrushes on snails of different colours to be correlated with the seasonal variation of vegetation and the longevity of different genotypic types of moths to be measured in terms of concrete units of time. That is how selection actually operates.

Astonishingly out of date is the statement (p 284) that "the entire discussion of sexual selection is anthropomorphic in its basic conception, for whether the coloration of a bird is judged to be either beautiful or monstrous it is by human standards that the judgment is made. It is now quite clear that the beautiful and monstrous colours in question, to which must be added structures, attitudes and behaviour patterns used in courtship function, as Sir Julian Huxley, N Tinbergen and many others have proved, as stimuli by which a threshold physiological condition in the partner is reached and a release mechanism set in motion. There is no question of any anthropomorphic aesthetic choice.

It is quite correct that many of the examples which Darwin in thought conformed to the principle of sexual selection have since been found to owe their origin to other than epigamic causes, such as warning marks, recognition or threatening defensive characters. But some characters, as those of the male peacock ruff, or argue pheasant, are good examples of the

sexual selection in Darwin's sense, as Sir Julian Huxley showed more than twenty years ago. Yet Dr Himmelfarb concludes (p 300) that "Sexual selection has all the faults of natural selection and more: the suspicious faculty with which it can be made to explain anything and everything, the manipulation of evidence for whatever purposes are convenient, and the invocation of ignorance when all else fails." Here again the historical present tense is used but there is nothing to show that the author does not intend it to apply to the present and that the remarks made represent the actual state of scientific knowledge.

Turning now to another discipline of science we find Dr Himmelfarb stating (p 271) that, "Geology, however, has been notably unforthcoming and instead of being the chief support of Darwin's theory, it is one of its most serious weaknesses." It is difficult to believe that such a phrase could have been written in 1959 for 1959. She goes on to say that "It might have been expected that in those cases where the geological record is more or less complete we would find closely graduated varieties of species existing at the beginning and at the close of the period. Yet even here we do not find such a graduated series." It can only be concluded that she has not held in her hands the series of ammonites from *Laproceras* through *Androgynoceras*, *Amaltheus* to *Pleuroceras* demonstrated by L F Späth nor the series of *Alveolites* demonstrated by D Nichols. As for the series of horses Dr Himmelfarb's information is not more recent than that of T H Huxley in 1870. Actually the fossil series of ancestors of the horse is now so good that George Gaylord Simpson has been able to measure the time required for the conversion of a species into another and the length of life of a species (two million years in horses). T S Westoll had done the same for fish which evolve at different rates. Simpson was also able to show that the geological record in some places is so good that it is now possible to calculate the degree of variability of fossil species and to prove that it is not correlated with their evolution rate. This is further evidence that natural selection not mutation, controls the rate and direction of evolution.

The statement that the geological record is one of the most serious weaknesses of Darwin's theory is ridiculous. Even in his day, the Mesozoic mammals of the Stonesfield Slate had been discovered and that most beautiful of all known fossils, *Archaeopteryx* was known showing such a perfect transition between the reptilian and the avian stages of that line of evolution that it can be regarded as ancestral to all later birds. It also demonstrates the way in which one vertebrate class became converted into another, by piecemeal transformation of bits of the body one by one, a process called mosaic evolution. Other examples of representatives of precursors are *Jamoythus* between the lowest chordates and the fishes, *Ichthyostega* between fishes and amphibians, *Seymouria* between amphibians and reptiles, *Ichthyosaurus* between reptiles and mammals, *Australopithecus* between apes and man. All these and countless others are a striking vindication of Darwin's view.

The sudden appearance in the geological record of representatives of important groups (such as the gastropods or vertebrates) is no fly in the ointment of Darwin's theory, and it receives a logical explanation from the obligatory rarity of tentative initial types and from the principle of candelstick evolution.

tion' of young stages without hard parts and therefore not preserved as fossils until they became adult in their new state. As for the abrupt appearance of fossils in "the lowest fossiliferous strata", the number of fossils discovered in Pre-Cambrian deposits goes on increasing and now includes algae and fungi in which eight amino-acids could still be recognized although they are 1,700,000,000 years old.

Dr Himmelfarb states (p 310) that chemists showed that all the pieces of the 'Piltdown find' revealed the same fluorine content. This was not the case. The earliest estimations by K. P. Oakley and C. R. Hoskins showed fluorine percentages varying from 3.1 to less than 0.1, estimations correct to within a range of ± 0.1 . This proved that all the 'specimens' were not Lower Pleistocene. Subsequent estimations by more refined methods showed that the latest of these were not even Upper Pleistocene. But if Dr Himmelfarb really thinks that the exposure of the Piltdown fraud "leaves the theory (of evolution), after a century of search, without the much desired link", *Proconsul*, *Australopithecus*, *Pithecanthropus* and Neanderthal man are there to bear witness to what Sir Wilfrid Le Gros Clark has demonstrated from them about the so-called 'much desired link'.

If ever the cult of personality should attempt to invade science, it would cease to be science, and if scientists hold Darwin in honour to-day, it is because the evidence, all the evidence, and nothing but the evidence, provided by the observations and experiments of biologists who have undertaken research in this field, has shown that the natural selection of mutant and recombined genes is the mechanism whereby the evolution of plants and animals in Nature has been brought about.

GAVIN DE BEER

THE FAITH OF A REALIST

Blaise Pascal

The Life and Work of a Realist. By Ernest Mortimer. Pp 240+4 plates (London: Methuen and Co., Ltd., 1959) 21s net.

MUCH of Pascal's work, and several books about him, are readily available. What is not so easy to obtain is an assessment of his place in history in keeping with the pedestal upon which his fellow-countrymen are nearly unanimous in placing him. Furthermore, to find an answer to the question as to how much he means to us to-day is assuredly a rewarding task. These things the author has done and the result is a notable achievement. Pascal emerges as a character of gigantic intellectual and spiritual stature, weak of body, indomitable of will, and relentless in his quest for truth.

In the present context, we may perhaps leave aside the well-known facts of his mathematical genius, his contacts with great minds like those of Descartes, Fermat and Desargues, and concentrate upon his theory of knowledge (Chapter 11), which developed from the intense strife going on within him, and which burnt itself out as a consuming fire. Pascal was no mere dreamer, but on the contrary passionately concerned with making things work. His technical skill, if he were alive to-day, would lift him to the summit of electronic computing, and to the highest triumphs of cybernetics and servo mechanisms. In this sense he was a realist,

his faith transcended it, however, as he reached out towards that greater truth only to be found in charity.

It is from some such position as this that we can best approach Mr Mortimer's treatment of Pascal's theory of knowledge, for it is essentially here that the present volume finds much of its *raison d'être*. Here too is Pascal's message for the world to-day.

The central concept is that of *le cœur*. By this Pascal did not envisage something "cardiac rather than cerebral". He uses the phrase to cover a species of synthesis, a type of thought in which analysis gives place to cognition. It seems as if this came out of a state of mind akin to despair, in that, for example, the propositions of Euclid needed acceptance of something "given" before any progress could be made, and thus real knowledge could never be obtained. In this, he was in effect anticipating Gödel's theorem, and the failure of Hilbert to construct a consistent system of mathematics purely mathematically. But for Pascal, truth is not apprehended by reason alone, which can only yield statistical properties.

Mr Mortimer is at pains to point out that Pascal did not draw this inference himself, it is nevertheless the gist of his whole argument. Here indeed is a startling preview of twentieth-century science, quantum theory, operationism and all. Nevertheless, the part to be played by *le cœur* remains, and it stands supreme if we are to 'know' the world around us. But what is it, if it is not rational knowledge? Pascal gives his answer—"Le cœur a ses raisons, que la raison ne connaît point". Metaphysics may be out of fashion at the moment, it looks, however, as if the faith of a great realist may have elevated such a discipline to a position otherwise unheeded.

As people exclaimed in another setting altogether, "We have seen strange things to-day". The author has written a book modest in compass but great in concept. He has brought Blaise Pascal, his tempests stilled at the last, into the centre of contemporary thought.

F. I. G. RAWLINS

ENZYMES—KINETICS AND CHEMISTRY

Behavior of Enzyme Systems

An Analysis of Kinetics and Mechanism. By John M. Rimer. Pp xii+317 (Minneapolis, Minn.: Burgess Publishing Company, 1959) 6.50 dollars.

Proceedings of the International Symposium on Enzyme Chemistry

Tokyo and Kyoto, 1957, organized by the Science Council of Japan under the auspices of the International Union of Biochemistry (IUB Symposium Series, Vol 2). Pp 541 (Tokyo: Maruzen 1958) n.p.

LET Dr Rimer speak for himself. In his foreword addressed to "Timid Souls" he writes, "The foremost purpose of this book, accordingly, is to make it possible for anyone to begin the book knowing substantially nothing, and to finish it an expert for all practical purposes". This is a bold ambition, even when restricted to the field of enzyme kinetics. A major adverse criticism of this book is, in the reviewer's opinion, the almost complete lack of reference to

published experimental work, one has to turn many pages before one can see on the name of an enzyme and there are virtually no numerical data given. Dr Reimer a ideal reader the ignorant but intelligent man but one, nevertheless, longing to learn would find himself bewildered by reality. Putting these criticisms aside this book is a serious piece of scholarship, and provides a useful introduction to the theory of enzyme kinetics.

In contrast to Dr Reimer's solo performance, the Proceedings of the International Symposium on Enzyme Chemistry relating to a conference which took place in Tokyo and Kyoto in October 1957, contains contributions from 228 authors. Apart from four special lectures delivered by Profs Chance (Cytochromes—their Nature and Function in Living Cells), Engelhardt ('Enzymology and Mechanism of Tissues and Cells'), Lynen ("Phosphatkreislauf und Pasteur Effekt") and Tamiya ("The Koji, an Important Source of Enzymes in Japan"), the Proceedings are divided into four sections.

The first section covers the mechanisms of enzymatic group transfer, the second, enzyme systems of hydrogen, oxygen and electron transport, the third, the formation of proteins and enzymes, and the fourth relates to enzymes and industry (interpreted to include pharmacology). Many of the contributions are in effect short reviews (2-10 pages) of specialized topics supplemented with what was in 1957 new experimental material. These articles are in general, of a high standard and are in the main very readable.

The title given to the Conference in no way restricted the range of topics, enzyme chemistry was taken to include any reaction catalysed by enzymes in animals, plants and microorganisms. Papers dealing with the action of thyroxine on isolated animal mitochondria and the role of chlorophyll in photosynthesis occur in the same section.

The majority of contributions are in English, a few in German and even fewer in French. Almost inevitably some of the papers from veterans of international conferences have appeared in substantially the same form before or since.

J. B. CHAPPELL

CHEMISTRY OF PHOSPHORUS

Phosphorus and Its Compounds

By John R. Van Wazer Vol 1 Chemistry Pp xii+974 (Now York Interscience Publishers Inc., London Interscience Publishers Ltd 1958) 208s.

THIS volume must be unique, for it gives in wide scope and considerable detail an account of the structure, the physical and chemical properties and the chemical reactions of phosphorus and all its main classes of compounds both inorganic and organic. It is also outstanding not only for the wide range of the modern scientific information which is so clearly presented, but also for the historical background of this information—each main topic has a historical introduction so that, for example, the discussion of the structure of one class of compound may range from a brief review of the theories of a century ago to a more detailed discussion of the most recent evidence supplied by nuclear magnetic resonance spectra.

The first two chapters deal respectively with the nuclear and atomic structure of the phosphorus atom and with interaction between atoms. The second chapter discusses in detail bond-energies and lengths, dipole moments, polarity of molecules, ionic radii etc. The following chapters discuss in turn various classes of phosphorus compounds. The detailed information available may be assessed from the 380 pages devoted to phosphoric acid and its compounds divided into five chapters on condensed phosphates, orthophosphoric acid, chain phosphates, ring and branched phosphates and amorphous phosphates respectively. This treatment ranges in these five chapters from the physical and chemical properties of phosphato minerals on one flank to those of the nucleic acids on the other. Throughout the book the constant comparison of the properties of the purely inorganic compounds of phosphorus and those of their organic substitution products makes fascinating reading and may well serve both to widen and to readjust the mental balance with which inorganic and organic chemists have hitherto in their different ways assessed the chemistry of phosphorus.

In the preface, the author makes an eloquent plea that the present division of descriptive chemistry into two parts, organic and inorganic, should now be widened to include a third part namely phosphorus chemistry. Many chemists will shrink from this suggestion but it must be admitted that although phosphorus chemistry contains on one hand a number of reactions which can be regarded as normal reactions of inorganic compounds and on the other hand many reactions typical of organic compounds, there lies in the centre a host of reactions and aspects of behaviour which are peculiar to phosphorus. The same statement might possibly be made of the chemistry of other non-metallic elements but the specific chemistry of phosphorus is in its range and nature much greater than that of any other element except carbon. This quality is one of the major factors underlying the vast increase in the academic and technical interest in phosphorus chemistry which has occurred during the past twenty years.

The price of this book may appear high by English standards but the volume contains an immense amount of information liberally illustrated by X-ray structure diagrams, phase rule diagrams etc. and by a wealth of valuable tabulated material. The final three appendices list in turn phosphato minerals (40 pages) giving details of each based largely on Dana's 'System of Mineralogy'; single bond energies and distances with electronegativity differences; and thermodynamic data on the compounds of phosphorus.

The book, however, is emphatically not a mere catalogued compilation of facts. In spite of the size of the book, the author has maintained to the end a critical treatment of the material under discussion and this treatment combined with the author's pleasant and lucid style gives the book a personal flavour which heightens the reader's interest throughout the volume.

The publishers are to be congratulated on the general format and printing of the book and in particular for printing references at the bottom of pages where they can be immediately noted by the reader instead of printing them in a vast huddle at the end of each chapter.

The book will be appreciated by all types of chemist, inorganic, organic, physical and phosphoric.

F. G. MANN

Suggestions to Authors of the Reports of the United States Geological Survey

Fifth edition Pp xu+255 (Washington, D C Government Printing Office, 1958) 1 75 dollars

IN the eighty years that have passed since the foundation of the United States Geological Survey, more than 3,500 volumes of scientific and technical literature and more than 20,000 different maps have been published under its auspices—an output far surpassing that of any other geological institution in the world. Throughout this long history, continuous efforts have been made to promote lucidity, consistency and uniformity in these publications, and the code of practice established by the Survey for its authors, first published in 1909, has found wide spread use outside official circles. The much enlarged fifth edition of this manual outlines the successive literary steps which a geologist-author will normally take from the beginning of an investigation to the final proof-reading of his text, maps and illustrations. It advises on matters of ethics and professional etiquette, enumerates the requirements of a well prepared manuscript, deals at length with questions of typographical style, and gives a great deal of detailed information on the form and content appropriate to reports of various kinds. More than 50 pages are taken up with sensible advice on composition and expression, forming a sort of "A B C of Plain Words" directed specifically at geologists. Not all the suggestions will be acceptable to British readers, who may be somewhat puzzled by the preferred use of 'geologic' and comparable '-ic' endings in a country with a Geological Survey and a Geological Society. But there is no similar guide produced on the eastern side of the Atlantic, and, with appropriate warnings, the work could profitably become prescribed reading for all post-graduate students of geology, as a brake on the present over-production of 'geologese'.

C F DAVIDSON

Causes de la Répartition des Etres Vivants

Paléogéographie, Biogéographie Dynamique. Par Raymond Furon (Evolution des Sciences, No 10) Pp 168 (Paris Masson et Cie, 1958) 1,000 francs

THIS book is well described by its author, in his preface, as "ce petit livre de 'morceaux choisis' n'est donc dans mon esprit qu'une esquisse de ce qui pourrait être un beau livre qui n'existe pas in 'Traité de Biogéographie'", for it touches upon almost every aspect of its subject. Unfortunately the touch is too light to permit the suggestion of solutions to the many problems it describes, and this almost inevitably excites, rather than calms, the doubts that haunt most biogeographers as to whether the chaos of facts with which they are confronted can ever be reduced to final order.

Moreover, so vast a subject can be compressed within the limits of a single short book only by the most careful and balanced selection of information, and of the sources from which this comes, and in this respect also the book leaves more than a little to be desired.

With the author's main conclusions, that the present distribution of organisms chiefly reflects the catastrophic consequences of the Pleistocene glaciations, and that to understand the history of the living world its distribution in the Tertiary must be reconstructed, few biogeographers will disagree. They are likely to agree also that palaeogeography and

palaeontology are the keys to this reconstruction, but they are likely to feel some disappointment that an author so well qualified to comment on these particular aspects of the matter does not give a clearer lead as to how they may be more profitably pressed into service.

The great value of the book is as a source of much useful, and not infrequently unusual, factual information, and as such it can be recommended to all who are interested in the distribution of plants and animals.

RONALD GOOD

Die Banderschnecken

Eine Studie zur Evolution der Tiere. Von Prof. Dr. F. A. Schülder und Dr. Maria Schülder. Schluss: Die Banderschnecken Europas. Pp iv+93-206 (Jena, Gustav Fischer Verlag, 1957) Broschert, 30 30 DM

IN this third and final part of their monumental work on polymorphism in the banded snails (*Cepaea*), Prof. F. A. and Dr. Maria Schülder have tried to give an account of the variation in all parts of the ranges of the four species, and to draw some evolutionary conclusions. The booklet contains much useful information but suggests that such a task requires many more workers. The maps summarizing the data may be adequate for some areas of Germany, but it is well known that the proportions of the different colour and banding forms can vary greatly between adjacent colonies, for some large areas far too few colonies have been investigated for any reliance to be placed on mean frequencies from them as truly representative.

The conclusion reached is that the different forms in the polymorphisms have spread out from centres of special abundance. Lamotte's work is quoted as proving that visual selection by predators can never be of importance. The authors seem unaware of published criticisms of both Lamotte's conclusions, which are certainly invalid for Britain, and of their own inferences from their previous work on *Cepaea*. They combine data from colonies for making inferences about selection, although some at least of these colonies are in disturbed habitats and certainly not in genetical equilibrium with their environments. The composition of such colonies in relation to their habitats need give no indication that selection of any sort is acting, even though in fact it may be very strong. The data are given only to the nearest 10 per cent, and are too inaccurate for re-working.

A J CAIN

The Sea-Horse and Its Relatives

By Gilbert Whitley and Joyce Allan. Pp ix+84 (Melbourne, Georgian House, Pty., Ltd., 1958) 30s net

A PART from a cosy introductory chapter which oozes with unsubstantiated sentimentalities, Whitley and Allan's book will be of value to interested ichthyologists as well as the children for whom it is primarily intended. Besides an account of the lore and legends of sea-horses, there are good descriptions of the structure, behaviour and reproduction of this remarkable fish which Sir J. Arthur Thomson once described as the "most 'kopspeckle' creature of the sea". The systematics of the sea-horse show that about a hundred species have been recorded, and these are distributed over four genera. About half the book is concerned with these and the rest with pipe-fishes, trumpet fishes, flute-mouths, bellows fishes and razor fishes. These, like the sea-horses, are illustrated by some remarkably fine drawings, most of which have been prepared by the authors.

T H HAWKINS

RADIATION OBSERVATIONS WITH SATELLITE 1958₃ OVER AUSTRALIA

By DR. A. J. HERZ, DR. K. W. OGILVIE and J. OLLEY

The F.B.S. Falkiner Nuclear Research Laboratory School of Physics* University of Sydney

AND

R. B. WHITE

Radio Research Board Commonwealth Scientific and Industrial Research Organization
University Grounds, Sydney

In June 1958 the School of Physics of the University of Sydney received a cabled request from the Academy of Sciences of the U.S.S.R. asking for help with the recording of signals from *Sputnik III* (195832). As a result of this request signals from many transits during July and August were recorded with equipment kindly put at our disposal by the Radio Research Board of the Commonwealth Scientific and Industrial Research Organization.

Unfortunately, details of the instrumentation aboard the satellite and of the code used did not reach us until late September 1958, and even now we do not have all the information needed for a complete analysis of the data. We believe, however, that our results are of sufficient interest to be reported at this stage.

Description of Apparatus

It is now well known^{1,2} that among the equipment carried by *Sputnik III* is a scintillation counter. Because of the large size of the crystal (a cylinder of sodium iodide, 40 mm. high and 39 mm. in diameter) the detection efficiency for low-energy photons is high, and fast charged particles give very large pulses, corresponding to the loss of several MeV or more. In particular, the counter responds with high efficiency to bremsstrahlung photons emitted as the result of the absorption of electrons with energies of about 100 keV which collide with the sputnik.

A block diagram of the photon counter and its associated telemetering apparatus is shown in Fig. 1 and Fig. 2 gives the pattern of the signals. The second and third pulses carried the information from the scintillation counter. We do not know what information the first pulse carried.

Fig. 1 is largely self-explanatory. The anode current of the photo multiplier is integrated and fed to a bistable circuit which switches relay A at intervals corresponding to a loss of energy in the crystal of 2×10^6 eV. The current to the seventh dynode similarly controls relay C, which switches at intervals corresponding to an energy loss of 18×10^6 eV. In addition, the last dynode was connected to a scaler which controlled the switching of relay B.

Table 1 POSITIONS OF 195832 DURING OBSERVATIONS

| Epoch | Time (UT) | Altitude (km.) | Latitude | Longitude |
|---------|-----------|----------------|----------|-----------|
| July 10 | 06500 | 2050 | 1 605 | 20° S |
| July 19 | 07431 | 2059 | 1 753 | 4 9° S |
| July 23 | 81550 | 1920 | 1 703 | 23° S |
| July 23 | 81359 | 1092 | 1 507 | 27° S |
| July 30 | 74514 | 1763 | 1 794 | 20° S |
| July 30 | 74501 | 1758 | 1 800 | 22° S |
| Aug 4 | 70550 | 1656 | 1 782 | 27° S |
| Aug 4 | 70764 | 1659 | 1 750 | 34° S |

At the time our observations were made the scaling circuit had ceased to operate so that relay B remained in a fixed position throughout. So channel 2 (the second pulse) transmitted information about the position of the anode-current relay A, and channel 3 about the seventh-dynode-current relay C. On most of our records the marker and the first-channel pulse are missing as part of the modulating equipment was operating only intermittently, but the data given in this report are all taken from records in which all the pulses are present.

Positions of the Satellite during Observations

The positions of 195832 used by us were calculated with the aid of the elements of the orbit published by the Smithsonian Institution and with an orbital period found from a least squares fit to the transits observed at Sydney.

The results of these calculations are given in Table 1 and displayed in Fig. 3.

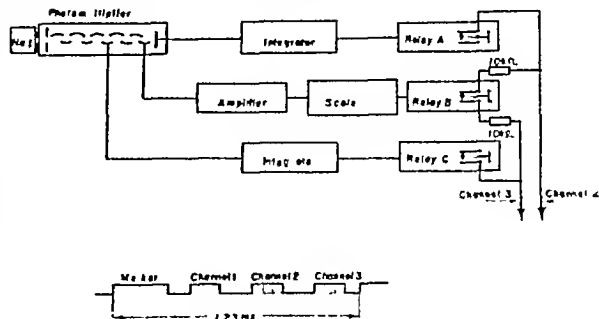


Fig. 1 (above) and 2 (below)

* Also supported by the Nuclear Research Foundation within the University of Sydney

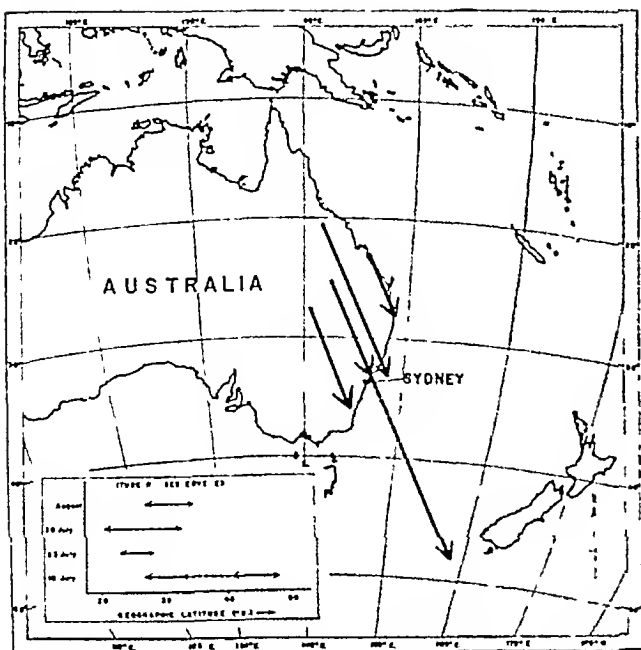


Fig 3

Results and Conclusions

The rates of energy loss in the crystal during our five recording periods are plotted as function of time (τ) in Fig 4. Combining these with the positions of the satellite (Fig 3 and Table 1) we find a minimum of radiation intensity at a geographic latitude of about 35° S. The intensity appears to increase by an order of magnitude when the latitude changes by approximately ten degrees on either side of this minimum. Similar observations over Australia, made with satellite 1958 α (*Explorer IV*), have been reported by Van Allen *et al*², who suggested that these minima correspond to outward-projecting 'horns' in the contours of constant radiation intensity. The minima can presumably be interpreted as the gap between the inner and outer radiation belts which have recently been discovered by means of the Russian artificial planet⁴ and by Van Allen and co-workers using the American lunar probes.

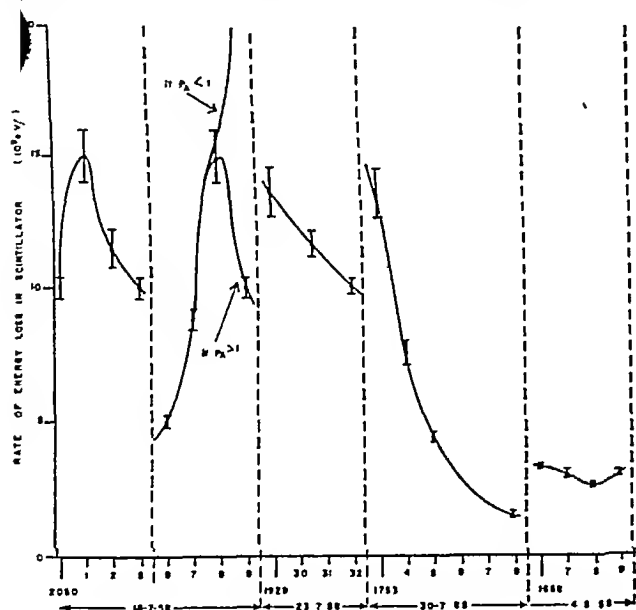


Fig 4

Our data also suggest a time variation in the radiation intensity. The mean intensity during the first part of the transit of July 19 (see Fig 4) is about five times the mean for August 4 although the satellite moved through almost exactly the same region in the two cases. We do not know whether the distribution of absorbing matter around the scintillator is such that tumbling of the sputnik could cause such large fluctuations, but, in any event, we do not believe that the fluctuations are so caused since our observations of the signal strength suggest a tumbling period not greater than about 40 sec — much less than our intervals of observation.

We tentatively conclude that the intensity of radiation in the region observed may show very considerable variations with time. This may be of particular significance as the region in question straddles the gap between the two radiation belts.

Our remaining conclusions concern the ratio of the switching rates of relays A and C. It appears to us that the telemetering equipment was not designed to handle the high switching rates, especially of relay A, which corresponds to the intensities of radiation encountered by the satellite. The switching rate of relay A almost always overloaded channel 2 during our periods of observation. We were, however, able to obtain adequate data on the rates of loss of energy through channel 3—these are the ones plotted in Fig 4.

When a large charge passes through the later stages of a photomultiplier, its anode current response becomes non-linear, and for extremely large flashes of light the current from the dynodes also becomes a non-linear function of the light input. The ratio of the switching rates of relays A and C therefore depends on the average magnitude of the light flashes at low counting rates, and on the average light output from the scintillator at counting rates so high that the interval between the individual events in the crystal is less than the decay time of the light pulses (about 5 μ sec in sodium iodide). According to Vernov *et al*¹ the ratio of the switching rates of relays A and C is 9:1 if the photomultiplier operates in the linear region of its response curve, it will be less if an appreciable number of the pulses is caused by particles which lose large amounts of energy in the crystal, and it will also be less if the number of photons detected in unit time is extremely large.

It was therefore of interest to try to find values for the switching rate of relay A, and we were able to do this as we explain in detail below. The results show that the ratio of the switching rates was of the order of 4:1, with fluctuations in the range 3.8:1 to 6:1. Individual results are shown in Table 2, they suggest that the ratio decreased with time. As we have no information about the response curves of the apparatus we cannot draw conclusions about the nature of the radiation from this.

Table 2 THE RATIO p_C/p_A

| Epoch | Time (τ) | p_C/p_A |
|--------------------------------|-----------------|---------------|
| July 19 86800 to July 19 87431 | 2050 to 2050 | 5.0 \pm 0.3 |
| July 23 81250 to July 23 81789 | 1929 to 1932 | 4.4 \pm 0.1 |
| July 30 74514 to July 30 74861 | 1753 to 1758 | 3.0 \pm 0.2 |
| Aug 4 70556 to Aug 4 70764 | 1656 to 1659 | 3.0 \pm 0.2 |

Recording Method

The receiving aerials were two horizontal dipoles placed at right angles to each other. Each dipole



Fig 5

fed a communications receiver and the rectified signals from the second detectors were further amplified by two separate d.c. amplifiers. The two outputs were then summed by a resistive mixing network and the resultant was applied to the deflecting plates of a cathode ray tube. The spot was photographed on 35 mm film moving perpendicular to the direction of deflection at a speed of 0.6 in./sec (1.52 cm/sec).

Characteristics of the Signal

A sample of one of our records, showing complete pulse trains with marker pulses and first pulses is given in Fig 5. The pulse-lengths were measured with the aid of a travelling microscope. A sample of a pulse length distribution (for the transit of July 23) is shown in Fig 6.

The various combinations of positions of relays A, B and C lead to pulses of nominal lengths 50, 100 and 150 μ sec, which we designated short, 'medium' and 'long'. As the position of relay B was fixed the second-channel pulses were either long or short, depending on the position of relay A only, and the channel 3 pulses were of either short or medium length. It is clear from Fig 6 that in both channels there occurred a number of intermediate length pulses—these were caused by the switching of a relay while a pulse is being transmitted.

With the aid of time markers recorded on the film we were able to measure the pulse lengths. The results are given in Table 3.

Table 3. LENGTHS OF PULSES AND PULSE TRAINS

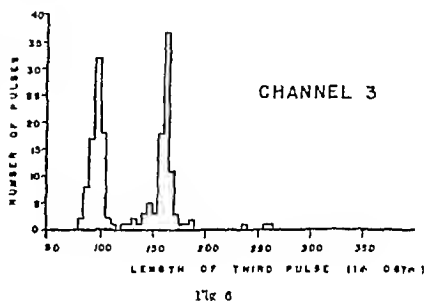
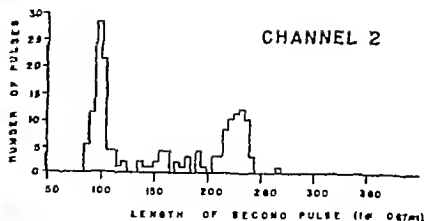
| | Nominal value (μ sec) | Mean used (μ sec) |
|------------------------------|-------------------------------|---------------------------|
| Short pulses | 50 | 60 ± 9 |
| Medium pulses | 100 | 115 ± 8 |
| Long pulses | 150 | 161 ± 10 |
| Pulse train including marker | 1,250 | $1,210 \pm 20$ |

Vernor et al. (ref. 1)

Analysis of the Records

In the system of telemetering used the positions of the relays are sampled at regular intervals of 1.23 sec (the cycle length). A change in the length of the appropriate pulse occurs whenever the number of switchings during the preceding cycle was odd, no change is found when the number of switchings was even. If a relay is switched during transmission of the pulse the length of which it controls, a pulse of intermediate length occurs.

If the relay is switched at intervals which are large compared with the length of the sampling cycle every switching results in a change of pulse length. Common sense suggests that the converse is also true—that changes in pulse length at intervals large compared with the cycle length denote an equal



number of switchings, each of which occurred during the cycle immediately preceding the change. Although not strictly true as we shall see below this turns out to be almost always correct.

For more detailed analysis we plot (Fig 7) the interval between pulse length changes as a function of the interval between switchings of the relay. It is clear that if the interval between switchings were really constant and if there were no additional information we should not be able to deduce a unique value of the switching frequency from the observations of changes in pulse-length. Fortunately, however the intervals fluctuate and we have other data as well.

The published information shows that if the photomultiplier is working in the linear region of its anode current characteristic the ratio between the switching rates of relays A and C is 9:1. Over loading cannot increase this ratio, so that we accept only those pairs of switching rates which have ratios of 9:1 or less. Secondly as Fig 7 shows the lengths of the intervals between changes are very sensitive to changes in the switching rate when there is more

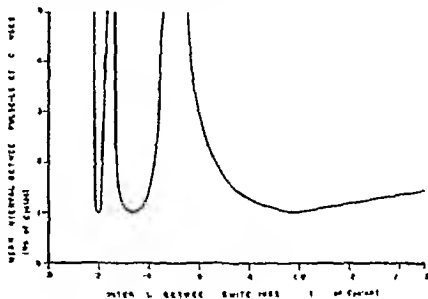


Fig 7

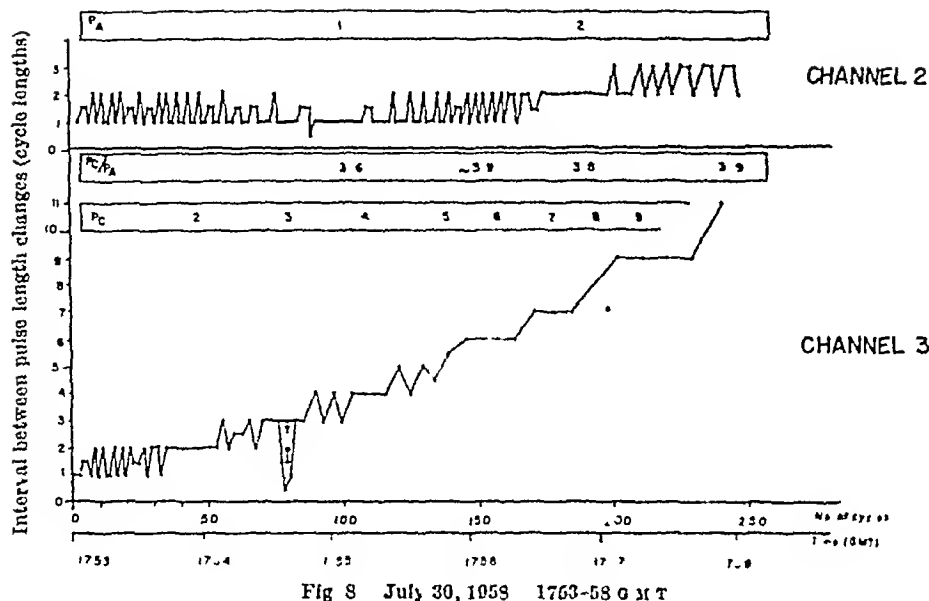


Fig 8 July 30, 1959 1753-58 GMT

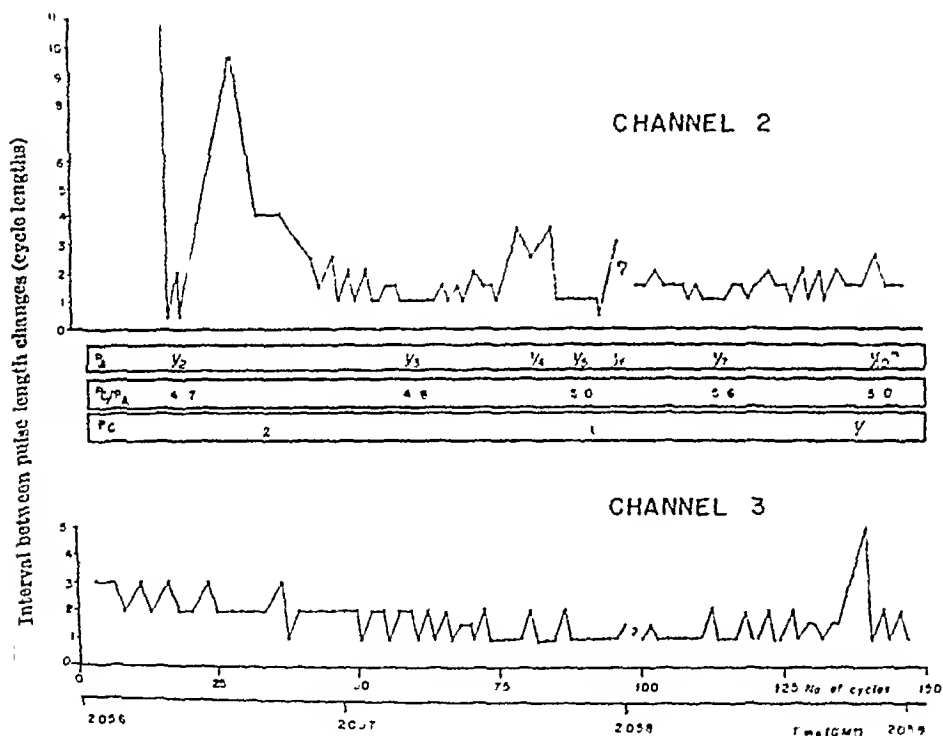


Fig 9 July 10, 1959 2050-59 GMT

than one switching per cycle. In the presence of fluctuations it is thus quite unlikely for high switching rates to give rise to long successions of pulses of equal size, that is, to consistently long intervals between changes in pulse-length. We conclude that if the intervals between pulse-length changes are consistently longer than the sampling cycle, the frequency of the changes is equal to the switching frequency of the relay concerned. During most of our observation time the less-sensitive channel 3 operated in this way so that we could deduce the radiation intensity directly from the frequency of pulse-length changes in it.

With one exception, at 1758 UT on July 30 (see Fig 4), the intervals between the switchings of relay A in channel 2 were always less than the length of the sampling cycle. The intervals between pulse-length changes thus rarely exceeded two cycles, and

we could not obtain information about the rate of switching from the average magnitude of these intervals alone. However, for the reasons discussed earlier we felt it worth while to try to estimate the switching frequency of relay A.

The possible values of the interval p between switchings can be obtained from Fig 7, and the smaller values of the intervals p_A (between the switchings of relay A) can usually be eliminated because of the requirements that the ratio p_C/p_A cannot be greater than 9. In most cases we were still left with several possible values of p_A from which a choice had to be made using the patterns of pulse sizes in both channels.

Two additional pieces of information helped us here. First, the ratio of the switching rates is not likely to show violent discontinuous changes. Secondly, in spite of fluctuations, there will be a brief series of equal-width pulses (no changes) whenever the number of switchings per cycle is nearly equal to an even integer ($p = 1/n$ cycle lengths where n is even). Whenever there is an odd number of switchings per cycle there will be a series of pulse-length changes every cycle. This effect, though not very pronounced, is clearly observable.

In our analysis we used a graphical method of display, of which we show examples in Figs 8 and 9. Along the horizontal axis we plot the times of occurrence of changes in pulse-length, while the ordinate gives for every change the time elapsed since the immediately preceding one.

We also indicate on the diagrams our estimated values of p_A and p_C and of the ratio p_C/p_A . The intervals p are measured in units of one cycle-length.

Fig 8 shows the record corresponding to our lowest detected radiation intensity—the only case when we found p_A to be undoubtedly greater than unity. It can be seen clearly that p_C/p_A is approximately equal to 3.8—much less than the nominal value 9.

Fig 9 is a display of data from an observation period during which the radiation intensity was high and changing rapidly. According to our estimates, p_A varied from approximately $1/2$ cycle to $1/10$ cycle during the time covered by the diagram, and the record shows particularly clearly the peaks in the plot associated with even integral values of $1/p_A$, and the runs of pulse-length changes every cycle which occur when $1/p_A$ is odd.

We should like to thank Prof H Messel for the excellent laboratory facilities made available to us, and Dr G H Munro, the officer in charge of the Sydney Section of the Radio Research Board, for making possible the recording of the sputnik transmissions. To Academician L I Sodov we are grateful for an informative discussion during his recent visit to Australia, and for the reprints he presented to us. We are much indebted to Miss Xenie Federoff for the careful and conscientious way in which she

carried out the tedious work of reading the records. One of us (J O) would like to thank the Commonwealth Scientific and Industrial Research Organization for the award of a studentship.

¹ Vernov S N, Yakulov, P V, Gorchakov Ye V, Logachev I I, and Chudakov, A Ye (in Russian), "Collection of Papers on Sputnik Results" 2 (Moscow: U.S.S.R. Academy of Sciences 1953).

² Chudakov A Ye (privately circulated information).

³ Van Allen, J A, McIlwain C L, and Ludwig G H *J Geophys Res* 64 271 (1959).

⁴ Vernov S N and Chudakov A Ye (privately circulated preprint).

ROBERT HOOKE AND BOYLE'S AIR PUMP

By DR. H D TURNER

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IT is just three hundred years since Robert Hooke built Boyle's air pump. This event has been described by Gunther¹ as "the most important research ever brought to a successful issue in Oxford", and it is perhaps appropriate to mark the tercentenary by examining the truth of this statement and, incidentally by somewhat belatedly giving Hooke the acknowledgment which is his due for his share in the enterprise.

Robert Hooke who was born on July 18 1635 at Freshwater in the Isle of Wight, was the son of the local curate. He was a sickly child and never robust, but he gave early evidence of that mechanical aptitude which led to his being described as "certainly the greatest mechanick this day in the world".² After the death of his father, Hooke went, at the age of thirteen, to Westminster School, and in 1653 he went to Christ Church, Oxford as a chorister, being admitted to the degree of Master of Arts in 1663. During the latter part of his stay in Oxford Hooke was employed as a laboratory assistant by Boyle, and in 1659 he built the air pump shown in Fig 1.

At this time Hooke was very much interested in the mechanical properties of the air, and very dissatisfied with the behaviour of the air pump then available, that due to Otto von Guericke. In 1660 Boyle wrote his famous treatise on the "Spring of the Air".³ In this book, which was dedicated to his nephew Lord Dungarvan, he says:

"As few inventions happen to be at first so complete, as not to be either blemished with some deficiencies needful to be remedied or otherwise capable of improvement. so when the Engine we have comes to be more attentively considered there will appear two very considerable things to be desired in it.

"For first the Wind Pump (as somebody not im- properly calls it) is so contriv'd that to evacuate the Vessel there is required the continual labour of two strong men for divers hours. And next, (which is an imperfection of much greater moment) the Receiver or Glass to be employ'd, consisting of one entire and uninterrupted Globe and Neck of Glass; the whole Engine is so made that things cannot be convey'd into it whereon to try Experiments. So that there seems but little (if anything) more to be expected from it than those very few Phenomena that have been already observed by the Author and recorded by SCHIOTTUS."

Boyle then goes on to say that he asked Hooke to contrive a more effective air pump

"Wherefore to remedy those Inconveniencies I put both Mr G(RATORIN) and R HOOK (who hath also the honour to be known to your Lordship and was with me when I had these things under consideration) to contrive some Air Pump that might not like the other, need to be kept under water (which on divers occasions is convenient) and might be more easily managed. And after an unsuccessful tryal or two of wavs propos'd by others, the last named Person fitted me with a Pump upon to be

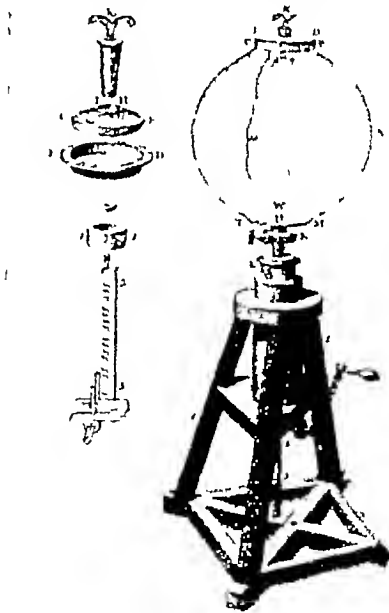


Fig 1. Boyle's air pump built for him by Robert Hooke in 1659. This was a notable advance on O. v. Guericke's pump since the evacuated enclosure was easily accessible and the receiver system enabled one man to operate the pump without undue effort. Hooke later built a double-acting pump which was even more effective and flexible in operation.

described. And thus the first imperfection of the German Engine, was in good measure, though not perfectly remedied."

The cylinder of the pump was bored in London, but the rest of the machine was constructed by Hooke in Oxford. The technical difficulties were evidently enormous. Boyle goes on to say:

"Your Lordship will, perhaps, think that I have been unnecessarily prolix in this first part of my Discourse. But if you had seen how many unexpected difficulties we found to keep out the external Air, even for a little while, when some considerable part of the internal had been suck'd out, you would peradventure allow that I might have set down more circumstances than I have, without setting down any, whose knowledge, he that shall try the experiment, may not have need of."

Once an efficient air pump was available, there were many experiments which could be performed. One of the first investigations carried out by Boyle was into the relationship between the pressure and volume of a gas.

This led to the enunciation of 'Boyle's Law' or 'Boyle and Mariotte's Law' after its confirmation by Mariotte in 1676. Although Boyle does not explicitly name Hooke as his assistant and collaborator in this work, Gunther¹ believes that he was. At this time Boyle was suffering from weakness of eyesight, and he also complained of a lack of skill in geometry which made him "both unwilling and unfit to engage in any Study where the conversing with Mathematical Schemes is necessary." The suggestion is that Hooke, a skilled experimenter and a very able geometer, was, in fact, mainly responsible for the enunciation and proof of Boyle's Law.

Hooke himself carried out many experiments with the air pump. In 1662, having been released by Boyle, he went to London as curator of experiments to the newly formed Royal Society. In this capacity he had to demonstrate different experiments two or three times a week for the delectation of the Fellows, and in many of these he used either the air pump, or the condensing engine, a compressor which he built in 1662-23. For example, in April 1663 we find Hooke experimenting with water freed of air which, according to Huygens, did not subside in a Torricellian tube, and later, air was removed from above and within water containing various fish to see which would die soonest.

This work with fish undoubtedly stimulated an interest in the general problems of respiration and combustion, and we may suspect that this was not unconnected with the interest that the Royal Society was then taking in the problems of diving. In 1664 we find Hooke giving an account of an experiment with two birds, one of which was kept in compressed air and the other in air at ordinary atmospheric pressure. He also constructed a container, large enough to hold a man, which could be partially evacuated by the air pump. Hooke experimented on himself in this device, thus anticipating modern investigations into human behaviour under reduced atmospheric pressure. He tells us that when a quarter of the initial air had been extracted he was able to endure for "somewhat above a quarter of an hour without any other inconvenience than feeling some pain in his ears, and finding himself deaf." During this experiment Hooke took a lighted candle into the container and discovered that it was extinguished long before he experienced discomfort. Other experiments carried out at this time involved

the development of an air gun, the measurement of air pressure and experiments with diving bells, but the most important aspect of this period of experimentation is undoubtedly the insight which the use of the air pump gave Hooke into the mechanism of combustion and respiration. The culmination of this work was, in fact, the publication by Hooke in 1664 in "Micrographia", of his theory of combustion².

In 1680 Denis Papin, who invented the 'digester' (the prototype of the modern pressure cooker), joined Hooke as his assistant. He later developed a 'steam pump' in which water was forced, by expanding steam, into a container from which it was ejected, under pressure, on to the paddles of a water-wheel, and this has been regarded by some French authors as the first steam engine.

Papin's claims in this direction, however, must, one feels, rest on his contributions to the development of the atmospheric engine. For some time on the Continent there had been interest in the possibility of producing power by using the pressure of the atmosphere to force a piston along an evacuated cylinder. Various ways of producing the vacuum had been tried. Guericke³ had described an experiment in which a cylinder had been evacuated by using his air pump. Huygens⁴ had blown the air out of a cylinder by the detonation of a small charge of gunpowder, and Papin⁵ had used the apparatus shown in Fig. 2 to produce a vacuum by the condensation of steam. Like many other members of the Royal Society at this time, Papin was aware of the enormous problem of clearing flooded mines.

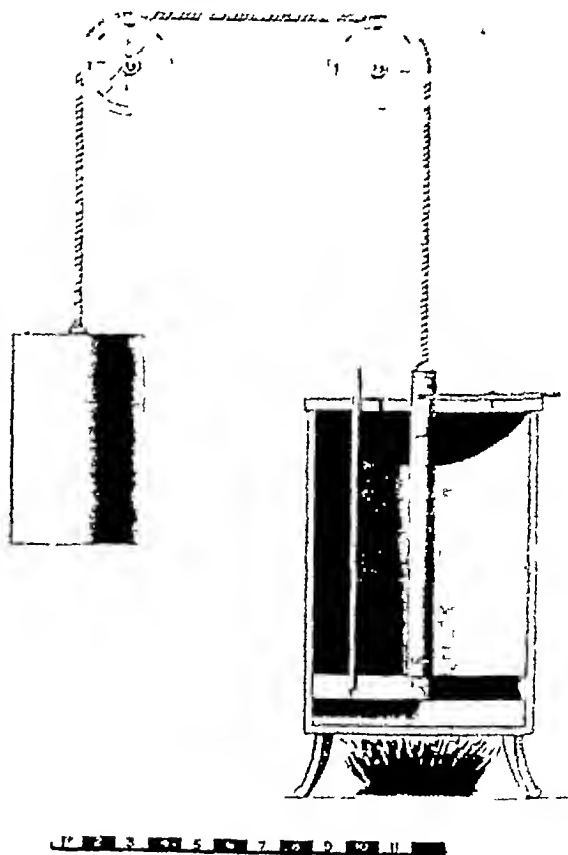


Fig. 2 Papin's cylinder and piston device, 1680 (Crown copyright). From an exhibit in the Science Museum, South Kensington. Steam generated by heat from the fire allowed the piston to rise to the top of the cylinder, where it was locked in position by the movable rod. The device was removed from the fire, the steam condensed by pouring cold water on the cylinder, and on releasing the piston it was forced down by air pressure, thus raising the counterbalanced weight.

which were frequently distant from sources of water power. In 1686 he proposed a scheme for the transmission of power over considerable distances. A water wheel was to drive two large air pumps, the air contained in pipes attached to these would be alternately rarefied and compressed at the mine the suction and pressure would alternately lift water from the mine and then expel it. In 1688 he proposed a modification of this in which a conveying pipe was to be evacuated by a water-driven air pump, at the mine the conveyance pipe was connected by branched pipes and valves to two vertical cylinders fitted with pistons these were connected by ropes to an axle carrying a winding wheel around which was wound another rope carrying buckets at each end. As each cylinder was evacuated in turn, external air pressure would force its piston down, thus turning the wheel first clockwise then anticlockwise and hence the buckets would be alternately raised and lowered.

Hooke's influence on these projects and his contribution to the ultimate development of the atmospheric engine is now, unfortunately, undocumented. Our only evidence of his interest and suggestions comes from references made by Dr Robison⁶ of Edinburgh. Among the latter's papers after his death was found a "List of Dr Hooke's Inventions" which contained the following sparse note, "1678 proposed a Steam Engine on Newcomen's principle", which implies that he had anticipated later developments in this field. Robison also claimed to have seen among the Royal Society's collection of Hooke's papers memoranda of a letter addressed to Thomas Newcomen, of Dartmouth these memoranda were however not in the possession of the Royal Society in 1880. According to Robison, Newcomen and John Cawley, a glazier, were anxious to make an engine on the lines suggested by Papin in 1688. Newcomen was in touch with Hooke and wrote to ask his advice. Hooke had already criticized both Papin's projects on the ground that the great compressibility of the air in the conveyance pipe would result in negligible effects at the mine unless the water-driven pumps had inordinately long strokes. In replying to Newcomen Hooke said "Could he [Papin] make a speedy vacuum under your second cylinder your work is done".

This suggestion was taken up by Newcomen and Cawley, who probably knew of Papin's piston and cylinder experiment and who certainly knew of the methods employed by Savery in operating his pumping machine "The Miner's Friend". According to Stuart¹⁰, "They therefore made the experiment of introducing steam under a piston moving in a cylinder and formed a vacuum by condensing the steam by an affusion of cold water on the outside of the steam vessel and the weight of the atmosphere pressed the piston to the bottom of the cylinder".

This method of producing a vacuum by the condensation of steam had been patented by Savery. An agreement was therefore entered into between Savery, Newcomen and Cawley and they were all associated in the grant of a monopoly for the atmospheric engine which was made in 1705.

The construction by Hooke of the first efficient air pump undoubtedly exercised a profound effect on the development of science and technology in the second half of the seventeenth century. Not only did the use of this machine lead to an understanding of the physical properties of gases and to a theory of combustion which is strikingly similar to the modern theory, but also it focused attention on the properties of systems of pistons and cylinders and the pressure of the atmosphere. This was certainly important in providing the climate of opinion in which the atmospheric engine could develop and as we have seen, there is reason to believe that in this development too, Hooke played a decisive part.

¹ Gunther E. T. "Early Science in Oxford" 6, 8 (Oxford 1930).

² Gunther E. T. "Early Science in Oxford" 6, 6 (Oxford 1930).

³ Boyle, R. "New Experiments Physico-mechanicall touching the Spring of the Air and its Effects Made for the most part in a New Pneumatick Engine (Oxford 1660)".

⁴ Gunth E. T. "Early Science in Oxford" 6, 7 (Oxford 1930).

⁵ Hooke R. "Micrographia" 103 (London 1664).

⁶ Querkele G. von "Experimenta nova" (1672).

⁷ Huygens C. "Oeuvres Complètes" 8, 22, 7 (The Hague 1893).

⁸ Papin D. "Fasciculus dissertationum de novis subdandis machinis" (Amberg 1693).

⁹ Robison J. article on The Steam Engine "Encyclopaedia Britannica", Third Edition "A System of Mechanical Philosophy with Notes" by D. Brewster (Edinburgh 1822).

¹⁰ Stuart E. "A Descriptive History of the Steam Engine" 59 (London 1824).

Information about Hooke's experiments on respiration and combustion and with the air pump has been taken from "Early Science in Oxford" vols 6 and 7.

CANCER AND THE RESPIRATORY GRANA

By PROF CARL C LINDEGREN

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WARBURG'S¹ theory of the origin of cancer proposes that tissue specificity can be achieved only by the synthesis of substances which make tissues specifically different through oxidative metabolism in the grana which carry the oxidative enzymes. Accordingly, the loss of tissue specificity begins with the loss of oxidative capacity through injury to the grana. Since a source of energy is essential the cell can only survive the loss of its oxidative apparatus if the oxidative apparatus is replaced by the adaptive development of the fermentative apparatus. The loss of oxidative capacity is not reflected by an immediate loss of tissue specificity but when the

injured cell divides and the daughter cells begin to grow, they do not achieve tissue specificity because the energy produced by fermentative metabolism cannot produce it. Warburg has focused attention on the oxidative grana of the cell, mutation the carcinogenic poisons, viruses, mechanical irritations, anaerobiosis, radiation and all other indirect causes of cancer and influences similar to hormonal control are assumed to affect the autonomous grana and thus to affect tissue specificity only through their action on the grana. Warburg has unified all ideas concerning the origin of cancer into a single concept involving material organelles capable of

observation and metabolic investigation, thus making it possible to bring the phenomenon under test and observation. In this respect, the theory is (as Warburg says) the only explanation of the origin of cancer cells which can be "metabolically specified". The essential aspects of the theory are summarized by Warburg: "Cancer cells originate from normal body cells in two phases. The first phase is the irreversible injuring of respiration... there is only one common cause into which all other causes of cancer merge, the irreversible injuring of respiration."

"The irreversible injuring of respiration is followed, as the second phase of cancer formation, by a long struggle for existence by the injured cells to maintain their structure, in which a part of the cells perish from lack of energy, while another part succeeds in replacing the irretrievably lost respiration energy by fermentation energy. Because of the morphological inferiority of fermentation energy, the highly-differentiated body cells are converted by this into undifferentiated cells that grow wildly—the cancer cells."

Although Warburg's theory concerns the problem of dedifferentiation, it does not explain how the cell became differentiated. It has been pointed out by others that the cancer cell is not dedifferentiated back to the embryonic level but always retains some characteristics which make it identifiable with regard to origin. Thus the loss of tissue specificity does not involve complete but only partial 'dedifferentiation'.

Differentiation is also achieved in organisms in which defined cells do not exist, since the Ascomycetes, which are coenocytial, are highly differentiated. Even though the nuclei flow freely through the false septa throughout the thallus, differentiation into mycelium, conidiophore and conidium is achieved in circumstances so fluid that no specific cell can be identified. This differentiation requires, like all other differentiation, the activity of many genes, since many nonconidial forms of *Neurospora* are known each of which is the phenotype of a different recessive allele. It may be inferred that differentiation is effected differently in cellular and noncellular organisms.

Although we all speak freely about 'yeast cells', it should be pointed out that phylogenetically yeasts are also noncellular organisms which graduate from mycelial or coenocytial forms to budding varieties all of which seem to be relatively closely related. The so-called yeast 'cell' and its bud is simply a coenocytial form which partitions single nucleate buds with a surrounding wall, much as *Neurospora* forms microconidia. Although this might seem like splitting hairs, it is a vital point in cell theory. The 'cell' that Warburg means is the cell of a multicellular organism.

A dominant scientific theory remains the dominant theory until it is replaced by a subsequent theory, because scientific effort can only be carried out under the aegis of a theory which restricts the activities and directs the efforts toward the examination of fundamental principles. Warburg's theory is to-day the dominant theory, by unifying the concept Warburg has made all other ideas concerning the origin of cancer subsidiary to his. In the absence of an alternative theory, one does not reject a theory by indicating extreme dissatisfaction with it (for example, Weinhouse¹), since no scientific activity is conceivable without a guiding theory. The most adverse criticism notwithstanding implies acceptance *ipso facto*.

The first step in criticism of the theory is the specification of the assumptions upon which it is

based. Warburg has assumed (1) that the ascitic tumour cell is a typical cancer cell, (2) that differentiation and tissue specificity in cellular organisms are achieved by oxidative metabolism of the grana (the respiratory grana have functions other than tissue differentiation, since they play an active part in the metabolism of yeasts), (3) that the grana are autonomous, and, therefore, (4) that the oxidative apparatus cannot be synthesized *de novo* (recent, unpublished, experiments in this laboratory have revealed that respiratory-deficient yeast cells, which never recover respiratory capacity spontaneously, can in certain unique conditions become respiratory-sufficient by exposure to yeast homogenates), (5) that cells which have lost oxidative capacity may obtain their energy by fermentation, (6) that division of these fermentative cells leads to the loss of tissue specificity, since they cannot obtain the oxidative energy essential to differentiation, (7) that such cells can neither fit into the tissue to perform the tissue function nor be restricted by the agents which restrict the differentiated cell and, therefore, form tumours, (8) that oxidative capacity can be injured (a) by oxidation of narcotics on the grana, (b) by direct action of specific poisons, (c) by anaerobiosis, (d) by radiation and (e) by various other items which are carcinogenetic. Research aimed at understanding cancer (as distinguished from applied research aimed at methods relieving the symptoms, study of surgical procedures, discovery of drugs for destroying cancer by large scale canvases, etc.) requires an investigation of the validity of these assumptions and a reformulation of theory depending on the results of such investigations.

Warburg's theory presupposes that the aerobic apparatus is a recent phylogenetical achievement. It is clearly a late, almost certainly the last, great advance made by the free cell in evolution, since it could only occur after photosynthesis had made oxygen available. Its recent integration into the cell probably accounts both for its autonomy and its vulnerability. (The respiratory grana and the chloroplasts are both autonomous structures which were obviously integrated into the cell recently, presumably before multicellular organisms evolved. It is reasonable to suppose that the chloroplast was the original symbiont added to the cell—or to the coenocyte—and that it later evolved into the respiratory granum with the advent of oxygen.) Since the autonomous aerobic apparatus seems universal, it may have been perfected when cells existed only as free cells, before the advent of the differentiated multicellular Metaphyta and Metazoa. The adaptive enzymic fermentation in yeasts, which is normally achieved by oxidative metabolism, may also be achieved by fermentative metabolism, albeit more slowly and less efficiently. Warburg might say that enzymic adaptation in single celled microorganisms is a 'cytoplasmic' activity and thus different from 'true' tissue specificity in multicellular organisms. On this theory, true tissue specificity may have appeared after the advent of oxygen.

A striking difference between yeast cells and mammalian cells lies in their means of obtaining energy. Yeast cells, unlike mammalian cells, have two separate fully functional systems for supplying adenosine triphosphate—an oxidative and a fermentative system. Yeasts can grow oxidatively or fermentatively without previous preparation, unlike the mammalian cells which can adjust themselves to a fermentative mode of existence only (according to Warburg).

by slow degrees. In this sense, mammalian cells are almost obligate aerobes. No obligately aerobic yeasts are known since the anaerobic metabolism in yeasts is always available as a source of energy. In some yeasts (in which the aerobic pathway has been lost) the anaerobic pathway is the only source of adenosine triphosphate. Yeasts are markedly different from the filamentous fungi, like *Neurospora*, in which it is difficult to demonstrate the fermentative pathway and which resemble mammalian tissue in growing only poorly, if at all under anaerobic conditions.

This discussion suggests that the yeast cell can provide a fruitful research object for study of the sensitivity of the respiratory apparatus and thus a guide in the evaluation of carcinogens. Many kinds of poisons have been tested with this view in mind. An interesting poison which was introduced to us by Dr Seymour Hutner is propamidine isethionate. It is widely used in the tropics as a specific for kala azar. It is thus important to know whether or not it may be carcinogenic. Our present indications are that it destroys the respiratory apparatus too completely, too rapidly and too specifically to be a carcinogen—if the data from yeast cells are transferable to humans. When yeast cells are smeared on the surface of an agar plate and a paper filter pad saturated with a solution of 1760 p.p.m. of propamidine isethionate is placed in the middle of the plate a zone (several cm wide) appears around the disk in which the yeast cells grow abundantly but in which none of the cells is capable of utilizing oxygen. Since the original cultures were respiratory sufficient, it is inferred that propamidine isethionate has destroyed the respiratory apparatus. The living cells in the zone around the disk have been irreversibly transformed into obligate anaerobes. This is demonstrated by inoculating the cells from the zone into a peptone yeast-extract broth containing sodium acetate as the major source of carbon. The medium contains phenol red as an indicator, and if a single cell with an intact respiratory apparatus is introduced into this medium it will grow and the medium will turn deep red due to the increase in pH.² Although cells from the area surrounding the disk grow well in glucose broth transfers to the acetate broth never produce an alkaline reaction proving that all the cells have lost their ability to respire acetate and hence are respiratory-deficient. The conclusion that propamidine isethionate has destroyed the respiratory apparatus irreversibly seems irrefutable. It also appears to have achieved this end with relatively little harm to the cell otherwise.

This experiment is simplified by using a yeast which is incapable of synthesizing adenine since strains of this kind with an intact respiratory apparatus are pink while the respiratory deficient strains are white.³ When this experiment is performed with a pink yeast, the yeast which appears in the zone surrounding the disk is white although it remains adenine-dependent. White cells from such a plate always fail to grow after transfer to the acetate broth, justifying the inference that all the cells have lost their respiratory apparatus since a single cell with an intact respiratory apparatus would be able to utilize the acetate and grow in the acetate broth. A poison of this type which acts abruptly and completely on the respiratory apparatus might be assumed on Warburg's theory not to be carcinogenic because it acts so quickly and completely that the mammalian cells (which do not have a fully formed anaerobic pathway available and waiting) would not be able to adapt

themselves to anaerobic growth. The phenomenon demonstrates the extreme sensitivity of the respiratory apparatus to a poison which has little or no effect on the survival of the cell.

Warburg's theory assumes that low oxygen tension can lead to crippling of the autonomous grana and thus to cancer. Warburg's inference that respiratory deficiency could be induced by anaerobiosis was confirmed by Hino and Lindegren⁴ using yeast (Respiratory-deficient yeasts induced by anaerobiosis or by a variety of other treatments are completely capable of maintaining their structural integrity permanently from generation to generation although all the cell's energy is supplied only by fermentation. Warburg quoting Pasteur stated that not even yeast which is one of the lowest forms of life can maintain its structure permanently by fermentation alone; it degenerates to bizarre forms.⁵ This view concerning the stability of yeast grown exclusively anaerobically is in error but this fact has no bearing on the validity of Warburg's theory of the origin of cancer since it neither supports nor invalidates any of the assumptions upon which the theory is based.) Both Sarachek⁶ and Harris⁷ failed to confirm the induction of respiratory deficiency in yeast by anaerobiosis. In three haploid cultures Hino and Lindegren found that the frequencies of respiratory-deficiency under aerobiosis were, respectively 1.7, 3.8 and 3.3 per cent, while the same cultures grown anaerobically produced respectively, 14.9, 8.6 and 8.0 per cent. Two diploid cultures under aerobic conditions produced respectively, 0.8 and 0.0 per cent respiratory-deficiency and 1.9 and 0.2 per cent under anaerobic conditions. In one tetraploid culture the frequency of respiratory deficiency rose from 0.0 under aerobiosis to 0.3 per cent under anaerobiosis. It is clear that the haploid state provides the clearest demonstration of the effects of anaerobiosis on respiratory-deficiency, and it is not surprising that neither Sarachek nor Harris detected this effect since they did not use haploid cultures. Anaerobiosis (unlike propamidine isethionate) induces only a low frequency of respiratory deficiency; the effect of propamidine isethionate is total. Anaerobiosis produces relatively minor damages which might be progressive. If repeated since only a few of the grana are affected in most cells and only rarely are all destroyed. Anaerobiosis is inferred to be an effective carcinogen since it only reduces partially the energy available from aerobiosis and thus enables the cell to survive long enough to adapt the dormant fermentative system.

Recent work in this laboratory⁸ has provided an example of another kind of induction of respiratory deficiency in yeast. Caffeine induces respiratory deficiency in yeast cells sensitive to caffeine with much higher frequency than in cells resistant to caffeine. Growth in caffeine is only achieved by an adaptive process, presumably an enzyme adaptation. Both resistant and sensitive yeast cells pass through the adaptation but the adaptation of sensitive cells is characterized by the simultaneous induction of an extremely large number of respiratory-deficient cells. Although one may assume that the total induction of respiratory deficiency by propamidine isethionate is due to the direct action on the grana the induction of respiratory deficiency which occurs when caffeine sensitive cells become adapted to caffeine may be due to injury of grana, not by direct action of caffeine upon the grana but through the metabolic stress imposed by oxidative

The metabolic stress of adaptation can be observed cytologically. Several years ago when interest in the laboratory centred on adaptation of yeast to galactose, yeast cells were critically observed during adaptation. In the early stage of adaptation most cells were not budded and did not stain with methylene blue (Non-stainability is the standard criterion for viability). Just before adaptation was achieved (as indicated (1) by the absence of budding, (2) by the failure to accumulate glycogen, (3) by slow utilization of galactose) nearly all cells became stainable with methylene blue. In other circumstances this would indicate that the cells were non-viable. Shortly thereafter, however, at least 80 per cent of the cells produced buds, lost their stainability with methylene blue, and vigorous fermentation of galactose occurred. This is interpreted to mean that the stress of adaptation had exhausted most of the reducing reserves of the yeast cell, permitting it to stain with methylene blue, but that this deficiency was made up as soon as sufficient galactose became available.

An important use of Warburg's theory is for predicting the possibility that an agent is a carcinogen from its action on the respiratory grana. On this theory, propamidine isethionate is predicted not to be carcinogenic whereas anaerobiosis and caffeine are. The dye janus green, which acts specifically to stain the respiratory grana and which is singularly effective in preventing sporulation in yeasts, is predicted to be non-carcinogenic. Incidentally, the sporulative process in *Saccharomyces* is an especially useful point for testing the effectiveness of various toxic agents on the respiratory grana, since it is a highly specific kind of differentiation which is achieved only aerobically. The view that viruses may cause cancer can also be deduced directly from Warburg's theory. Warburg inferred that a great variety of metabolic disturbances could inactivate the respiratory apparatus, and experimental evidence from yeasts supports his views. Since many viruses grow in the cytoplasm

without killing the cell, they are disturbers *par excellence* of cytoplasmic metabolism and might be expected readily to cause the destruction, inactivation or malfunction of the grana. Viruses inhibiting the nucleus would be predicted to be not nearly so effective.

Ephrussi⁸ was the first to speculate concerning the chemical mechanism by which the respiratory grana of the yeast cell could be destroyed. He assumed that since acriflavine has an affinity for nucleic acids it was mutagenic and he found that it induced respiratory deficiency. Ephrussi was unaware of the fact that Stier and Castor⁹ had previously induced respiratory deficiency with cyanide, and Whelton and Phaff¹¹ had shown that ethylene oxide is extremely efficient in producing the same effect. It has become increasingly evident that a great variety of substances induce respiratory deficiency in yeasts: copper and manganous salts are recent additions. Whether these substances act directly as propanidine isethionate appears to, or indirectly as temperature¹² and caffeine adaptation, it seems clear that study of the phenomenon should be revealing in terms of the nature of the respiratory grana and therefore, of carcinogenesis.

This work has been supported in part by a research grant from the American Cancer Society.

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⁷ Harris, M. J., *Cell and Comp. Physiol.*, 48, 95 (1956).

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THE NEW MARINE BIOLOGICAL STATION ON HELIGOLAND

By DR J. N. CARRUTHERS

National Institute of Oceanography, Wormley, Surrey

MANY years before the island of Heligoland passed from British to German ownership in 1890, it was popular with distinguished scientists from Germany and other Continental countries for marine biological pursuits, because the waters bordering the German mainland yield only a small part of the faunal range characteristic of the open sea.

In the Baltic, the low salinity of the German waters there is a limiting factor and in the North Sea the turbidity is such. Moreover, in the North Sea the wide belt of mainland shore which dries out at low tide militates against the establishment of a first-rate German marine biological station there. Well before 1850, men whose names were to become world-famous in the domain of marine biology were frequenting Heligoland because of the much better natural conditions which exist there.

So long ago as 1835, Ehrenberg had investigated the origin of bioluminescence while working on the island and, ten years later, Johannes Muller had

there formulated new ways of investigating the life of the open sea. In 1865 Anton Dohrn (later of Naples fame) and Ernst Haeckel of Jena were conducting researches from the island, and, within two years of its cession to Germany, a marine biological station had been founded with F. Heineke as first director. During the twenty-eight years of his tenure of the post, his famous work on the natural history of the herring and on the plaice was carried out. In those days the Station was housed in more than thirteen separate buildings and its own staff of eight scientists and sixteen technical assistants had to find room for sixteen guest workers. Not until it was possible (in 1920) to take possession of a large building freed from naval use did it become possible to conduct tuition courses, and the first of these was attended by a class of thirty.

Many British oceanographers will well remember Heineke's successor—the genial and talented W. Mielek, who was head of the Station during

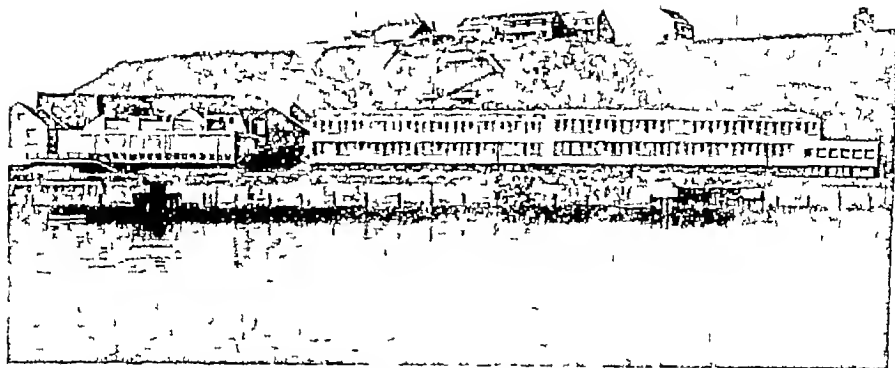


Fig 1 General view from the water front

1920-33 When its enlargement was completed in 1937, the name "Wilhelm Meelok Haus" was given to part of the multi storied construction. The last director of the Station to be appointed before the Second World War was A. Hagmeier, who held the post on the island from 1934 until after hostilities had broken out. He remained the nominal director of the Station until his death in 1953. Until shortly before that time, he had been resident in Sylt at the dependant Ellenbogen Station near List. While there Hagmeier spent much effort in the furtherance of marine biological research and was able to adapt a vacated army building in List to provide a two roomed laboratory on the harbour side in which instructional courses could be given. Already by 1949 the number of visiting students had reached 170. When, in 1952, the island of Helgoland was made free of access again and declared ready for building operations to start Hagmeier was already prepared with plans for reconstituting the renowned Biologische Anstalt on it. Though it is not by any means the case that all German marine scientists were in favour of the project, the marine biologists for the most part were so.

In pre 1930 days, the "Biologische Anstalt Helgoland" came under Prussia and one may read, in old reports of the Government, of that State having furnished 400,000 marks for the rebuilding which began in the winter 1925-26 when serious thought was given to rebuilding the completely demolished Station some years after the end of the Second World War, however, the island had come under

Schleswig-Holstein. This Land not being financially able to shoulder the expense of such an ambitious project, it came about that the Bund Ministry of Land Food and Forests eventually did so.

Much space would be needed to give an adequate account of the impressive proceedings of June 1958, when the fine new Station which has arisen on the ruins of the old was formally declared open in the presence of a large concourse headed by Bundesminister Dr. Lübcke who has since been elected President of Western Germany in succession to Dr. Heuss. Ministers of Schleswig-Holstein were present. German oceanographers were there in number, guests from the Netherlands, Italy and Britain attended and an English fisheries research vessel (*Sir Lancelot*) had come from Lowestoft. The Director of Fisheries Research in Britain was present greatly to the gratification of Dr. A. Büch-

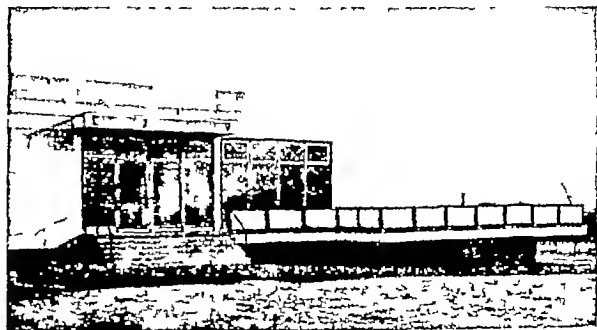


Fig 2 Entrance to the aquarium with (on the right) the veranda around the seal basin

mann, director of the new Station, who recalled the close associations between Lowestoft and Heligoland during the years between the wars. Most of the guests had been carried from Cuxhaven in the very fine German research vessel *Anton Dohrn*, which has already much first-class work to her credit despite her youth.

Speeches and a tour of the new Station were the business of the first day—followed by a reception and supper aboard the *Anton Dohrn*. The second day (June 20) was devoted to a scientific conference in the commodious lecture room. After a *Festvortrag* by Dr J. Verwey of Den Helder, he opened a general discussion on what should be the scientific activities of marine stations. After this topic had been debated very widely with no lack of participants, Dr A. Buckmann gave a very detailed account of the programme of work which he has in view for his new Station. From what he said it was quite clear that great care had been taken to build as economically as possible in erecting the long low buildings which are such a contrast to those standing when the former building programme ceased in 1937. Because practically everything had to be transported from the mainland at great additional expense and with dependence upon weather, it is perhaps not surprising that the cost to the *Bund* Ministry was in the neighbourhood of six million DM (about £6/11 million).

The divisions of activity provided for under the general leadership of Dr A. Buckmann who remains resident in Hamburg, where he is professor of fisheries biology in the University of Hamburg are: zoology, animal physiology, botany, microbiology, planktonology and fisheries biology. The first of these divisions has a staff of three scientists with the Director as leader. The other divisions have two scientists each, except for microbiology, which has only one. It seemed surprising that there is no special provision for the hydrographical work which is essential before a proper study can be made of the relationships between the marine fauna and flora and the environment. An island like Heligoland must afford wonderful opportunities for studying what differences exist in the marine life as between what must usually be the lee and weather sides.

There are many things of great interest with which a worker trained in the physical side of oceanography could occupy himself working from the new Station. Questions elicited the remarks that expense had to stop somewhere, but that visiting workers on any aspect of oceanography would always be made most welcome—as evidenced by the great amount of laboratory space set aside for guests.

It is a very praiseworthy feature of post-War German marine science that excellent collaboration exists between the Heligoland activities led by Dr Buckmann, the German Hydrographic Institute, the German Scientific Commission for Marine Research, the Institute for Fisheries Biology of the University of Hamburg, the Bremerhaven Institute for Marine Research and the University of Kiel. This close working together has led to really notable achievements in respect of investigations on the high seas, and German oceanographical investigations made during the Polar Front Survey within the International Geophysical Year programme are of high merit.

Along the southern face of the main block of the new Station are the laboratories in use by the staff and the rooms used for the dispatch of animals to universities and other customers. The northern face

contains the laboratories for guest workers and students. The public aquarium, with all its complicated technical 'plumbing', and the aquaria for research and growth studies constitute a separate block. An impressive feature of the aquarium which those with memories of the pre-War Station will recall has been provided anew and in duplicate. Quite detached and centrally placed are a pair of circular 'tanks' in the form of very large glass vertical cylinders rising to a considerable height from the floor. Co-axially placed within each of them is an opaque vertical cylinder of considerable diameter which has a sanded surface. As a result, fast-swimming fish such as herring, mackerel and hake can swim swiftly around and around in the annular water space without knocking into the external glass or being crowded into corners. It is a wonderful sight to see the fish incessantly swimming around on their (to them) endless journey. Great value is attached to the fine supply of excellent sea-water pumped in from the end of a mole, and to the fact that all the 'plumbing' is of plastics. One sees handsome arrays of bright green and red piping more or less everywhere. The Station's cutter *Uthorn*, which is 24.5 metres long, of 6.4 metres beam and of draught 2.6 metres, does 8 knots under the drive of her 150 h.p. engine. She is excellently equipped with instruments and is of great use in enabling the scientists to dredge in the Heligoland Rinne, which is one of the deepest parts of the southern North Sea and has a fauna of particular interest. Two motor boats are also available.

It was emphasized that to run a marine biological station to day is a vastly different affair from what it was in Anton Dohrn's day. The mass of expensive and costly apparatus which had already become necessary a decade and more back has been much added to by the requirements for work with carbon-14 and other isotopes. The new Heligoland Station is well equipped for work with eight or more tracer elements.

Heligoland was always a favourite holiday resort, and already some eleven hundred permanent inhabitants are housed again on the island to make the most of it. 'Day tripping' from the mainland is also a very intense and paying business. During the summer the multitude of visitors contribute to the Station's funds by way of their payments to visit the aquarium. In winter when the visitors no longer come, the scientists of the Station can use the large annular 'tanks' described above of 25 m³ capacity for studies on the swimming of migratory fish.

About fifteen guest investigators pursuing quite different lines of work can work in association with the thirteen scientists of the Station, and great help is given in the matter of lodging to guests whose visits take place in summer. By throwing two large classrooms into one, thanks to a movable partition, a lecture room with ample accommodation for fifty students becomes available. Provision is made for visiting university teachers to bring students to the Heligoland Station for classes lasting some weeks, and facilities are afforded for teachers of biology and others to attend refresher courses.

The complex of buildings, which has a total frontage of 120 metres, includes a special basin in which a seal will live. This, with glass 4 cm thick, is most ingeniously constructed. Outside, walking on a balcony, paying visitors will be able to look down on the seal from above. From inside the building the visitors will look into the tank illuminated by daylight from

above and will see many smart movements imposed upon the seal by the clever internal 'architecture' of the tank. This fine haasm recalled the modest accommodation which the seal living in the Helgoland aquarium many years ago had to be content with.

As with the Station of former times the very appropriate speech from Goethe is in evidence. It now faces us set into the wall in large bronze capitals as we enter through the main public door: 'Alles ist aus dem Wasser Entsprungen alles wird durch

das Wasser erhalten, Ocean gönn uns Dein ewiges Walton.

It was due to the kind generosity of the Bund Ministry that I was able to attend the impressive re-opening. For those who would know very much more about the new Biologische Anstalt Helgoland, a full account written by its director exists¹ and a shorter one by one of his assistants².

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² Hempel G. *Die Umschau* 12 353-4 (Frankfurt am Main 1950).

OBITUARIES

Prof E Percival

A GREAT blow has been dealt to marine and freshwater biology in New Zealand by the death on July 16, in Christchurch, of Prof Edward Percival. Prof Percival who was born in 1893 was elected to the chair of biology at Canterbury University College, as it was then called, in 1928 after serving as lecturer in the Department of Zoology at the University of Leeds, where he was assistant to the late Prof Walter Garstang. During 1928 he worked as a temporary naturalist in the Plymouth Laboratory on the ecology of the Rivers Tamar and Lynher and he will be well remembered by those who knew him then. The son of a Cheshire farmer, Percival spent his boyhood in Lancashire, where he took the national diploma in agriculture at the Harris Institute, Preston, and he found much to interest him when he came to New Zealand. His early work on the ecology of rivers in Yorkshire led him to play a prominent part in trout management in acclimatization society work in New Zealand and his experience in marine biology in the United Kingdom was put to good use in guiding his research students and in advising the policies of various government departments.

His published work, amounting only to about a score of papers, is not a sufficient criterion by which to judge the man. He had declined various academic honours since he maintained that such things were of no use to him. He did, however, consent to be elected a Fellow of the Royal Society of New Zealand.

First and foremost he was a teacher. From the elementary to the postgraduate level he never failed to bring out the best in the human material set before him. His particular philosophies on the teaching and appreciation of biology will be long remembered by all those who came in contact with him, even if only as incidental associates.

For his advanced students he held a twice-yearly field expedition to Monzie's Bay, one of the isolated little coves on Banks Peninsula, and he took his students into the field on almost every other week end during term, bringing a certain spartan approach to the pleasures of animal observation which helped one more fully realize what is meant by ecology. His aim was to produce, at the postgraduate level, a student well balanced in outlook, able to think, not to be a storehouse of facts but to know where to turn to find what is already known, and potentially able to go on in almost any field of biological endeavour. How successful he has been in this can be seen by the wide distribution of his honours students in various positions throughout the world.

The informal, and often quite unzoological discussions which he held in the field and in the well remembered atmosphere of his rooms, together with his novel methods of allowing notes to be taken into the examination room all helped to bring out what powers of expression and thought were available in his students. Indeed, he often remarked that he wished he could conduct his examinations in the University library for he would know even more easily the worth of his candidates.

Physically he was outstanding for a man near retirement, and in the field his stride and energy in every activity proved more than a match for even the most athletic of his followers.

At the first encounter he presented a rather forlorn aspect and was inclined to be of uncertain temperament but this, particularly in his later years, was a variation on the theme of not suffering fools gladly. If one genuinely wanted help, advice or encouragement and if one had exorcised all one's resources before approaching him, Percival became the proverbial tower of strength and it was difficult not to find oneself being cast in his mould.

Apart from his long term studies on lakes in the Canterbury foothills and his interests in marine matters, his scientific work will long be remembered for his fine studies on the embryology of the Brachipoda. Percival was fortunate in having a locality close by where these animals could easily be taken between tides on the rocky shore and he was able to use his advantage to the full in producing his studies on their development and growth. He was never afraid to admit that he was wrong or that he did not know, an attitude of mind which had its effects particularly on his elementary students contemplating a career in teaching.

Percival's influence extended far beyond the cloisters of the University of Canterbury, and it would be hard to exaggerate just how widely his teaching and stimulation have been, and will continue to be felt.

ELLIOT W. DAWSON

Dr M. R. Schafroth

DR. MAX ROBERT SCHAFROTH and his wife, Käthi Schafroth (née Gempferle) died on May 20, they were killed in an aeroplane crash in Northern Queensland, Australia.

Dr Schafroth was born in Burgdorf, Switzerland on February 8, 1923. He passed his matriculation at the Gymnasium in Bern in 1940. He then entered the University of Bern in order to study mathematics and physics later changing to the

Swiss Federal Institute of Technology in Zurich. He graduated at the latter in 1948, obtaining a diploma in mathematics and physics.

Thereafter he commenced research work under the direction of Prof W Pauli, who was professor of theoretical physics at the Institute and Nobel prize-winner of 1944. Dr Schafroth obtained his doctorate degree in 1949 and was thereafter appointed as assistant to Prof Pauli—a post he held until 1953. During that time he continued research in collaboration with Prof Pauli in quantum field theory and solid state physics.

At this stage the Schweizer Arbeitsgemeinschaft für Mathematik und Physik offered him an overseas travel grant for two years, which he decided to spend in the Department of Theoretical Physics of the University of Liverpool with Prof H Fröhlich. After one year in Liverpool, however, he left Europe to accept a lectureship offered him by Prof H Messel in the then newly expanded School of Physics at the University of Sydney. He remained at the University of Sydney until his death, having been promoted to a senior lectureship on January 1, 1955, and to a readership on January 1, 1957. In May 1958 he was invited to accept the chair of theoretical physics at the University of Geneva, Switzerland, which invitation he had accepted and intended taking up this post on September 1, 1959.

Starting mainly with his stay with Prof Fröhlich in Liverpool, Dr Schafroth became interested in the theoretical understanding of the phenomenon of superconductivity. This was also his chief research interest during his five years at the University of Sydney. He published several penetrating papers on this subject himself and also inspired contributions

from others in the School. There can be no doubt that his work in this field will go down in science as having been a major contribution to the understanding of superconductivity. Several papers by him are yet to appear. These include a review of the field in the series "Solid State Physics", edited by Profs Soltz and Turnbull.

Apart from this particular field of research, Dr Schafroth was an expert and inspiring lecturer in the fields of statistical mechanics, solid state physics in general and quantum field theory. He brought into his lectures something of the qualities of his old teacher, Prof Pauli.

The death of Robert Schafroth and of his wife Kathi will be a great loss to all who knew them.

S T BUTLER

Mr H. W. Greenwood

THE death of Mr H W Greenwood occurred on April 30 at the age of seventy-seven. In the course of a very active life, Mr Greenwood was associated with three industries. Before the First World War he was a mining plant superintendent in the south of Spain. In 1919 he joined Leto Photo Materials Company, manufacturers of photographic paper, and continued with the firm after their amalgamation with Wellington Ward and their later amalgamation with Ilford, Ltd. Since 1937 he had been associated with Powder Metallurgy, Ltd.

Mr Greenwood wrote profusely in all three subjects, papers and books of a popular but well-informed nature. For many years he was an important contributor to the *British Journal of Photography*.

W D JONES

NEWS and VIEWS

Electrical Engineering at Newcastle upon Tyne

Prof J. C. Prescott

PROF J C PRESCOTT, professor of electrical engineering at King's College, Newcastle upon Tyne, retires this year. He was elected in 1937, succeeding W M Thornton, who was the first holder of the chair. After studying at the University of Liverpool under Prof E W Marchant, he entered a college apprenticeship with the British Westinghouse Company in 1915, continuing later with that Company as research engineer. He saw service with the R N V R during the First World War, being attached to H M Mining School at Portsmouth. After the War, he returned to the University of Liverpool as lecturer in electrical engineering, where he was to remain for 18 years. His early researches were concerned with the behaviour of constant-current dynamos, and this led by way of a study of the free period of coupled alternators to researches on the inherent instability of parallel connected synchronous electrical machinery. His papers of this period reveal that electrical measurement and measuring instruments were also occupying a substantial part of his time. For this work he was awarded the degree of doctor of engineering by the University in 1931. In Newcastle his research work has been concerned with synchronous governing of alternators, and further studies of the stability of parallel-connected alternators have been made, latterly he has been engaged in an investigation into

the performance of turbo/alternator governors, which is still in progress.

The Department of Electrical Engineering at Newcastle has grown greatly in size during Prof Prescott's tenure of the chair. Under his direction the expansion has been conducted so as to preserve a balance between so called 'light' and 'heavy current' electrical engineering, and to avoid too early specialization in undergraduate courses. Always playing a large part in the teaching activities of his Department, he has consistently emphasized the necessity for the teaching of fundamentals in university courses and has always insisted upon the maintenance of a high academic standard in his Honours School. Like his predecessor, he has been active in the affairs of the Institution of Electrical Engineers, being chairman of the North Eastern Centre in 1943-44, and has taken a continued interest in the North East Radio and Measurements Group. Coming from a literary family, he is a man of uncommonly wide interests who holds the respect and affection of all who know him. His friends both inside and outside the University wish him many years of active and happy retirement.

Dr R L Russell

DR R L RUSSELL, who has been appointed to the chair of electrical engineering at King's College, Newcastle upon Tyne, in succession to Prof J C Prescott, graduated B Sc in 1938 and M Sc in 1939,

in mathematics at the University of Leeds. Soon afterwards, he took up work in the Admiralty Degaussing Department at Portsmouth and Holmsburgh and thus his first contacts with electrical engineering were made. In 1942 when the magnetic mine had been overcome and there was an acute demand for radio mechanics, Dr Russell accepted lectureships on radio training courses first at the Royal College of Science and Technology, Glasgow and then at Robert Gordon's Technical College, Aberdeen. He went from Aberdeen to the Research Department of the British Thomson Houston Co. at Rugby. In 1946 he was appointed as lecturer in the Department of Electrical Engineering in the University of Bristol, and in 1955 he was promoted to a readership.

Towards the end of the War he published certain papers of a semi-geometrical nature mainly arising out of problems in radio engineering. As time has proceeded, he has turned his essentially geometrical mind to a number of problems first in electrical measurements and then in relation to electrical machines. Many papers have been published in the *Proceedings of the Institution of Electrical Engineers* arising out of this work, which led to Russell receiving the degree of D.Sc. from the University of Leeds a few months ago. Dr Russell's most individual contribution to electrical engineering has been to observe the possibilities which arise from feeding a three phase winding simultaneously at both ends with voltages of different frequencies. This principle has already had several applications, and it is of interest to note that Russell's predecessor in Newcastle, Prof J. C. Prescott, adopted the idea in relation to synchronous governing. A recent Ph.D. thesis on synchronous governing presented at King's College incorporated just such a double fed device.

Agricultural Botany at Leeds Prof J. H. Western

Dr J. H. Western has been appointed to the newly instituted chair of agricultural botany within the Department of Agriculture in the University of Leeds. He was educated at Avoncroft Agricultural College, Evesham, and the University College of Wales, Aberystwyth, where he graduated in botany with agricultural botany. In 1937 he was awarded the degree of Ph.D., the subject of his thesis being 'Some Aspects of Biological Specialization in the Oat Smut Fungus'. In that year he also took up an appointment at the Welsh Plant Breeding Station, Aberystwyth, where he undertook research on diseases affecting herbaceous plants. In 1939 he was appointed lecturer in agricultural botany and advisor in mycology in the University of Manchester, leaving in 1946 to take up appointment as provincial plant pathologist to the Northern Province, Ministry of Agriculture and Fisheries, Newcastle upon Tyne. In 1951 he was appointed to his present post of senior lecturer in agricultural botany in the Department of Agriculture in the University of Leeds. His investigations have included the problem of the 'choko' disease of cocksfoot (*Dactylis glomerata*) caused by the fungus *Epichloa typhina*, and he has been responsible for numerous publications.

Physiology at King's College, London
Prof R. J. S. McDowall

The retirement is announced of Prof R. J. S. McDowall from the Halliburton chair of physiology at King's College, London. This he has held for thirty

six years. He has perhaps become best known for his books. The most outstanding is "Control of the Circulation of the Blood", a monumental work with more than 9,000 references, but his 'Handbook of Physiology' of which he has produced eleven editions, has been the bible of a generation of medical students. His 'Sane Psychology' has been reprinted four times. Prof McDowall's interests have been chiefly in the circulatory system in which he has been an untiring worker and is a recognized authority. He gave the Oliver Sharpay Lecture of the Royal College of Physicians in 1939 on this subject. He has also been largely responsible for the formation of the Asthma Research Council and in recognition of this he was made president of the fourth European Congress of Allergy held in London in September. His enthusiasm and powers of inspiration are reflected by the fact that thirteen of his pupils have become professors and of these six have been in the University of London.

Prof J. L. D'Silva

Prior J. L. D'Silva has been appointed to succeed Prof R. J. S. McDowall. Prof D'Silva first graduated in 1929 from King's College in chemistry. His early interests were in organic chemistry and he was elected Sir Halley Stewart Fellow in 1933. His attentions then turned to physiology, and appointments leading to the readership in physiology at St. Bartholomew's Hospital Medical College followed. Here he pursued his particular interests in the effects of adrenaline and adrenaline-like substances on serum electrolytes. In 1948 he was appointed to the chair of physiology at the London Hospital Medical College where his research contributions to the understanding of respiratory mechanics again reflected his early interest in the physical sciences.

University of Malaya in Kuala Lumpur

Prof R. S. Huang

In the article under the title 'University of Malaya in Kuala Lumpur' in *Nature* of August 1, p. 306, it was stated that Prof R. A. Robinson had been appointed to the chair of chemistry. It has now been announced that Prof Robinson has declined the appointment, which has been accepted by Prof R. L. Huang, reader in chemistry in the University.

Prof Rayson Lising Huang was educated in Hong Kong first at Munsang College and then at the University of Hong Kong. After a year as demonstrator in chemistry at Kwangsi University, China, Dr Huang went to the University of Oxford with two scholarships from the Rhodes Trust and the British Council to study under Sir Robert Robertson. He gained his doctorate as a result of this period of research on synthetic hormones. Dr Huang then visited the University of Chicago with a postdoctoral fellowship and studied for two years under the late Prof M. S. Karasch and then joined Prof Konrad Bloch as a research associate for a further year. During these periods Dr Huang worked on free radicals and on the biosynthesis of cholesterol respectively. He joined the University of Malaya early in 1951 and has been awarded the degree of D.Sc. for his researches mainly in the field of free radicals. A citizen of the United Kingdom and Colombia, Dr Huang has a good knowledge of classical and modern Chinese, and speaks several Chinese dialects. His scholarship in a wide field will be a most valuable contribution to the professorate of the new Division of the University of Malaya.

The Second Russian Space Rocket

A RUSSIAN multi-stage rocket was launched at about 9 hr UT on September 12 and its final stage, weighing 1,511 kgm (3,331 lb) when empty of fuel, was projected towards the Moon with a speed of 7 miles per sec. At 18h 40m UT on September 12, when it was about 90,000 miles from the Earth, the vehicle emitted a cloud of sodium vapour. This was observed from eastern Europe and Asia as a glow, which lasted about 5 min and was of stellar magnitude 5 in the constellation of Aquarius. At an unspecified point on its journey, the vehicle divided into two parts, an instrumented sphere weighing 390.2 kgm (860 lb) and the spent rocket. The sphere carried instruments to measure the magnetic fields of the Earth and Moon, the zones of radiation around the Earth, cosmic rays in space, the impacts of micrometeorites and the composition of interplanetary gas. It was stated that these experiments were successfully accomplished. The vehicle carried radio transmitters operating on some of, or all, the frequencies 19 993, 19 997, 20 003, 39 986 and 183.6 Mc/s. The radio signals ceased abruptly at 21h 02m 24s UT on September 13, when the instrumented sphere struck the surface of the Moon at long 0°, lat 30° N, near the crater Archimedes.

While the vehicle was above the horizon in Britain, it was tracked by the Jodrell Bank radio telescope. The measurements made, of the direction, the Doppler frequency and the moment of impact, all confirmed that the vehicle followed very closely the trajectory given by the Russians. This second space rocket was similar to the first (launched on January 2, 1959, see *Nature*, 183, 83), which had a total weight of 3,245 lb, including 797 lb of instruments in a spherical container, and performed similar experiments. The trajectories of the two rockets were also similar—both took about 35 hr to reach the vicinity of the Moon—though the first rocket instead of colliding with the Moon, flew past it to become the first artificial planet.

Rocket Studies of Emissions caused by Solar Flares National Science Foundation Grant

THE National Science Foundation has made a grant of 250,000 dollars to the U.S. Naval Research Laboratory for rocket observations of ultra-violet and X-ray emissions from solar flares. Principal investigator of the project is Dr. Herbert Friedman, superintendent of the Atmosphere and Astrophysics Division of the National Research Laboratory. The effect of the Sun's emissions upon the ionosphere and the resulting radio communication problems are of great theoretical and practical significance. Measurement and understanding of the origin of these emissions will be basic to an understanding of the solar flares themselves. Dr. Friedman will therefore launch a series of instrumented *Nike-Asp* rockets to make the necessary observations. The investigation will explore wave-lengths and altitudes at which only rudimentary observations have so far been made. Previous work by Dr. Friedman, Dr. Richard Tousey, and their co-workers at the National Research Laboratory has established the existence of intense radiations from the Sun in the wave-length regions under consideration. Dr. Friedman and his group at the Naval Research Laboratory were pioneers in the use of rockets for astronomical research, and astronomers credit his work with being among the most exciting and significant at present.

being carried on in the field. Instrumentation for the series of rocket observations will include Geiger counters to measure X-rays in the 1–10 Å range, X-ray detectors for wave-lengths of 8–20 and 44–60 Å, scintillation counters sensitive to hard X-rays in the 20–500 kV range, and ion chambers sensitive to the helium emission lines at 584 and 314 Å.

British Aid for Nato Scientific Courses

MR. H. NICHOLLS, Parliamentary Secretary to the Ministry of Works, stated in the House of Commons that the United Kingdom contribution to the fund established by the North Atlantic Council to promote international gatherings for the advanced study of special scientific topics would be about £7,000 in the first year and would be borne on the vote of the Department of Scientific and Industrial Research. This was a written answer on June 25 in response to a request for a statement regarding United Kingdom participation in the new North Atlantic Treaty Organization scheme for advanced study institutes. The funds would mostly be used for contributions to the teaching and administrative expenses of selected courses at institutes in a Nato country which offered intensive courses, usually at postdoctoral to professional level, in branches of the natural sciences and technology. Assistance might also be given to the travelling and scholastic expenses of participants from Nato countries.

Graduates and National Service

IN answering a question in the House of Commons on June 8, the Minister of Labour, Mr. Ian MacLeod, said that he was not prepared to extend the deferment arrangements for science and engineering graduates to men with other qualifications. This was the advice of his Technical Personnel Committee, which had considered last autumn difficulties said to be created for firms engaged in nuclear engineering and other industries by the call up of non-graduates engaged on research. It was extremely difficult to distinguish between all the different professional qualifications that non-graduates have, but Mr. MacLeod said he would be willing to receive a deputation of research directors to discuss a definition which might be as effective as the graduate definition, if Mr. Blenkinsop, his questioner, cared to organize such a deputation.

Research and Development Charges in Civil Nuclear Power

A QUESTION was asked in the House of Commons on June 15 regarding the proportion of research and development charges for the civil nuclear power programme borne by public funds through the Atomic Energy Authority. The Paymaster General, Mr. H. Maudling, in reply said that all research and development expenditure incurred by the Atomic Energy Authority was originally borne from public funds. However, it was intended that the expenditure attributable to the civil power programme should be recovered in due course in the form of royalties payable on the electricity stations and as part of the price charged for fuel elements. The Authority also recovered the cost of the consulting services from the electricity boards.

Nuclear Reactor RB Accident in Yugoslavia

VOLUME 9 of the Bulletin of the Boris Kidrich Institute of Nuclear Sciences contains twenty-five articles and two laboratory notes of technical interest contributed by members of the physics, physical

chemistry and radiobiology laboratories of the Institute. They are prefaced by a statement in French by the director of the Institute Prof P. Savic, concerning the unfortunate accident which occurred to the nuclear reactor, *RB*, on October 15 1958, at the Institute. Six people who were very close to the reactor, received strong doses of neutron and ionizing radiations and two others who were not so close, doses above the permissible level. The six were given medical treatment at the Curie Hospital in Paris but one V. Zivota, a nuclear physicist, died on November 15. The reactor *RB*, is of zero energy and is fuelled with natural uranium and moderated with heavy water. Details of the construction of the reactor are given in the first article in the volume. The safety system consists of a control key safety rods, alarm dose rate meters and an automatic shut down. The approach to criticality is made by gradually raising the heavy water level. The accident occurred when the reactor went out of control in becoming critical. Prof Savic includes in his statement the conclusions of the committee of inquiry set up by the president of the Federal Commission for Nuclear Energy to report on the accident. On October 15, the committee reports, neither the alarm dose-rate meters nor the automatic control were functioning and the personnel were judging the state of the reactor by the amount of ozone they could smell in the air. The rise in power of the reactor had been detected by the strong increase in gamma radiation within an interval of ten minutes on automatic recorders of the activity in the atmosphere, placed at 540 metres from and in direct line with the reactor. An estimate of the radiations received by the injured persons is given in the article and shows that a total dose of about 0.83 rems was received of which about 388 rems was by neutrons. The amount received individually varied according to the distance of the person from the reactor, and was about 15 per cent less than the quoted value for the farthest distant.

The Japanese Nuclear Power Station

The March number of the General Electric Company's *Atomic Energy Review* (2, No. 1) includes an artistic impression of the 150 MW nuclear power station designed to be erected at Tokai Maru, 65 miles north-east of Tokyo, and which will be Japan's first nuclear power station. The General Electric Co. Ltd. has been selected exclusively to negotiate a contract for its erection. The station will be powered by a single gas-cooled graphite-moderated reactor of the same basic type as the two reactors at present being built at Hunterston, but will include many novel features, particularly with regard to structural and control considerations. It will take approximately four years to build and is expected to be in operation by mid 1963. Other articles in the issue include a description of the General Electric Company's atomic energy division by K. J. Wootton, manager of the division; a discussion of the first sixteen months civil engineering construction at Hunterston by F. W. Evans; examples of corrosion problems in gas-cooled reactors by M. W. Davies; and an account of two methods of reducing the permeability of reactor quality graphite by D. A. Boyland.

Technical Books

The Atomic Energy Commission of the United States has issued a catalogue of 80 technical books

published by the Commission, 1947-59. (Technical Information Service. Technical Books sponsored by the US Atomic Energy Commission. Pp. 40. Washington D.C.: United States Atomic Energy Commission, 1959.) The list is arranged by subjects and the contents of each volume are indicated. The second part of the catalogue similarly lists 26 books in the press or in preparation on April 1, 1959.

Nutrition Meeting

The Nutrition Meeting for Europe of the Food and Agriculture Organization of the United Nations at Rome, June 23-28, of which the report has now been published (Report Series No. 21. Report of the Food and Agriculture Organization Nutrition Meeting to Europe. Rome, Italy, 23-28 June 1958. Pp. ix+28. Rome: Food and Agriculture Organization of the United Nations. London: H.J. Stationery Office, 1958. 2s. 6d. 0.50 dollar), was concerned with food consumption with special reference to fat consumption and with education and training in nutrition. With regard to the first the meeting recommended the Organization to take all possible steps to foster improvements in the techniques of food consumption surveys, and of the reporting and analysis of their results so as to ensure their maximum utility. It also recommended periodic meetings of European nutrition workers and that an expert committee or study group in co-operation with the World Health Organization should consider the problem of fat consumption and coronary disease in European and other countries. The need for further extensive studies of the fatty acid content of foods is emphasized in the report and also of further research to establish satisfactory tables for fatty acid composition. The present situation was reviewed with respect to education and training in nutrition, stressing the lack of suitably trained teaching staff. The contact between competent research groups, educational authorities and teachers was also considered. Further, reference was made to the narrow and unbalanced approach in teaching nutrition and the absence of refresher courses for teachers dealing exclusively or incidentally with nutrition. The meeting strongly supported the plea for a seminar in 1959 to study these questions in greater detail and to suggest better practical approaches. The main purpose of the seminar would be to examine the scope and effectiveness of education and training in nutrition in Europe. It would also formulate proposals for developing and orientating such training by government departments and other agencies, and to promote co-operation and coordination between the disciplines and agencies concerned and between those engaged in training and research. The report outlines an agenda for a seminar of 12-14 days for 50 to 60 people.

Central African Scientific Research

A further 105 papers published in 1957 by members of the staff and research workers associated with the Institute for Scientific Research in Central Africa are listed in the second part of the tenth annual report of the Institute making a total of 793. Brief abstracts of these papers constitute the rest of this part of the report (Institut pour la Recherche Scientifique en Afrique Centrale. Dixième Rapport Annuel 1957. Pp. 228. Bruxelles: Institut pour la Recherche Scientifique en Afrique Centrale, 1959). In the administrative report which is illustrated, the director Prof J. van den Berghe and

cates briefly the general character of the scientific work of the Instituto during the year Prof van den Berghé continued his own study of the biology of the tsetse flies of *Bugoseia* and *Mimuli* (Ruanda) and at Jiangi, and also on the sexual and asexual cycles of *Plasmodium atherui*. Other work was concerned with the isolation of factors of growth of trypanosomes, and a histopathological study of the hypophysis of small African mammals. In nutrition, besides an extensive study of maternal milk and the variation of its content of amino-acids and proteins as a function of the period of lactation, the nutritional value of native beers was also investigated in the region of Lake Kivu and Ruanda-Urundi and the experimental kwashiorkor of swine was studied. An investigation of the fauna of the Belgian Congo and Ruanda-Urundi was launched and also of the methods and seasons of reproduction of the birds of Tshubati. In physical anthropology a study of the growth of Africans in Ruanda-Urundi was initiated and besides an inquiry into the rural economy of Ruanda-Urundi, one was commenced into the low birth-rate of the people of the Mongo tribe. In the physical sciences observations of solar radiation and of the radio-electric activity of the Sun continued, as well as studies of the functional efficiency of dwelling houses at Bagira, Kabunambo and Usumba.

International Council of Scientific Unions

THE Yearbook of the International Council of Scientific Unions, 1959 (Pp 77 The Hague International Council of Scientific Unions, 1959), provides a comprehensive reference work on the unions. Besides lists of members of the Executive Board, national members of the Council, of countries adhering to the Union, and of officers of the International Scientific Unions, it gives the membership of the Special Committees and other organs of the International Council. There is also an alphabetical list of these officers and members, the Statutes and Rules of the Council, the text of the agreement between the International Council and the United Nations Educational, Scientific and Cultural Organization and the reports for 1957-58 of the Secretary-General of the International Council. The Commissions of the Unions are also detailed and there is a calendar of arrangements for 1959.

No 2 of Volume 1 (1959) of the *International Council of Scientific Unions Review* includes D L V Berkner's presidential address to the eighth General Assembly of the Council. It also includes the remarks of Sir Harold Spencer Jones, the secretary general, on some affairs of the Council and the reports of the Special Committees for the International Geophysical Year, for Oceanographic Research and for Antarctic Research. The constitution of the Committee on Contamination by Extra-Terrestrial Exploration and of the Committee on Space Research is recorded and the report of the former committee is also given. This Committee believes that there is a real danger that exploration attempts made within the next few years may produce contamination of extra-terrestrial bodies, which would complicate or render impossible more detailed studies when the technological problems of landing sensitive scientific instruments on the Moon and planets have been solved. It recommends that a specific code of conduct representing a reasonable compromise between the early initiation of lunar and planetary exploration and the need to safeguard future research should be drafted with the minimum of delay.

Council for the Preservation of Rural England

THE twenty-eighth annual report of the executive of the Sheffield and Peak District Branch of the Council for the Preservation of Rural England for the year 1959 (Pp 28 Sheffield Council for the Preservation of Rural England, Sheffield and Peak District Branch, 1959) is seriously concerned as to the preservation of the National Parks. It emphasizes the importance of public opinion exerting effective pressure through such bodies as the Council for the Preservation of Rural England if the Peak District National Park, and other national parks, are not to be seriously damaged. At the present time the executive is seeking to prevent the desecration of the Manifold valley by a motor road and is opposing a major attack on the Green Belt of the Sheffield Development Plan—at Middleton in the Don valley. With the local authorities and others the Branch vigorously opposed the proposals to prospect for open-cast coal in the Troway valley, but the recent Government statement that areas of natural beauty will no longer be mined for this purpose should put an end to prospecting in this area. It is pointed out, however, that absence of national funds prevented the Peak Park Branch from petitioning against the Waterworks Bill which proposes to submerge the Oler valley, one of the few remaining valleys leading to the heights of the Peak District National Park.

Society of Environmental Engineers

A SOCIETY of Environmental Engineers has been formed to provide a forum, by meetings, publications and visits, for the exchange of information and views among these engineers who are concerned with the development of equipment to withstand shock, vibration and other forms of environmental conditions, and who carry out research in these fields. The first meeting was held in London on May 29. Some fifty members and guests attended and papers reviewing the field of work were presented by Mr D A Nutt (Armstrong Whitworth Aircraft, Ltd), Mr F I L Knowles (Ministry of Supply) and Dr P Grootenhuys (Imperial College of Science and Technology). Future meetings are to be on November 25 and February 17 at the Imperial College. The first annual general meeting of the Society will be held on March 30 at the Royal Society of Arts. Further information can be obtained from the Secretary, Society of Environmental Engineers, 42 Manchester Street, London, W 1.

Progress of Chemical Engineering

IN the presidential address to the Institution of Chemical Engineers on April 28, Sir Hugh Beaver discussed the development and progress of chemical engineering in Britain, particularly in comparison with other countries. Pointing out that chemical engineering was now acknowledged as the fourth great technology, Sir Hugh thought that the Zuckerman Committee's estimate of our requirements of chemical engineers was too low. The figure of about 4,400 was below the present membership of the Institution—5,900 in 1959, and recent calculations of membership put the figure for 1965 at 8,800 and for 1967 at 11,100. Although the rate of increase had changed greatly in the past eight years, only in the past two or three had it approached the rate of increase in the United States. All these calculations, however, involved a change of attitude and policy as

well as of methods in British industry as would enable industry to absorb these numbers, and Sir Hugh regarded the increased application of chemical engineering as a measure of the use of modern techniques of manufacture. Referring to the training of the chemical engineer, Sir Hugh favoured our system of three, or at most four, years college education followed by practical training. He also said that the works training must be scientific and methodical carefully thought out and systematically applied and the system of education, while avoiding the specialization of the Continent, must produce a sufficient proportion of research students. None of the industrialists he consulted had any doubts as to the need for a broad based training but Sir Hugh stressed the need for an open mind on this subject. With regard to research he felt that much more should be sponsored, especially industry. Further, liaison between industry and university was essential for our national progress.

Haida Carvers

A deposit of the hard, dark shale called argillite was discovered in the Queen Charlotte Islands in the 1820s, and Haida Indian carvers soon began to exploit it as a material for a variety of objects, which they sold as curios. This has continued to the present day. Many of the objects are miniature copies of the larger carvings in wood, especially totem poles and totem poles, but tobacco pipes, bowls and plates were often made and are common in museum collections. There are also rarer objects, such as flutes.

Prof Marius Barbeau was well known for his work on the North West Coast Indians and has recently published another of his many monographs on the subject (Canada Department of Northern Affairs and National Resources National Museum of Canada Bulletin No 130 "Haida Carvers in Argillite" By Marius Barbeau Pp viii+214 Ottawa Queen's Printer, 1957 3 dollars). It is a sequel to his previous book, "Haida Myths illustrated in Argillite Carvings", and it deals as its title implies, chiefly with the carvers themselves but it is a complete work in itself. It is packed with information but is somewhat haphazardly arranged. There are numerous illustrations but no list of them, and there is a table of contents but no index, the nature of the material puts difficulties in the way of providing an adequate index but the book would have been easier if a list of the objects illustrated had been given, grouped according to their present location. A brief account of the carvers at the village of Skidegate is followed by five sections each dealing with a particular type of object, and the remainder consists of notes on individual carvers. The book is full of interest and the carvers many of whom the author has known personally, live again under his hand. There has been a tendency to deprecate these argillite carvings on the ground that they were mostly made for sale and hence were a product of acculturation and not truly indigenous. Prof Barbeau has done a great service in directing attention to their value as works of art in their own right, made by skilled carvers who not only worked faithfully in their own traditions, but were also capable on occasion of representing extraneous objects in their own style.

New Floristic Studies

Attention may be directed to two new and considerable floristic studies C Schweinfurth

has added a further contribution on the 'Orchids of Peru' (published in *Fiediana Botany* 30 No 2 Chicago Natural History Museum March 1959 4 dollars 50 cents). The work is in the usual format for this series and is mainly devoted to two considerable genera namely *Pleurothallis* and *Epidendrum*. Ten other genera with a smaller number of species are also considered. All the available information has been used in preparing this volume, though some of the records are understandably still rather scanty. The publication is well illustrated by line drawings.

J P M Bronan has made a further contribution to the 'Flora of Tropical East Africa', the portion now published dealing with Leguminosae subfamily Mimosoidae (publ Crown Agents for Oversea Governments and Administrations London, May 1959 price 12s). The main features of the subfamily are set out together with a bibliographical commentary and there is an analytical key to the genera based on vegetative and fruit characters. There are also analytical keys to the species within individual genera. The text contains much useful descriptive matter dealing with distribution habitat etc., and is illustrated by line drawings.

Royal Commission for the Exhibition of 1851

The following awards have been made for 1959 Senior Studentships D W Barnes (University of Oxford) for research in pure mathematics at Tübingen P J Goodford (University of Oxford) for research in pharmacology at Oxford A V Grimstone (University of Cambridge) for research in zoology at Cambridge D O Hayward (Imperial College of Science and Technology) for research in physical chemistry at the Imperial College of Science and Technology M Wells (University of Cambridge) for research in physics at Cambridge. The Senior Studentships are of the value of £800-£900 a year and tenable ordinarily for two years. Overseas Scholarships G F O Langstroth (Dalhousie University) for research in physics at University College, London A J McComb (University of Melbourne) for research in plant physiology at King's College London J W White (University of Sydney) for research in physical chemistry at Oxford Miss S G Page (University of New Zealand) for research in biophysics at University College London, A Chisholm (University of New Zealand) for research in physics at Liverpool M H Proctor (Trinity College, Dublin) for research in biochemistry at Cambridge A J Ganguly (University of Delhi) for research in organic chemistry at the Imperial College of Science and Technology London M Jancel (University of Karachi) for research in physics at Cambridge. The Overseas Scholarships are of the value of £550-£650 a year and tenable for two or three years.

American Academy of Arts and Sciences Foreign Honorary Members

The American Academy of Arts and Sciences, at its 170th annual meeting on May 13, in Boston, elected 113 new Fellows from the United States, and 21 new Foreign Honorary Members as follows: Sir John Eccles, Australian National University, Canberra, Jean Brochet Université libre de Bruxelles Georges Braque Paris Albert Camus, Paris; Jean Lory, Collège de France, Paris Max Born Bad Pyrmont, Germany George Keith Batchelor, Cambridge, Sir Isidore Berlin, Oxford Sir Lawrence Bragg Royal Institution London; Frank C Francis, British Museum London Anna

Freud, London, David Keilin, Cambridge, P B Medawar, University College, London, Sir George White Pickering, Oxford, Ronald Syme, Oxford, Federico Chabod, Croce Institute, Naples, Hitoshi Kihara, National Institute of Genetics, Misima, Carlos Chavez, Mexico City, M G J Minnaert, University of Utrecht, Alf A Sommerfelt, University of Oslo, A N Kolmogorov, Academy of Sciences, Moscow

At the same meeting Dr Kirtley F Mather, emeritus professor of geology, Harvard University, was re-elected president for another year

University News

Bristol

THE following appointments have been made Dr J T Martin to a readership in chemistry of insecticides and fungicides Lectureships have been conferred on Dr E W Abel (inorganic chemistry), Dr R F Burbridge (electrical engineering) and R H C Penny (chemical pathology, veterinary)

University College, Dublin

Dr A L KAPOOR of the National Chemical Laboratory, Poona, has been appointed an ICI Fellow in Chemistry at University College, Dublin

Liverpool

THE following appointments have been made to take effect from October 1 Dr B Collinge, reader in physics, Dr P M Sheppard, reader in genetics The following have been appointed to senior lectureships Dr A K Holliday, inorganic and physical chemistry, Dr N S Jones, marine biology, Dr T M Flett, pure mathematics, Dr A Ashmore, physics, Dr H D Parbrook, physics-acoustics, Dr V H Leek, electronic engineering, Dr R S Benson and Dr N G Calvert, mechanical engineering, Dr F T W Jordan, veterinary preventive medicine

University College of North Staffordshire

Dr D J E INGRAM, at present reader in electronics in the University of Southampton, has been appointed professor of physics, to take effect from October 1

Nottingham

THE following appointments have been made to take effect from October 1 Dr K J Standley, to a readership in physics, Dr G E Lamming, to a readership in animal physiology, Dr M Woodbine, to a readership in agricultural microbiology

Sheffield

THE following appointments have been announced Dr D E Bourne, lecturer in applied mathematics, Dr R S Duff, senior lecturer in medicine, I E Gillespie, lecturer in surgery, D W Warrell, lecturer in obstetrics and gynaecology, L Grimshaw, lecturer in psychiatry

Swansea

PROF F LLEWELLYN JONES, professor of physics, University College of Swansea, has been appointed acting principal of the College until such time as a new principal takes office

Announcements

Dr P T HASKELL has been appointed deputy director of the Anti-Lecust Research Centre, London, in succession to Dr T H C Taylor, who became

director on the retirement recently of Dr B P Uvarov (see *Nature*, 183, 1160, 1959) Dr Haskell has been at the Centre since 1955, and was previously lecturer in entomology in the Imperial College of Science and Technology, London Most of his published work has been concerned with sensory physiology, especially the production and perception of sound in insects

Dr CARL F KOSSACK, formerly head of the Department of Mathematics and Statistics at Purdue University, has joined the research organization of the International Business Machines Corporation at the Lamb Estate Research Center in the Town of Cortlandt, New York Dr Kossack is manager of the newly formed Statistics and Operations Research Department Dr Kossack gained his B A and M S degrees in mathematics at the University of California and his Ph D degree in mathematical statistics from the University of Michigan

A JOINT meeting of the Challenger Society and representatives from the marine laboratories (Development Commissioners' scheme) will be held at the Guildhall, Conway, North Wales, on October 28 and 29 Further particulars of the meeting can be obtained from Dr H O Bull, Dove Marine Laboratory, Cullercoats, Northumberland

THE USSR Academy of Sciences began to publish in the Russian language in 1959 the following new journals (in brackets, the first figure indicates number of issues per annum, the second figure, the price in roubles per annum) *High Molecular Compounds* (12, 150), *The Geology of Ore Deposits* (6, 72), *Palaeontological Journal* (4, 60), *Radiochemistry* (6, 72), *The Physics of the Solid Body* (12, 150), *Cytology* (6, 72), *Soviet Slavic Studies* (4, 50)

THE Commonwealth Scientific and Industrial Research Organization of Australia has issued a pamphlet listing the Organization's Divisions and Sections, as at January 1, 1959, giving the address of each and its laboratories, and the names of the Officers-in-Charge State Committees are also listed Publications of the Organization, to December 31, 1958, including those of its predecessors, are listed in a separate pamphlet

VOLUME XV of the Collected Papers of the Rowett Research Institute (Bucksburn Rowett Research Institute, 1959) contains an account of work of the Institute, lists of members of its governing body and scientific staff and of 88 published papers, reprints of most of which are available, as well as a summary, by the Director of the Institute, of the contents of published papers of the Institute 1957-58 so arranged as to indicate the scope, continuity and integration of the research programme Two subject reviews are also included by J J Bullen on experimental reproduction of enterotoxaemia of sheep and by J Duckworth on Institute research on the skeleton in lactation and growth

THE Department of Scientific and Industrial Research will shortly resume publication of its *Technical Digests*, last issued in 1957 Their object is to direct attention to useful ideas appearing in technical literature, and following an initial free distribution to industrial firms they will be available at an annual subscription of £3 3s A reduction will be offered for supplies in quantity The digests will be published monthly, each being printed on a separate sheet of paper

THE TWO CULTURES AND THE SCIENTIFIC REVOLUTION

SIR CHARLES P. SNOW'S Rede Lecture* for 1959 carries forward to a significant extent the old arguments concerning those subjects commonly spoken of as the humanities on one hand and the sciences on the other. The teaching of the history and sociology of science to arts students and the teaching of the history of art and literature to science students is better than nothing though it is difficult to see how the history of science can make much impact without a knowledge of the methods and results of scientific investigation. The corpus of knowledge of all types is now so vast that it is foolish to look back to a Hellenic or Thomistic attempt at a synthesis.

Sir Charles Snow is both a literary man and a scientist and is able to see each side of the problem from the other. He seems to find the snug, self-contentment of many of the literary men more dangerous and irritating than the failure of some scientists to realize the implications of their own work in the broader field of human knowledge and aspiration. "Why do most writers take on social opinions which would have been thought distinctly uncivilized and démodé at the time of the Plantagenets? Wasn't that true of most of the famous twentieth century writers? Yeats, Pound, Wyndham Lewis run out of ten of those who have dominated literary sensibility in our time—were they not only politically silly, but politically wicked? Didn't the influence of all they represent bring Auschwitz that much nearer?"

But it is ill-considered of scientists to judge writers on the evidence of the period 1914-50. Literature changes more slowly than science. It has not the same automatic corrective and so its misguided periods are longer.

At one pole, the scientific culture really is a culture not only in an intellectual but also in an anthropological sense. Its members need not always completely understand each other—biologists more often than not will have a pretty hazy idea of contemporary physics—but there are common attitudes, common standards and patterns of behaviour, common approaches and assumptions. This goes surprisingly wide and deep. It cuts across other mental patterns, such as those of religion or politics or class. In their working and in much of their emotional life their attitudes are closer to other scientists who in religion or politics or class have the same labels as themselves. At the other pole the spread of attitudes is wider. It is obvious that between the two as one moves through intellectual society from the physicists to the literary intellectuals there are all kinds of tones of feeling on the way. But I believe the pole of total incomprehension of science radiates its influence on all the rest. That total incomprehension gives much more pervasively than we realize living in it, an unscientific flavour to the whole traditional culture, and that unscientific flavour is often, much more than we admit, on the point of turning anti-scientific. Once or twice I have been provoked (by the 'non scientists') and have asked the company how many of them could describe the Second Law of

Thermodynamics. The response was cold—it was also negative. Yet I was asking something which is the scientific equivalent of 'Have you read any work of Shakespeare's?'

Little purpose is served by cataloguing the dismal ignorances in many arts people of the simplest fundamental principles of science. "The separation between the scientists and non scientists is much less bridgeable among the young than it was thirty years ago then they managed a kind of frozen smile across the gulf. Now the politeness has gone and they just make faces. It is not only that the young scientists now feel that they are a part of a culture on the rise while the other is in retreat. It is also to be brutal, that the young scientists know that with an indifferent degree they will get a comfortable job, while their contemporaries and counterparts in English or History will be lucky to earn 60 per cent as much. No young scientist of any talent would feel that he is not wanted or that his work is ridiculous as did the hero of Lucky Jim, and in fact some of the disgruntlement of Amis and his associates is the disgruntlement of the under employed arts graduates."

Sir Charles insists that we should completely re-think our education. "Nearly everyone will agree that our school education is too specialized. But nearly everyone feels that it is outside the will of man to alter it. Other countries are as dissatisfied with their education as we are, but are not so resigned. Because of our intense specialization alleged by schoolmasters to be dictated by the Oxford and Cambridge Scholarship examinations we have set ourselves the task of producing a tiny élite—far smaller proportionately than in any comparable country—educated in one academic skill." Snow takes as an example the old Cambridge Tripos which seemed to be perfect in all respects save one. The one exception was—so the young creative mathematicians such as Hardy and Littlewood, kept saying—that the training has no intellectual merit at all. They went a little further and said that the Tripos had killed serious mathematics in England since dead for a hundred years.

While we are beginning after many years, to understand the scientific and social implications of the industrial revolution and to understand the development in teaching technology in Germany in the nineteenth century and in the United States and U.S.S.R. in later years we are still far from grasping the meaning of the scientific revolution by which is meant the transformations made in industry and its effects because of electronics, atomic energy, automation and modern forms of machine tools.

We have failed to keep pace with the new scientific revolution—roughly if we compare like with like and put scientists and engineers together we are training at a professional level per head of the population one Englishman to every one and a half Americans to every two and a half Russians. In Russia the gap between the cultures does not seem to be as wide as it is with us. If one reads contemporary Soviet novels, for example one finds that their novelists can assume in their readers—as we cannot

—at least a rudimentary acquaintance with what industry is all about” The latest figures of graduates trained per year (scientists and engineers combined) are roughly United Kingdom, 13,000, United States, 65,000, U.S.S.R., 130,000. One-third of Russian graduates in engineering are women. “It is one of our major follies that we do not in reality regard women as suitable for scientific careers. We thus divide our pool of potential talent by two.”

“We are left with a population twice as large as we can grow food for, so that we are always going to be *au fond* more anxious than France or Sweden, and with very little in the way of natural resources—by the standard of the great world powers, with nothing. The only real assets we have, in fact, are our wits. Those have served us pretty well, in two ways. We have a good deal of cunning, native or acquired, in the arts of getting on among ourselves: that is a strength, and we have been inventive and creative, possibly out of proportion to our numbers. Given these two assets, and they are our only ones, it should have been for us to understand the scientific revolution first, to educate ourselves to the limit and give a lead. In some fields, like atomic energy, we have done better than anyone could have predicted. Within the pattern, the rigid and crystallized pattern of our education and of the two cultures, we have been trying moderately hard to adjust ourselves. The historical warnings are all there. For instance,

the Venetian Republic in its last half-century was guided by patriot men, who had immense political skill, who knew that the current of history had begun to flow against them. They were fond of the comfortable pattern of their life, just as we are fond of ours. They never found the will to break it.”

There is yet another danger. The large masses of poor in the undeveloped countries will not allow themselves to live for ever in a world in which large sections have become rich through industry. A new missionary spirit, both human and technical, is essential.

“Closing the gap between our cultures is a necessity in the most abstract intellectual sense, as well as in the most practical. When those two senses have grown apart, then no society is going to be able to think with wisdom. For the sake of the intellectual life, for the sake of this country’s special danger, for the sake of the western society living precariously rich among the poor, for the sake of the poor who need not be poor if there is intelligence in the world, it is obligatory for us and the Americans and the whole West to look at our education with fresh eyes. This is one of the cases where we and the Americans have the most to learn from each other. We have each a good deal to learn from the Russians, if we are not too proud. Incidentally, the Russians have a good deal to learn from us too.” W. L. SUMNER

COAL SCIENCE

THE third biennial International Conference on Coal Science was held at Valkenburg, in the Netherlands, during April 27–30. The Municipality kindly allowed the Conference to be held in the Municipal Theatre, and the greatest hospitality and interest were shown throughout by the burgomaster, F. A. A. H. Breckpot.

On this occasion the number of participating countries increased to fourteen, newcomers being East Germany, Czechoslovakia, Australia and India. Authors submitting papers were required to complete a form indicating, in telegraphic style, their main new conclusions and results, the methods and observations from which these were deduced, and any special limitations or assumptions involved in their interpretation. This information was found by the organizers to be more helpful than the conventional summary (or on occasions the paper itself) in deciding whether a paper was acceptable; it was also useful in evaluating the conclusions of the Conference and the interrelation of papers. The proceedings of this Conference will not be published as a whole, but papers will be submitted by their authors to journals of their own choosing.

Discussion was unusually lively and fruitful, and a large proportion of novel work was presented. In several cases widely accepted ideas were apparently undermined, though it would be premature to assess the importance of the new evidence. For example, a suggestion arose, from the work of S. Ergun and I. Wender on the X-ray scattering of vitrinites reduced with lithium in ethylene diamine, that partially reduced aromatic and/or alicyclic molecules may lead to reflexions in the angular region where the (10) and (11) reflexions of aromatic mole-

cules occur. This awaits direct experimental test, but if correct it may throw doubt upon the derivation of aromatic layer sizes in coal, for example, by Hirsch and Diamond. Ergun and Wender also demonstrated an increase of layer spacing on reduction, even in graphite.

Similarly, an interpretation of data obtained on coal by high-resolution magnetic resonance spectroscopy, by J. K. Brown, W. R. Ladner and N. Sheppard, yielded a structural distribution of non-aromatic carbon atoms which may prove incompatible with the present consensus of opinion on the chemical structure of coal. As a third example, R. L. Bond and D. H. T. Spencer illustrated the inadequacy of existing interpretations of sorption data obtained with inert gases on coal and of heats of wetting of coal in polar liquids, a question thought by many to have been settled, at least in principle.

These, and the other thirty-three papers presented, were grouped under four heads, as follows.

Chemical Reactions of Coal

E. S. Hammack, H. G. Davis and F. B. Brown estimated the content of phenolic hydroxyl in vitrinites by titration with sodium aminoethoxide in ethylene diamine, by trimethylsilylation and by acetylation. They found reasonable agreement between these methods and noted the importance of particle size. Acetylation was studied by S. Delavarenne, A. Halleux and H. Tschamler, who also confirmed the presence of quinone groups in coal extracts, by reductive acetylation and reduction with copper/hydrogen sulphide. They observed the corresponding changes in the infra-red spectra and showed that the

reduction was to a large extent reversible. In both papers tests of the quantitative accuracy of the methods by experiments on model compounds such as quinones were reported. Evidence for the presence of thioether groups in coals to the extent of 15-90 per cent of the organic sulphur content was put forward by L Wąpłowska. The difficulty of combining all known observations on the chemical and physical nature of coal, together with the elementary analysis, in a structural model was emphasized by P. H. Givon, who by comparison of data and experiments with atomic models had been able to find only one satisfactory pattern of structure. The essential feature of this was that any pair of aromatic fused ring clusters is bound together by two methylene bridges.

E. J. Greenhow and J. W. Smith showed that pitch can be regarded as a solution of phenolic or basic compounds of medium molecular weight in a relatively non polar solvent, results suggested that the physical properties were influenced by intermolecular association.

There were three papers on chromatographic separation of oxidation products of coal. By F. Michol, J. E. Germain and F. Valadon, and G. J. Lawson and S. G. Ward. The first author had isolated small yields of anilino anthracene substituted anthraquinone, tetraphenol and fluoranthene from air or nitric acid-oxidized coals, the second group had identified various benzene polycarboxylic acids and the third malonic succinic and tartaric acids. S. Landa had studied hydrogenation of model substances, montan wax and humic acids extracted from brown coal, with tungsten and molybdenum sulphide catalysts. Hydrocarbons with two to three fused aromatic rings and side-chains were found among the products from treatment of the humic acids.

Ultra fine Structure of Coals and Chars

M. Wąpłowska discussed the influence of sorption on coals of organic vapours on their elasticity and the consequent dimensional changes. S. Ergun, W. F. Donaldson and I. Bregor showed that apparent changes in rank induced in coals by α particles originating from natural impregnation by uranium differed from those caused by normal coalification processes.

J. L. Soule and S. Durif demonstrated, by measurements of small angle X-ray scattering, the presence in a wide range of coals of pores of sizes 22-25 Å and the variation of this characteristic with temperature of carbonization, they also deduced absolute values of specific internal surface. In the carbonization temperature range 500-700°C these surface areas agreed with those estimated by P. Chiche and S. Prégermain from adsorption of water and methanol vapours.

Sorption of pyridine by carbonization products, their solubility in it and their swelling in various organic liquids were studied by A. Ladam and P. Payen. Important changes were indicated in the region 400-500°C. S. J. Gregg and M. I. Popo had studied the effect on the electrical conductivity of coal artefacts, of pressure and of exposure to atmospheres of various humidities. J. J. Kipling and R. B. Wilson from a study of the sorption of gases and vapours on chars prepared by carbonizing synthetic polymers demonstrated the presence of microcapillaries of 5-10 Å diameter, molecular sieve properties of the structure, and the effect of steam activation in opening up this structure. A. Camoron and W. O. Stacey combined measurements of internal

surface area, apparent density and measurement of internal volume with the porosimeter to demonstrate the presence of two distinct pore systems in chars prepared from brown coals. The presence in 600-900°C chars of cavities of some 25 Å linked by passages less than 10 Å wide was inferred.

Spectroscopy of Coals

There were two papers on mass spectroscopy. One by J. C. Robb and H. W. Holden, was concerned with the volatile products either volatilized or liberated by pyrolysis when coal was heated in the ion source. Interesting identifications in relation to temperature range were made. The other by R. I. Reed and W. Snodden, was chiefly concerned with the fragments produced from aromatic compounds and thus widened the background available for interpreting results with coals. Electron magnetic resonance spectroscopy had been used to study coals in course of carbonization under vacuum, by J. Smidt and D. W. van Krevelen. In addition the time of relaxation T_1 was measured as a function of temperature. J. Uebersfeld had applied combined nuclear and electron magnetic resonance measurements and found evidence of interaction between protons and free radicals in coals of low rank, exchange interaction in those of high rank. Light spectroscopy was represented in two papers, by R. A. Durio and J. Szewczyk and by S. Ergun and J. T. MacCartney. The first was concerned with a long wave length absorption edge which moves into the infra red with increasing temperature of pyrolysis. The magnitude of a corresponding energy gap in the structure was discussed in relation to the graph of polynuclear aromatic structures. In the other paper an attempt was made to establish specific reflectance of coals as a significant structural parameter, related to the hydrogen/carbon ratio and to the diamond and graphite structures as extremes.

Carbonization

C. Kröger, R. Bräcker, M. Klatt and E. Bado had studied the maceral species oxinito and vitrinito by pyrolysis under high vacuum. They discussed the origin of the liquid and gaseous products determined. A. M. Wandless and G. W. Fenton described coking tests, on coals of 84, 85 and 87 per cent carbon content that indicated a beneficial effect on the coke strength of the maceral inertinito as a constituent in the coal blend at the two lower levels of rank. D. W. van Krevelen, F. J. Huntjens and A. H. Wilms presented a thorough study of strength of coke in relation to particle size of coal carbonized. A. D. Dainton, W. G. Kaye and J. W. Phillips described the effect of macerals on volume changes in briquettes during carbonization. A. F. Boyer and P. Pavon throw doubt on the interpretation of an apparent exothermic peak found in the differential thermal analysis of certain coals. They considered this to result from an increase of conductivity due to agglutination. Finally in this series there was an outstanding paper by P. M. J. Wolfe, D. W. van Krevelen and H. I. Waterman on the carbonization of synthetic polymers containing aromatic units linked by methylene bridges labelled with radioactive carbon. Their fate on pyrolysis could be readily followed. The course of chemical decomposition was thus related to other measurements on the polymer, for example in a dilatometer test and a thermobalance.

M F Kessler and V Večeřikova reported a variety of physical and physicochemical measurements on cokes and related them to hardness and reactivity. J H Ehretsmann and R C Seymour had studied the gaseous products and thermochemistry of the formation and decomposition of surface oxides on charcoals. H Guérin and M Bastiek demonstrated the importance of microporosity during gasification of coke between 800° and 1,000° C. C Heuchamps, L Bonnetain, X Duval and M Letort showed that the apparent energy of activation of the combustion of graphite varied with temperature and extent of combustion, and was a complex function of heterogeneity, porous structure, impurities and reaction mechanism.

It is appropriate after three successive occasions when the burden of organization has largely been borne by the Dutch State Mines to add an appreciation of the magnificent arrangements made by the

scientific and administrative staff of that body. The never failing resourcefulness of Mr W J R Berke in all aspects is especially worthy of mention. The moving spirit behind these conferences has been the president Prof D W van Krevelen, and it must be recorded with regret that he has now resigned the presidency in view of his pending transfer from the coal to the plastics industry. To mark the occasion, tributes were paid at the end of the Conference by R Loison, I G C Dryden and M-Th Mackowsky on behalf of the French-, English- and German-speaking sections of the audience. Prof van Krevelen's impact on coal science has occurred only within the past ten years, yet, owing to the original and prodigious output of his research teams, he has left nothing unchanged. The Conference wished him every success in his new field of endeavour.

I G C DRYDEN

CURRENT RESEARCH ON NOISE

IT is only within recent years that acoustic noise, once studied simply for its effect on hearing and annoyance, has proved important in physical systems. Noise has long been a source of annoyance, its effects on working efficiency have been clear when it has interfered with speech communication, less clear in causing fatigue, and for years it has been realized that continued excessive noise can cause permanent deterioration of hearing—'boilermaker's deafness' has long been known.

These effects are still with us, in intensified form, since with the increased power of machines to-day, noise—as a by-product of this power—is increasing also. For this reason, the physical aspects of noise have come to the fore. The intense fluctuating pressures in the noise field near a jet engine can fatigue and fracture the structure of the aircraft. The forces on a missile flying through rough air may consist largely of random constituents, which need to be analysed in some detail to determine whether any frequencies are present which may damage the equipment in the missile. Such analysis is, of course, similar to that used in many other fields, such as radar, and thus acoustic noise problems find their counterparts in other studies.

These different aspects of noise were explored recently in two symposia held by the Acoustics Group of the Physical Society. The first, "Recent Studies of Noise Problems", was held at the Imperial College of Science and Technology, London, on March 24, with four papers on psycho-acoustic problems, and two on physical acoustics.

Human Response to Noise

The general effect of the first group of papers, curiously, was that work in many aspects of the subject culminated some five years ago in the United States, and little advance has been made since. This was particularly true of the account of noise and hearing loss given by Prof W Burns (Charing Cross Hospital Medical School). This subject is still heavily in debt to the classic report (Z24-X-2) of the American Standards Association, and little more has been learnt about safe noise-levels. However, work is continuing on the effect of age on normal hearing, this will give a better 'base-line' for the

estimation of hearing damage and is a subject on which the American report was not very satisfactory.

Procedures for evaluation of the loudness of a complex sound, however, have progressed very little in any country. This was discussed by Mr N Fleming and Mr D W Robinson (National Physical Laboratory). The National Physical Laboratory equal-loudness contours remain unchallenged, but they are for pure tones only. The various ways of dividing and weighting the spectrum, in order to calculate loudness, do not seem very productive, while annoyance is a factor even harder to measure objectively.

Much of this difficulty may be due to the fact that pure tones have in the past been considered of major importance. But as speech, and even music, are in effect successions of transients, many noises should be considered in the same way, and a study of the aural effects of transients may be a more fruitful approach.

The point was, however, made by Mr Fleming that the multiplicity of criteria in American psycho-acoustic studies may not be needed. He pointed out the equivalence between the 'equal-annoyance' contours for community noise, and the readings of representative noises on the *A* weighting of the sound-level meter. The *A* weighting is a valuable one for many approximate loudness studies: it is frequently used on the European continent in traffic noise problems.

Further points on community reaction to noise were dealt with by Mr H J Purkis (Building Research Station). The techniques for evaluating the annoyance of different types of noise, developed in America some years ago, still appear generally valid, although some alterations to suit the differing susceptibilities of English communities are needed. It is hoped to collate several case histories of noise annoyance, with the view of obtaining more applicable data.

Dr D E Broadbent (Medical Research Council) spoke on the effects of noise on working efficiency. This is a field in which it is most difficult to obtain conclusive results. A pattern is, however, beginning to emerge, connected with the effect of noise in interrupting attention, noise often seems to interfere with tasks necessitating short-term memory. An overall level of 90 db appears critical, and it is found

that, whatever may be the effect on efficiency at work, noise increases for example wastage rate and number of mistakes

Physical Acoustics

Two papers on physical noise problems were presented. Mr D M A Mercer (University of Southampton) dealt with the difficulties inherent in obtaining accurate measurements of aircraft noise. Such factors as ground reflexions, size and behaviour of source can cause errors of a few decibels. Comparisons of, for example, the performance of jet silencing devices may be quite misleading if these precautions are not taken.

Diesel engine noise was discussed by Dr A E W Austen and Dr D Friede (C.A.V. Ltd.). Speed and swept volume have been related to sound output; there is little variation with load, due to the characteristics of the diesel engine. A quite thorough survey has been made of the vibration of different surfaces of the engine and their effects as noise producers, and sound levels calculated from these are consistent with measured noise levels.

Aspects of Noise Analysis

The second symposium on "New Techniques in the Analysis of Noise and Vibration" was held in the Physics Department of the University of Southampton as a joint meeting with the Institute of Physics. The attendance of about 150, drawn from diverse fields of physics, engineering and electronics, indicated the considerable interest in the analysis of noise in the widest sense. The emphasis was on new and projected techniques; standard bandpass filtering methods received little attention.

The meeting was opened by Mr R A Eades (Signals Research and Development Establishment, Christchurch) who described the speech spectrograph, an instrument capable of examining and analysing short samples of sounds and presenting the analysis in a manner similar to that of the visible speech techniques. Mr Eades made the important point that, in much of this work, bandpass filters with sharp cut-offs are not desirable, due to the ringing they give; the lowered frequency discrimination of a filter of Gaussian or tuned circuit characteristics is amply repaid by freedom from ringing.

Mr G J Herring (Royal Aircraft Establishment, Farnborough) described an analogue-to-digital con-

verter which converted a fluctuating voltage into an input suitable for a Pegasus digital computer. The computer could then be used to make an analysis of the input wave form. This method was developed because purely analogue methods had proved unsatisfactory. This paper and the previous one led to considerable discussion; it was clear that the problem of analysis of random wave forms was important to many workers. One point, however, was that the distinction between wave forms with and without a periodic component—a difference important to the statistician—was not always made clear, with consequences perhaps of unnecessary difficulties in many analyses.

Mr D M A Mercer (University of Southampton) emphasized the practical point that in any analysis frequency discrimination, stability of estimates and ease of computing were all linked and could not all be maximized at once. Great care was needed in the planning stages of an analysis. Cross-correlation techniques were often able to give results unobtainable by straightforward methods.

Dr G M Jenkins (Imperial College of Science and Technology, London) discussed the statistical implications of obtaining a spectrum via an autocorrelation. It is desirable to examine the autocorrelation itself before the Fourier transform process; in any event some modification to it is often desirable to obtain a more stable spectrum, but in addition much information is often available at this stage and different applicable statistical criteria were described.

The ensuing discussion demonstrated much interest in the use of axis crossings of a random function. Presumably there is a major theoretical break-through to be looked for on this topic, but apart from this theoretical and experimental studies demonstrate that axis-crossings carry most of the information of a wave form (apart from magnitude of course). The limitations of the method, however, are not yet known.

The concluding impression of the symposium appeared to be twofold: first, that noise in the widest sense is a subject of considerable interest; and secondly, that there often appeared to be a considerable gap between the theoretical studies and the work of those concerned with practical noise and vibration analysis. This leads, at best, to correct analyses obtained with unnecessary difficulty and at worst analyses which are meaningless. Closing of this gap would be of benefit to all concerned.

DENWENT M A MERCER

BIOSYNTHESIS AND SECRETION OF ADRENOCORTICAL STEROIDS

At a symposium held on February 14 the Biochemical Society gathered together a group of investigators who described their own work and that of others on various aspects of the biosynthesis of the adrenocortical hormones. In an introductory paper, I E Bush described the chemical nature of the steroids under discussion and the application of various types of chromatographic procedures to the separation and identification of these substances. An important feature of steroid chromatography is the very large number of possible compounds and the danger of wrong identification if chromatographic properties are relied upon to the exclusion of others. This danger may be diminished by the use of numerous

microchemical and spectrophotometric techniques. The former include acetylation or oxidation (notably the removal of the C 17 side chain) on the 10–20 μm scale followed by observation of the chromatographic behaviour of the product on paper. Spots of steroid on paper give various well-known colours and very sensitive fluorimetric reactions. On the physical side a wide range of correlations between structure and absorption bands in the infra-red region has been established. Ultra-violet absorption spectra in sulphuric acid and alcoholic alkali provide useful information which, in conjunction with paper chromatography and comparison with reference substances, may provide identifications almost as reliable

as those from infra-red spectra. New work in Bush's laboratory has shown that useful generalizations about the behaviour of steroids in partition systems can be made using Martin's theory and the R_F function of Bate-Smith and Westall. For this theoretical approach Bush has collected numerous R_F values from the literature. Not all will agree with him on the reliability of these values. The chromatogram tank is not yet a precision instrument.

J. K. Grant then reviewed present knowledge of the biosynthesis of adrenocortical steroids. Here there are at least three questions to be answered. What is the nature of the secretion of the adrenal cortex, what sequences of reactions are involved in the syntheses of the steroids in the cortical cells and what are the mechanisms of these reactions? Complete answers cannot be given. The analysis of adrenal venous blood collected from animals and from human subjects undergoing adrenalectomy has provided direct evidence of the nature of the steroids secreted by the adrenal gland. Hydrocortisone, corticosterone and aldosterone are the principal C_{21} compounds found. The last of these, and a variety of others of less physiological importance, are present in trace amounts. There is indirect evidence that the adrenal cortex in man secretes a substance which, in contrast with aldosterone, promotes the excretion of sodium. A new steroid (3β , 16α -dihydroxy- 5α -pregnan-20-one), which produces this effect in rats, has recently been isolated by Wettstein from the adrenal glands of swine. There is also evidence that the adrenal gland secretes androgenic and oestrogenic steroids.

Application of a variety of techniques has clearly established that adrenocortical steroids may be formed in the gland from acetate or cholesterol by formation and subsequent hydroxylation of progesterone. An outstanding question of major interest is the possibility of alternative pathways to those originally proposed. These alternatives are concerned with the order in which the hydroxylations of the key intermediate progesterone proceed, with the possibility that cholesterol is not an obligatory intermediate in hormone formation, and with the direct transformation of cholesterol to C_{21} steroids. Hydroxylations commonly occur at C-17, C-21 and C-11 β in that order. It has been shown beyond reasonable doubt that a C-21 hydroxy steroid cannot undergo hydroxylation at C-17. Grant has, however, demonstrated that 11 β -hydroxylation of progesterone can proceed in good yield. Hydrocortisone may then be formed from 11 β -hydroxyprogesterone but at rates too slow to be of significance in normal biosynthesis. This alternative pathway may, however, be important in pathological states. Despite much suggestive evidence and numerous experiments with isotopically labelled compounds, it has not been possible to establish firmly the existence of alternative pathways from acetate to adrenocortical hormones which do not involve cholesterol. When such pathways appear to have been demonstrated, alternative explanations of the results have been possible if the existence of different metabolic pools of adrenal cholesterol is assumed. In other cases the results are unacceptable since the comparisons between the specific activities of precursors and products have been made at one point in time and not on a kinetic basis known to be essential in order to avoid misinterpretation of results. Despite intensive study, the mechanism of steroid hydroxylation has not been

elucidated. Molecular oxygen and reduced triphosphopyridine nucleotide are essential. It has not been possible to confirm that a transhydrogenase is involved in the formation of reduced triphosphopyridine nucleotide. It has been suggested that the reduced nucleotide is required for the reduction of an oxygen activating or transferring enzyme containing a heavy metal, but proof is lacking. There are, however, indications that the 11 β -hydroxylating enzyme system located in the mitochondria is complex. The observation that 2-methyl 1-(2-bis-(3-pyridyl) 1-propanone) (SU 4885) appears to be a specific inhibitor of 11 β -hydroxylation *in vivo* and *in vitro* has aroused considerable interest.

Adrenal glands of the rat, ox and man have been most extensively studied. The anatomy and histology of these glands were described by T. Symington. He directed attention to two features which have not until recently received adequate attention from biochemists: the unusual musculature of the adrenal veins which may, by restricting blood flow through the gland, influence steroid biosynthesis, and the marked differences in histology between the ruminant and non-ruminant adrenal cortex. The fascicularis and reticularis zones, readily distinguished in non-ruminants, are not distinguished in the ruminant. In the ox, which is typical of the ruminants, a broad zone of 'compact' cells fills the cortex from the medulla to the prominent glomerulosa beneath the capsule. In man, the fasciculata zone of variable width is filled with lipid-laden 'clear' cells and lies between the reticularis zone of 'compact' cells and the glomerulosa, which is very irregular, forming islands under the capsule so that glomerulosa cells are absent from some sections. The ox adrenal gland is for this reason a more satisfactory object than the human gland for the *in vitro* study of the synthesis of aldosterone which appears to occur in glomerulosa cells. The morphology and histochemistry of 'clear' and 'compact' cells and the influence of corticotrophin thereon have been studied in Symington's laboratory using glands removed surgically in two stages for the treatment of breast cancer. The use of these fresh glands has also permitted the study of enzyme reactions involved in steroid biosynthesis. These biochemical studies and in addition the results of analysis of adrenal venous blood obtained at the time of adrenalectomy have been correlated with the morphological and histochemical observations. It would appear from the results obtained that 'clear' cells of the fasciculata zone may function as stores of hormone precursor, and that the 'compact' cells of the reticularis zone, far from being the senescent cells described by others, may be the site of active hormone biosynthesis. 'Clear' cells are converted to 'compact' cells under the influence of corticotrophin, which stimulates corticosteroid secretion, influencing various steps in the sequence of biosynthetic reactions. Studies with the electron microscope in Glasgow have revealed important differences between the 'clear' and 'compact' cells, the most striking features of which are the microvilli, which form extensions of the cell membrane running out into the intercellular spaces. The function of the microvilli is unknown, but it is interesting to speculate that they may be concerned with secretory processes.

P. J. Ayres described the relation of steroid secretion to the histological zones of the adrenal cortex, with particular reference to the evidence which he has obtained in collaboration with Dr and Mrs. Tait that aldosterone is synthesized and secreted

by the cells of the glomerulosa zone. This work developed out of early observations on the rat, these supported the view that a steroid active in electrolyte metabolism was secreted by the glomerulosa zone relatively independent of the pituitary but influenced by electrolyte intake. Further indirect evidence followed the isolation of the steroid concerned, aldosterone, from whole adrenal extract by the Taits in 1952. It was possible to show that aldosterone secretion, but not that of corticosterone is diminished in rats on a low potassium diet. Hypophysectomy has a much more pronounced effect on corticosterone than on aldosterone secretion in the rat. After this operation in dogs the fasciculated reticularis zone of the adrenal gland atrophies and the secretion of hydrocortisone and corticosterone falls by contrast the glomerulosa zone and the secretion of aldosterone are unaffected. Direct evidence for the preferential production of aldosterone in the glomerulosa zone was obtained by the Taits and their collaborators by incubation of adrenal capsule strippings to which glomerulosa cells were adhering, and of tissue from the underlying zone. In the ox the 17-hydroxylating enzyme system appears to be in the zone lying under the glomerulosa only, whereas the 18-oxidase system necessary for aldosterone synthesis is confined to the glomerulosa zone.

A remarkable feature of the adrenal cortex is its ability to synthesize all known types of steroid hormones. R. V. Short discussed the biosynthesis and secretion of sex hormones by the adrenal gland. In his laboratory, methods have been developed for the separation and determination of the major and some of the minor steroid constituents of adrenal venous blood. These have been applied to the analyses of blood collected from human subjects by A. P. M. Forrest in Glasgow and from adult, now born and fetal domestic animals by Dr. Short's collaborators in Cambridge. Progesterone has been found in adrenal blood from women, cows, sheep and pigs in concentrations higher than in the peripheral blood. 17 α -Hydroxyprogesterone, a steroid which is sixty times as active as progesterone in some biological assays, has been detected in the adrenal venous blood of women and cows. The interesting observation has been made that young calves secrete 20 α -hydroxypregn-4-en-3-one. This disappears from the secretion some time after birth and is replaced by the 20 β -epimer in the adult animal. The significance of this is unknown. There is good indirect evidence for the secretion of oestrogens by the adrenal cortex, but they must be present in human adrenal venous blood in amounts too small for detection by present methods. Four androgens have been reported in adrenal vein blood in man. Dehydroepiandrosterone is probably exclusively of adrenal origin, but its precursors are still uncertain. Androstenedione is undoubtedly the most biologically active adrenal androgen and it may be present in adrenal venous blood in relatively high concentration. It is remarkable that androstenedione and dehydroepiandrosterone cannot be detected in even large samples of adrenal venous blood in cattle. 11 β -Hydroxyandrostenedione is probably present in the adrenal venous blood of the cow and sheep as well as in that of the rat and cat, but this compound, in common with the other known 11-oxo C₁₉ steroids, seems to possess little biological activity. These observations may be of considerable importance in veterinary medicine and cast doubts on the reports of adrenal virilism in cattle.

The amount of corticosterone and hydrocortisone secreted by the adrenal cortex is controlled by corticotrophin from the anterior lobe of the pituitary. How the pituitary obtains the information necessary to enable it to adjust the activity of the adrenal cortex to the body's requirements is a fascinating question which has recently attracted much attention. Knowledge of this matter was reviewed by Marinho Vogt. Few histologists consider the nerve supply to the adenohypophysis adequate for the control of corticotrophin secretion, and this control is therefore assumed to be humoral. It has been shown that substances such as adrenalin, which may be carried by the systemic blood, can promote the release of corticotrophin by the pituitary. There is also much evidence in support of the view that a stressing stimulus results in nervous activity in the hypothalamus which elaborates a 'corticotrophin releasing factor'. This is carried by a 'portal' circulation to the anterior lobe, where it stimulates corticotrophin secretion. The original suggestion that the corticotrophin releasing factor is identical with vasopressin has been modified by the independent observations of Saffran and Guillemain, who now propose that it is a polypeptide similar to but different from vasopressin. The purified material is active *in vitro* in nanogram amounts, and microgram quantities produce a similar effect on the rat pituitary stores of corticotrophin or on blood corticosteroids as severe stress. The active material contains seven of the eight amino-acids of lysine vasopressin and, in addition, serine and histidine. Dr. Vogt also discussed the nature of stimuli which activate or inhibit hypothalamic activity. The level of corticosteroids in blood is now regarded as a contributing but not the sole factor accounting for the control of corticotrophin secretion in stress. Recent work suggests that the suppressing effect of high doses of corticosteroids may be on the hypothalamus rather than on the pituitary. In addition to lack of corticosteroid in the blood, afferent nervous impulses, especially if they elicit pain or worry, stimulate the release of corticotrophin but the nature of the stimulus or stimuli which act in other forms of stress is unknown. General depressants of the brain inhibit the release of corticotrophin.

Dr. Vogt also reviewed knowledge of the control of secretion of aldosterone. This secretion is less influenced by corticotrophin than that of the glucocorticoids. Farrel has, however, recently found that certain preparations of corticotrophin increased aldosterone secretion in the decerebrate hypophysectomized dog but satisfactory evidence for the existence of a specific pituitary hormone which influences aldosterone secretion is lacking. The role of such a hormone would be limited since increased aldosterone secretion in the hypophysectomized dog has been obtained with a variety of stimuli. Experiments in Dr. Vogt's laboratory have demonstrated the rapid and reversible response of aldosterone secretion in the dog to expansion and contraction of the intravascular volume. Infusion of blood decreases whereas hemorrhage increases the secretion of aldosterone. The former effect was less easily elicited than the latter.

In the final paper, N. Saba dealt with the mode of action of corticotrophin from the biochemical point of view. He referred to the observations of Hechter that corticotrophin acts on the conversion of cholesterol to pregnenolone and the later independent work of Heald and Grant on the stimulation of

11-hydroxylation by the trophic hormone Saba's results obtained in collaboration with Hechter suggest that corticotrophin influences the spatial relationships of enzymes involved in the biosynthesis of adrenocortical steroids. More recent work by others has revealed an effect of corticotrophin on enzyme systems which effects the reduction of triphospho-

pyridine nucleotide. The requirement for reduced triphosphopyridine nucleotide for steroid hydroxylation has already been referred to. If this is an important effect of corticotrophin it is difficult to relate it to the specificity of action of this hormone.

J. K. GRANT

EDUCATION IN THE UNITED STATES (1957-58)

EDUCATION in the United States of America is based on three fundamental concepts: that the primary responsibility for public education rests with the States, that every person has an equal right to educational opportunities, and that educated citizens are essential to freedom and human welfare. Working within these concepts during 1957-58 the United States made further progress towards its goal of improving education for all*.

Evidence of progress is found in the increasing educational attainment of the population. The number of school years completed by the average adult 25 years of age and over increased from 9.3 in 1950 to 10.6 years in 1957. The group 25-29 years had completed 12.3 years of schooling, while the group older than 65 had completed only 8.3 years.

Although education is a State responsibility, no State administers its schools directly. Laws have been enacted in each State dividing the territory of the State into local school administrative units, commonly termed school districts. The powers of local district school boards to establish and maintain schools are prescribed by State law, but permit exercise of local initiative in exceeding minimum educational standards required by the State. Each State has its own department of education, which exercises controls and provides specialized services to assist local school districts in conducting the State programme of education.

At the beginning of the school year there were 1,152,500 instruction rooms in full-time public elementary and secondary schools, an additional 142,300 rooms were needed to relieve over-crowding and to replace unsatisfactory facilities. About 70,500 instruction rooms were scheduled to be built during the year. About 61,000 rooms will be needed to accommodate next year's enrolment increase and to replace rooms that will probably be abandoned.

Almost one-third of all pupils enrolled in the public elementary and secondary schools are transported to and from school at public expense. During 1955-56, more than 10 million pupils were transported. In most States pupils must live $1\frac{1}{2}$ miles or more from the school to be eligible for transportation for which the State helps to pay the cost.

Institutions of higher education classified by type of support and control are of two general types—publicly controlled and privately controlled. One-third of the approximately 1,900 higher institutions are publicly controlled and supported by public or government agencies, two-thirds are privately controlled and supported by individuals or ecclesiastical, philanthropic and other groups. The State exercises little control over institutions of higher educa-

tion, even those supported by public funds, and consequently both types of institution operate with a high degree of autonomy.

In 1957-58 expenditures for education in public elementary and secondary schools and in higher institutions totalled 20,000 million dollars, which was 5.5 per cent of the 1957 total national income of 358,000 million dollars. Funds to cover expenditure in public schools were provided by Federal, State and local governments.

For the fiscal year 1958 the Federal Government appropriated approximately 2,000 million dollars for educational purposes. The total included funds administered by the Office of Education and was distributed as follows: Office of Education, 7,000,000 dollars, vocational education, 40,888,412 dollars, higher education, 5,051,000 dollars, school construction and maintenance, 225,650,000 dollars, and library services, 5,000,000 dollars.

Since the States have primary responsibility for public education in the elementary and secondary schools they provide funds and authorize local school districts to provide local tax-funds for public schools. In the 1957-58 school year it is estimated that of the total revenue for public schools the Federal Government provided 4 per cent, the States, 41 per cent, and local districts, 55 per cent. In recent years the percentage from Federal and States funds has been increasing slightly.

As much as 93 per cent of local educational revenue is obtained from property taxes. Local communities use the property tax to secure funds for current operating expenses and for school construction. Some local districts also levy non-property taxes for schools, including local *per capita* taxes and taxes on wages, sales and amusements. Non-property taxes for schools produce 7 per cent of local revenue.

Total expenditure per pupil in 1957-58 averaged 431 dollars, an increase of about 7 per cent over the amount in 1955-56.

Tax revenues supply most of the funds for public institutions, private donations, student tuition and endowment supply most of the funds for private institutions. The 1957 budgets for both private and public institutions for educational and general expenditures, excluding auxiliary services, student aid and plant expansion, totalled 3,200 million dollars. Of this, students paid 950 million dollars as tuition, earnings on endowment provided 150 million dollars, private gifts, 250 million dollars.

The organization of public schools is determined by State and local authorities, but generally the basic 12-year programme is organized as an 8-year elementary and a 4-year secondary programme or a 6-year elementary and a 6-year secondary programme. Typically a 6-year secondary programme is divided into a 3-year junior and a 3-year senior high school. The most common type of school is one

* Progress of Public Education in the U.S.A., 1957-58 (Washington, D.C. Gov. Printing Office, available also from H.M. Stationery Office, London.)

attended by almost all children of school age in the community, regardless of social or economic status, sex or vocational aim. On all levels schools vary greatly in size, from one room rural schools to large urban schools enrolling several thousand students. Improvement of the school district organization in sparsely populated regions has resulted in a continued decrease in the number of small high schools.

All States provide public schools and permit students between the ages of 6 and 20 years to attend. Most States have enacted compulsory attendance laws for certain age groups. The compulsory attendance ages range from 6 to 18 years, but a majority of the States require attendance between the ages of 7 and 17 years. Of the total population of persons between 6 and 17 years old in October 1957, 96.5 per cent were enrolled in school. At that time 93 per cent of all school age children, generally defined as those between 6 and 17 years old inclusive, were enrolled. In elementary and secondary schools the proportion of boys and girls was about the same but in higher education institutions men made up about two thirds of the student body and women one third.

School enrolments increased for the thirteenth consecutive year. In 1957-58, 43,135,000 persons or about one out of every four in the population, were attending public or private schools and colleges, an increase of more than 4 per cent over 1956-57.

The latest available data indicate that about one half of the high school graduates now go to college about 42 per cent full time and 8 per cent part time. Attendance of students at institutions of higher education is altogether voluntary. Assuming that they meet admission requirements, students are free to choose the type of institution they attend—public or private, liberal arts or technical, 2 year or 4 year and to pursue any curriculum or prepare for any profession to the extent of their abilities. A student in an institution may of his own volition drop out

altogether or transfer to another institution. In the autumn of 1957, colleges and universities enrolled more than 3 million students, an increase of 4 per cent over the autumn 1956 enrolment and a 43 per cent increase over the 1952 autumn enrolment. The number of freshmen entering college in the autumn of 1957 represented slightly more than 30 per cent of persons in the country who were 17 years of age in 1956. About 58 per cent of the students enrolled were in public institutions. Enrolment in public institutions is increasing more rapidly than in private. About 800,000 of the students attending full time lived in dormitories provided by the institutions.

The degree granting colleges conferred a total of 411,000 degrees in 1957-58, 8.3 per cent more than in 1956-57. Of the total conferred, 82.8 per cent were bachelor's, 15.1 per cent master's and 2.1 per cent doctor's degrees. The average cost of a year in college was between 1,500 and 2,000 dollars, and the median award in scholarship aid was less than 300 dollars.

In 1957-58 between 30 and 35 million adults participated in adult education programmes sponsored by industry, labour unions, the Armed Services, farm organizations and other groups. In carrying out their programmes these groups had the co-operation of public libraries, public school systems, higher institutions, television systems and Government agencies.

Extensive research is carried on by public and private agencies such as colleges and universities, State departments of education and various philanthropic groups. Their research is directed toward solving some of the problems facing education; for example, it includes further investigation of the learning process and the character and extent of individual differences. State departments and local school systems direct their research primarily to solving local problems and colleges and universities direct theirs to broader problems in education.

THE PHYSICAL SOCIETY, 1958-59

THE annual general meeting of the Physical Society was held on May 21 at the Royal Institution, London, and immediately following the meeting Mr J. A. Ratcliffe delivered his presidential address entitled 'Recent Trends in the Theory of the Ionosphere'. The report of the council of the Society and the accounts and balance sheet for 1958 were adopted at the meeting and the composition of the new council to hold office for the session 1959-60 was announced.

The income of the Society during 1958 exceeded expenditure by £4,581 and was mainly due to the increase in price of the Society's publications when sold to the general public which the council authorized in 1957. Notwithstanding the rise in price, sales have increased. The membership rose from 2,060 to 2,130 but the increase was entirely in the student membership grade. The forty-second annual exhibition of scientific instruments and apparatus was held during March 24-27 in the two halls of the Royal Horticultural Society. The size of the exhibition and attendance were similar to those of the previous year. The sales of the exhibition handbook and the receipts from exhibitors resulted in a satisfactory surplus of

£5,005 of which £4,000 was transferred to the exhibition contingency fund and the remainder to the general income and expenditure account.

The council's report refers briefly to the activities of the Society during the year and in particular to the conferences of two or three days duration which were held on various subjects in Cambridge, Durham, Malvern and Swansea. The attendances were usually between 200 and 250 of which approximately half on the average were members of the Society. A few research students and others were financially assisted to attend these conferences by means of a grant allotted to the Society by the Royal Society. The decision to recombine the two sections of the Society's *Proceedings* was put into effect during 1958 and the volume of work published (208 original articles, 74 research notes and 21 letters to the editor) was substantially the same as in 1957. Vol. 21 of the *Reports on Progress in Physics* which was published during the summer contained nine articles and these articles were also available for purchase separately.

The informal discussions with the Institute of Physics which began in 1957 to consider the

close co operation between the Institute and the Society were continued. A mutually agreed document entitled "Memorandum to Members—Proposal to Amalgamate the Institute of Physics and the Physical Society" was circulated, together with an explanatory letter from the president. A joint amalgamation committee has been set up and is now engaged in more detailed discussions.

At the annual meeting, the president, Mr J A Ratcliffe, the honorary secretaries, Dr C G Wynne,

Dr H H Hopkins and Mr A G. Peacock, the honorary foreign secretary, Prof E N da C Andrade, and honorary treasurer, Dr D A Wright, were re-elected to serve for 1959-60. The newly elected vice-presidents were Prof F. Llewellyn Jones and Dr G B B M Sutherland, and the newly elected members of council Mr D W Fry, Dr V. E Cosslett, Prof F. C Frank, Prof W E Burcham, Dr R L F Boyd, Dr R A Smith and Prof D H Wilkinson. S WENTROUB

SCHOOL MEALS IN ASIA AND THE FAR EAST

VARIOUS Food and Agriculture Organization conferences, as well as regional nutrition meetings convened periodically in co-operation with the World Health Organization, have emphasized the importance of supplementary feeding as a means of improving the nutrition of vulnerable groups. The First Regional Nutrition Committee in South and East Asia, which met in Baguio, the Philippines, in 1948, recommended a type of meal which could be supplied to school-children in the region. This meal pattern emphasized the use of cheap, locally available foods that would provide the children with all essential nutrients.

The Fourth Regional Nutrition Committee of the two Organizations, which met in Tokyo in 1956, considered a number of important factors relating to school feeding programmes, it recommended that the Food and Agriculture Organization should convene a school feeding seminar for countries in South and East Asia, at which the future development of school-feeding along sound lines could be discussed by appropriate country representatives.

Much of the Food and Agriculture Organization's practical work in school-feeding has been done in co operation with the United Nations Children's Fund, the Organization providing the technical guidance in organizing and developing programmes based initially on dried skim milk and other supplies

made available by the Fund. This Fund has become increasingly interested in the long-term development of measures to improve the nutrition of children and has recently been authorized to increase the scope of assistance which it can provide. It was agreed, therefore, that the Fund should join the Organization in convening the seminar. Because malnutrition is often a serious problem among children of pre school age, it was also agreed that consideration would be given to this important group of the population.

The seminar was designed to bring together, from the countries concerned, workers associated with various aspects of child-feeding programmes, in particular school-feeding programmes, for consideration of the problems met in developing them and of measures needed to improve and expand them on a sound nutritional and financial basis. The Government of Japan extended an invitation for the seminar to be held in Japan, and it was held in International House, Tokyo, during November 10-19, 1958. The seminar was attended by delegates from twelve countries in the region, as well as by representatives from the World Health Organization International Co operation Administration, and Co operative for American Remittances to Everywhere. A report on the seminar has now been issued (H M S O, 2s 6d).

INDUSTRIAL HEALTH IN THE POTTERIES

DURING 1956-58, four members of the factory inspectorate carried out a survey of industrial health in the pottery industry in the Stoke-on-Trent area. The survey was undertaken with the advice of the Industrial Health Advisory Committee. This Committee was set up in 1955 by the Minister of Labour and National Service to advise him on measures to further the development of industrial health services in work-places covered by the Factories Acts.

On the advice of the Committee the Minister instituted two industrial health surveys, which were to be regarded as pilot surveys. The first was of all the factories in a particular area—the town of Halifax was chosen—and the report on that survey was published in 1958. The second was a survey of a specific industry—the pottery industry.

A number of considerations led to the choice of the pottery industry. Among them was the fact that it is geographically compact, and that, although over

a number of years much has been done in the industry to eliminate or reduce the known health risk, it was considered that a survey of the pottery industry would have particular interest in giving an opportunity to assess both the success of the measures so far taken and the continuing needs.

Although a survey of this kind offers no basis for comparing conditions in the pottery industry with those of other industries, it is possible to draw some comparison between present conditions in the pottery industry and those of the past. General conditions in the industry to day are markedly different from what they were. The industry has done a great deal, particularly in the years since the end of the Second World War, to improve working conditions and to reduce the health hazards connected with pottery manufacture.

The classic industrial disease of the pottery industry was lead poisoning, due in part to the lead glazes used. By the middle 1940's the use of low-solubility

or leadless glazes had become so widespread that it was considered practicable to prohibit the use of any glaze that was not either leadless or of low solubility. This was not an easy requirement for all firms to comply with and the glazed tile industry was faced with a particularly difficult problem. Intensive research enabled all firms to be in a position to comply with the requirement when it became law. The other source of lead poisoning was the colour used in decorating the ware. Higher standards of cleanliness and improved methods of dust control have so far, dealt with this hazard, with the satisfactory result that in recent years lead poisoning has virtually been eliminated from the industry.

Another major achievement of the industry, this time in reducing the risk of pneumoconiosis, has been the substitution of alumina for powdered flint in the placing of china for the biscuit fire. When it became clear that alumina was a satisfactory alternative the china industry, in spite of some technical problems involved, agreed that the flint should be replaced by alumina. By 1947, when this change was made compulsory, all firms in the industry had in fact changed over.

Work on the control of dust in the making processes where there is a health hazard from pneumoconiosis is continuing. For some years the British Ceramic Research Association has been working on the dust

problems of the industry and has done much valuable research work into the behaviour and control of dust given off in certain processes. The Research Association has already designed dust-control plant for the processes of towing and hollow ware fettling which is proving most effective. Work is in progress on the control of dust in the dust tile making processes and to determine the most suitable material for workers' overalls where there is need to protect them against dust.

To provide a continuing forum for discussion of the health and safety problems of the industry, the Chief Inspector of Factories in 1956 appointed a Joint Standing Committee of the Pottery Industry. With the help of the British Ceramic Research Association it has published an advisory booklet on dust extraction in the pottery industry. It has also directed the attention of industry to the dangers inherent in the use of hydrofluoric acid in cleaning gold, encouraging the use of other methods which it has made known.

The aim of the survey was to present an objective picture of existing conditions in the industry and to indicate outstanding problems. The visits made by the inspectors have been followed up by action to secure improvements. The work that requires to be done in order to deal with outstanding problems is under examination by the Joint Standing Committee (H.M.S.O. 5s.)

DEVELOPMENTS IN TRAINING

A SERIES of five papers on training were given at the Polytechnic, Regent Street, to an audience of two hundred directors and industrial executives during January and February, 1957. They have now been reprinted and form a valuable addition to the scanty information available for those concerned with all aspects of training in industry.*

The first, by Prof J. Z. Young, deals with the fundamental aspects of learning by drawing on biological studies of organisms at all levels of complexity. Developing the importance of perception in learning, W. D. Seymour of the Department of Engineering Production in the University of Birmingham, produces evidence to show that carefully devised training procedures for manual skills which take

account of recent findings will usually halve the normal learning period. In the third lecture, Mrs W. Raphael, assistant director of the National Institute of Industrial Psychology, describes the in-plant training being carried out in seven European countries and shows that the training provided for operatives exists largely in name only. F. A. Heller, head of the Department of Management Studies at the Polytechnic, shows how the development of managerial skills can be approached from the same biological and analytical points of view as any other skill training. Like other lectures in the series, he pays special attention to the methods rather than to the content of training programmes. The fifth lecture was given by S. D. M. King, director of Organization and Training, Ltd., who used case studies to illustrate the importance of relating training to a carefully devised policy at all levels of an organization.

* *New Developments in Training. Five Studies in the Efficient Communication of Skills.* Edited by Frank A. Heller. (New Development Series No. 5.) Pp. 60. (London: Polytechnic Management Association 1959.) 5s.

ERGONOMICS

THE development of modern industry with the substitution of mechanization for craftsmanship has brought new problems: the machine has reached the point where it is no longer the limiting factor in production and this in turn is imposing new stresses and strains on the operator who can no longer be left to get along as best he can. That this was beginning to happen began to be realized about fifty years ago, and early developments in fitting the job to the man like the motion study of Gilbreth were part of scientific management for

increasing production through reduction of fatigue. Most of the biological sciences began to become aware that people at work were worthy of study and that remarkably little was known about their capabilities and aspirations.

It took the added stress of two world wars to stimulate any real interest. A start was made in the First World War when groups of physiologists and psychologists such as the Industrial Fatigue Research Board in the United Kingdom started work. Between the wars progress was slow, perhaps because a general

labour surplus removed a demand for maximum economy in use of labour, but during and since the Second World War the research effort has been vastly intensified. Much of it gained its initial impetus from the armed forces and has, particularly in the United States, continued to be supported by them. In other countries research has been much more directed towards solving industrial problems as typified by that done by work physiologists in Sweden and Germany.

The fragmentation of the subject into a number of disciplines independently studying human work could not continue indefinitely, and the first fusion occurred in the United Kingdom in 1949 with the formation of an interdisciplinary society and the coming of the term 'ergonomics' to cover the study of human work. Although the British society

attracted adherents from all over the world it soon became clear that a truly international meeting was needed. The initiative was taken by the European Productivity Agency in the form of Project 335, the final aim of which is a tripartite international conference of scientists, employers and employees. As a preparation for this, two preliminary steps were taken. The first was to send a mission to the United States to report on the situation there, and the second was to hold a technical seminar to assemble information on progress in Europe. A report has now been issued, part one of which contains the report of the mission and part two a report on the seminar*. The tripartite conference has still to take place.

* *Fitting the Job to the Worker: A Survey of American and European Working Conditions in Industry* (Paris, O.E.C.D., 1959).

AN OCEANOGRAPHIC SURVEY OF THE ROSS SEA

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IN January 1959 an oceanographic survey of the Ross Sea was carried out by members of the New Zealand Oceanographic Institute, from the New Zealand Antarctic Supply Ship H.M.N.Z.S. *Endeavour*.

The route taken by the *Endeavour* and the distribution of the twenty-four stations occupied are shown in Fig. 1. A brief station list is also included, particularly for the information of workers planning investigations in the area in the near future.

The aim of the survey was to investigate the hydrology, the benthic fauna and the marine sediments in the area.

The routine procedure at each station was to lower a bathythermograph (275 m) and a cast of reversing bottles, make a vertical plankton haul from near the

bottom to the top, collect phytoplankton, make three lowerings with a twin orange peel grab sampler and collect epifauna from the bottom with a trawl. The grab sampler consisted of two modified four-blade orange peel grabs, each having a bucket capacity of 24.5 litres, suspended one at each end of a 4 ft bar.

In addition to these routine observations, surface water samples from stations A466 and A470 and a bottom water sample from A470 were obtained for determination of carbon-14 activity in order to study water movements in the Ross Sea and under the Ross Ice Shelf.

An underwater-camera and a bottom trawl were used at three stations (A468, A469 and A471) near Ross Island, to sample three different types of bottom community. Some of the photographs

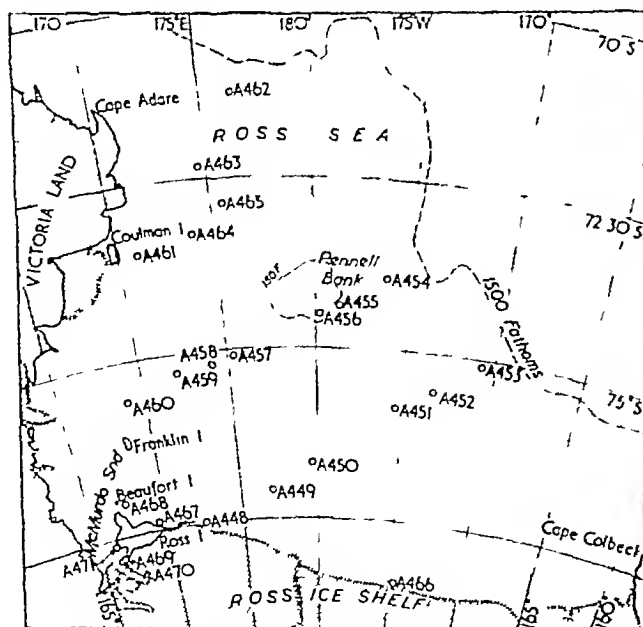


Fig. 1 Ross Sea, Antarctica, showing stations occupied from H.M.N.Z.S. *Endeavour*.

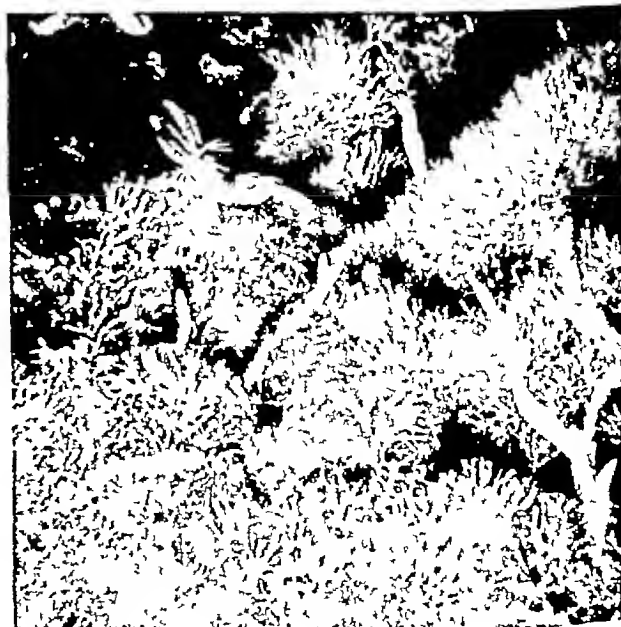


Fig. 2 Bottom photograph from station A468. Sponges, coral, and bryozoans predominate. Note crinoid top left (Depth, 110 m., foreground, 0.75 m. wide, depth of field, 1 m.).

Table 1 LIST OF STATIONS OCCUPIED FROM H.M.N.Z.S. *Endeavour* IN THE ROSS SEA

| V.Z.O.I. Station No | Position | Date | Provisional depth (m.) | Nature of bottom | Serial hydrological observations to (m.) | Trawls | Grabs | Phyto-plankton | Plancton | Other |
|---------------------|----------------------|---------|------------------------|------------------|--|--------|-------|----------------|----------|--------------|
| 1448 | 77° 27' S 172° 22' E | 10.1.59 | 752 | mud | 705 | x | x | x | x | |
| 1449 | 77° 05' S 172° 12' E | 11.1.59 | 562 | mud | 265 | x | x | x | x | |
| 1450 | 76° 42' S 170° 44' E | 11.1.59 | 472-518 | muddy sand | 515 | x | x | x | x | |
| 1451 | 76° 00' S 176° 25' W | 12.1.59 | 523 | gritty mud | 1,230 | x | x | x | x | |
| 1452 | 75° 35' S 173° 18' W | 12.1.59 | 1,230 | yellow brown mud | 1,400 | x | x | x | x | |
| 1453 | 75° 00' S 171° 00' W | 13.1.59 | 2 195 | yellow brown mud | 255 | x | x | x | x | |
| 1454 | 73° 55' S 176° 30' W | 14.1.59 | 014-628 | rocks | 320 | x | x | x | x | |
| 1455 | 74° 22' S 178° 35' W | 16.1.59 | 322-340 | stones | 180 | x | x | x | x | |
| 1456 | 74° 30' S 170° 40' W | 16.1.59 | 239-201 | muddy sand | 312 | x | x | x | x | fishing line |
| 1457 | 75° 02' S 175° 50' E | 16.1.59 | 315-342 | gritty mud | 430 | x | x | x | x | |
| 1458 | 75° 10' S 174° 00' E | 18.1.59 | 401-482 | mud | 510 | x | x | x | x | |
| 1459 | 76° 17' S 172° 20' E | 16.1.59 | 534-540 | muddy sand | 325 | x | x | x | x | corer |
| 1460 | 75° 38' S 168° 32' E | 17.1.59 | 415-430 | soft mud | 555 | x | x | x | x | corer |
| 1461 | 75° 32' S 171° 22' E | 18.1.59 | 578-566 | gritty mud | 1,750 | x | x | x | x | corer |
| 1462 | 71° 15' S 170° 30' E | 20.1.59 | 1,331-2 331 | sandy mud | 435 | x | x | x | x | |
| 1463 | 72° 20' S 174° 50' E | 21.1.59 | 469-465 | gritty mud | 375 | x | x | x | x | |
| 1464 | 73° 20' S 174° 00' E | 22.1.59 | 350-394 | barnacle plates | — | x | x | x | x | |
| 1465 | 72° 55' S 176° 30' E | 22.1.59 | 399 | sand pebbles | — | x | x | x | x | |
| 1466 | 78° 26' S 174° 50' W | 24.1.59 | 509 | barnacle plates | 570 | x | x | x | x | corer |
| 1467 | 77° 25' S 169° 28' E | 26.1.59 | 88-183 | mud | — | x | x | x | x | 10 sample |
| 1468 | 76° 50' S 167° 38' E | 26.1.59 | 110 | rocks | — | x | x | x | x | camera |
| 1469 | 77° 50' S 166° 33' E | 29.1.59 | 64 | gritty mud | — | x | x | x | x | camera |
| 1470 | 77° 50' S 166° 30' E | 4.2.59 | 377 | apicalia | 865 | x | x | x | x | 10 samples |
| 1471 | 77° 33' S 166° 20' E | 6.2.59 | 165-60 | muddy sand | — | x | x | x | x | camera |

revealed a surprisingly dense epifauna, dominated by sponges and Bryozoa (Fig 2)

A gravity corer was used at stations 1458, 1459, 1460, 1461 and 1462 short cores were secured.

Hourly surface water samples were taken on passage out of McMurdo Sound and continuous surface temperatures were recorded during the greater part of the cruise.

Of particular interest was the discovery of large deposits of calcareous barnacle plates. The plates were found sparsely distributed over the whole of the Ross Sea, but at stations 1463 and 1465 in approximately 400 m. and 400 m., respectively these plates, together with scattered rocks on which a live barnacle was growing formed the bulk of the bottom deposit. The deposit also contained a small

percentage of the calcareous remains of molluscs bryozoans and corals but as far as penetrated by the grabs and trawl was entirely free of mud or sand. The living and dead barnacles belong to the genus *Heclasma*. Estimates of the age of the barnacle plates are to be made from determinations of their carbon 14 activity.

The biological material collected is a substantial addition to that already available from Antarctic waters.

Results of the survey will be published by the New Zealand Department of Scientific and Industrial Research.

The wholehearted support the expedition received from the commanding officer and ship's company of H.M.N.Z.S. *Endeavour* is gratefully acknowledged.

CHANGE OF COSMIC RAYS IN SPACE

By PROF. H. V. NEHER

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THE advent of space rockets now makes possible direct measurements on quantities that have heretofore suffered from the interference of the Earth, its atmosphere or its magnetic field. Among these are measurements on cosmic rays. The absorption of the radiation in the Earth's atmosphere and the analysing effect of its magnetic field have, however, yielded valuable information on the total energy content and the individual particle energy. From such measurements together with a knowledge of their chemical composition one can deduce the intensity or number of primaries in space. When this is done using results collected over a period of years obtained with balloons at various latitudes one finds surprisingly large time variations in the numbers of primary particles. In what follows we discuss what such

measurements have so far disclosed about the absolute intensity and how it varies with time. Some preliminary measurements have already been made in rockets, and further measurements giving more complete checks on these calculations will undoubtedly come in the future.

A brief note concerning these large changes based on data taken in 1954 and 1957, has already been published¹. We wish here to present two additional methods of arriving at the numbers of primary particles in 1954 together with new results taken near the north geomagnetic pole in the summer of 1958 when the intensity there was even lower than in 1957.

The period 1954-58, when solar activity went from a minimum to a maximum of activity provided

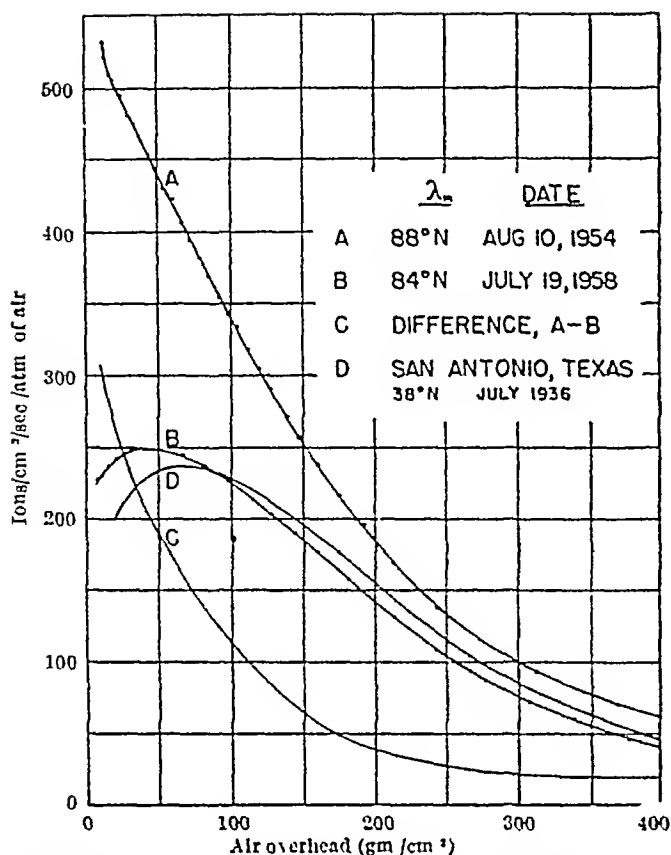


Fig. 1. Curves *A* and *B* show the extremes of the ionization so far measured with balloons near the north geomagnetic pole. Curve *A* represents data taken at the solar minimum of 1954, while curve *B* represents the situation near the solar maximum of 1958. The absorption in the atmosphere of the particles present in 1954 but which were absent in 1958 is given by curve *C*.

an excellent opportunity to study the changes produced in cosmic rays. Fig. 1 shows how large these changes have been near the north geomagnetic pole. The behaviour of curve *A* was typical of the curves from five similar balloon flights² made with ionization chambers in July and August 1954. All five records showed the same turn-up of the ionization curve at about 15 gm cm⁻². It was shown in ref. 2 that the behaviour of curve *A* at low pressures was consistent with the absorption of low-energy particles and that the turn-up was probably due to the absorption of protons with energies down to at least 150 MeV.

By 1958, the character of the radiation at the pole was radically different. The largest decrease occurred in the year 1956-57.¹ As shown by curve *B*, the ionization at high altitudes was less than half its value in 1954. In fact, the area under curve *B* is about 3 per cent less than the area under the curves taken in 1936 at San Antonio, Texas³ (geomag. lat. 38°N). It should be remarked that we feel confident that a direct comparison can be made between these years, for we not only have instruments which we have compared through the years but we have also checked their absolute calibration by using standard capacitors.

Our first method of estimating the number of primaries in 1954 is to calculate the number causing the difference between 1954 and 1958 and then adding to this the number present in 1958. To arrive at this latter figure we note that due to the nearly equal areas under curves *B* and *D* of Fig. 1 and to the similarity of shape, the number of primaries must be about the same. Taking the difference in area at the lower pressures and assuming a mean energy

of 3 BeV per particle causing this difference, we find that the number of primaries involved is approximately 0.007 cm⁻² sec⁻¹ sterad⁻¹. Previous calculations⁴ have shown that the number of primaries present at San Antonio in 1936 was 0.040 cm⁻² sec⁻¹ sterad⁻¹. This number is consistent with the measurements of MacDonald⁵ at the equator, together with the increase in energy brought in by the primaries as one goes from the equator to 38°N. We thus find that the number of primaries present in 1958 near the pole was 0.047 cm⁻² sec⁻¹ sterad⁻¹.

Referring now to Fig. 1, curve *C* shows the difference between *A* and *B* and represents the absorption in the atmosphere of those particles that were present in 1954 but were absent in 1958. A Gross transformation of this difference curve shows that the major part of the area under the curve is due to particles the effect of which varies nearly linearly with thickness of atmosphere. The fact that curve *C* has a tail that extends even to sea-level is undoubtedly due to mesons formed in the upper part of the atmosphere and especially by the higher-energy primaries that also change during a solar cycle.

Ignoring the high- and low-pressure ends, the bulk of the area may be accounted for by particles with a maximum range of about 300 gm cm⁻² in air. Assuming a range proportional to the energy, we may say with sufficient accuracy that the Gross transformed curve corresponds to a differential number distribution that is independent of energy.

We shall here assume that 15 per cent of the primaries responsible for curve *C* are α particles, 2 per cent of average $Z = 8$ and the remainder protons. We find that we need protons of mean energy 0.55 BeV, α -particles of mean energy 2.2 BeV and for $Z = 8$, a mean energy of 1.2 BeV per nucleon, for each to have a mean range of 150 gm cm⁻². We then arrive at a weighted mean energy of 1.5 BeV per particle. The area under curve *C* is 1.00 $\cdot 10^8$ eV cm⁻² sec⁻¹. Hence the number of particles per unit of horizontal area is 0.67 cm⁻² sec⁻¹. Thus per unit of solid angle we have, 0.21 cm⁻² sec⁻¹ sterad⁻¹.

To arrive at the total number of primaries at the pole in 1954 we add to the above the number present in 1958. We have already found this to be 0.047 cm⁻² sec⁻¹ sterad⁻¹. In this manner we find the total at the top of the atmosphere near the pole in 1954 to be 0.26 par sec⁻² sec⁻¹ sterad⁻¹.

Another method of arriving at the number of particles responsible for the difference between 1954 and 1958 is to estimate the mean specific ionization per particle at the top of the atmosphere and, knowing the ionization, the number of particles immediately follows.

Taking the mean energies of the protons, α particles and average $Z = 8$ for the heavy primaries, as given above, we find that the specific ionization relative to that for a minimum ionizing particle of unit charge has the values 1.3, 5.2 and 64 respectively. Using the relative abundances cited before and published curves on energy loss, we find the average specific ionization for these time-varying particles at the top of the atmosphere at the pole to be 210 ion pairs cm⁻¹ in air at 1 atm. If $\bar{\sigma}$ is this mean specific ionization and there are J particles cm⁻² sec⁻¹, then the ionization, $I = \bar{\sigma}J$. Since $I = 350$ ions cm⁻² sec⁻¹ atm⁻¹ of air from Fig. 1, then $J = 1.67$. The instrument is receiving particles from a solid angle of 2 π . Hence the uni-directional intensity is 0.26 par cm⁻² sec⁻¹ sterad⁻¹. This method then gives a

total of $0.31 \text{ par cm}^{-2} \text{ sec}^{-1} \text{ sterad}^{-1}$ at the pole in 1954

A third method of arriving at the numbers of particles is to take the increments in the area under the ionization depth curves for changes of latitude. This was done in 1954 from Boston to Thule, Greenland, using Bismarck as a base station to take account of temporal changes. The results of this analysis have been published*. These calculations gave a total of $0.24 \text{ par cm}^{-2} \text{ sec}^{-1} \text{ sterad}^{-1}$ at the pole.

These three values, 0.26 , 0.24 and 0.31 then give an average of $0.27 \text{ par cm}^{-2} \text{ sec}^{-1} \text{ sterad}^{-1}$ at or near the north geomagnetic pole in the summer of 1954. An application of Liouville's theorem tells us that with an isotropic distribution at infinity this was also the intensity in space at that time. The corresponding total intensity in space was then $3.1 \text{ cm}^{-2} \text{ sec}^{-1}$ through a sphere of unit area.

In 1958 the intensity at or near the pole was $0.047 \text{ cm}^{-2} \text{ sec}^{-1} \text{ sterad}^{-1}$ or $0.59 \text{ cm}^{-2} \text{ sec}^{-1}$ as discussed above. We thus arrive at the conclusion that the numbers of particles in space near the Earth but sufficiently far removed to be free from any of its effects, changed by a factor of 5 during this period of four years. This is probably a lower limit for we do not know how high the ionization would have gone in 1954 had our balloons gone higher.

So far data on the number of cosmic ray particles in space have been obtained by both the United States and the U.S.S.R. On the journey of *Pioneer I* which went near the Moon and is presumably now in orbit round the Sun the data at large distances gave 1.8 ± 0.3 particles $\text{cm}^{-2} \text{ sec}^{-1}$. (I am grateful to Prof. J. A. Van Allen for giving me this figure.) This rocket was launched on March 3, 1959. For the Russian cosmic rocket launched on January 2, 1959, the value measured* was $2.3 \text{ cm}^{-2} \text{ sec}^{-1}$. These values are to be compared with the above calculated values using ionization chambers of $0.59 \text{ cm}^{-2} \text{ sec}^{-1}$ in 1958 and $3.1 \text{ cm}^{-2} \text{ sec}^{-1}$ in 1954.

There are at least two reasons why the values measured in these rockets at the beginning of 1959 are higher than those calculated from terrestrial measurements in the summer of 1958. (1) Cosmic ray intensity near the orbit of the Earth appears to

have reached a minimum near the summer of 1958 and had definitely started to climb* by January of 1959. (2) The instruments in each of the rockets were surrounded by the material of the vehicle. One would therefore expect the number of secondary particles to be an important factor. This would be especially true for the Soviet rocket which was quite massive. To avoid the uncertainty of the contribution of surrounding matter the detecting instrument would need to be ejected from the vehicle and remain at some distance away.

For those interested in space travel an estimate may be made of the radiological intensity of cosmic rays in space. From Fig. 1 we see that the ionization at the pole was at least $530 \text{ ions cm}^{-2} \text{ sec}^{-1} \text{ atm}^{-1}$ of air at the highest altitude reached. In space where the shielding effect of the Earth is missing, this number would be just doubled. In terms of radiological units we would then expect at a solar minimum to have at least $1,060 \text{ ions cm}^{-2} \text{ sec}^{-1} \text{ atm}^{-1}$ of air = 1.8 mr (milliroentgens) per hr. At the solar maximum of 1958 we found the total intensity in space across unit sphere to be $0.59 \text{ par cm}^{-2} \text{ sec}^{-1}$. Assuming an average specific ionization of 300 ions cm^{-2} of path in air at 1 atm , we find an ionization of $120 \text{ ions cm}^{-2} \text{ sec}^{-1} \text{ atm}^{-1}$ of air or 0.21 mr per hr.

It is to be hoped that as time progresses data from instruments in rockets will give us more definite information as to the mechanism that causes these large changes in the primary cosmic radiation.

The assistance of the Office of Naval Research in making the necessary arrangements to carry out this programme is greatly appreciated. I would also like to thank the Office of Naval Research, the Atomic Energy Commission and the National Academy of Sciences through the International Geophysical Year for financial support.

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* Results to be published.

STUDIES OF COAL

By STAFF OF THE BRITISH COAL UTILISATION RESEARCH ASSOCIATION

Carbonization of Coals in the Presence of Activated Charcoal

IT has been reported recently by Adams *et al.*¹ that the pyrolysis products of coal if left in contact with a hot carbonaceous surface undergo further reactions. Experiments in our laboratories² have yielded further results of a similar kind with respect to the behaviour on heating of coal mixed with, or overlaid by, charcoal.

Measurements of the amount of tar like pyrolysis products omitted on burning briquettes made from mixtures of a low rank coal and an activated charcoal (prepared from a coal char) showed a decrease as the proportion of coal in the mixture decreased but more markedly than was to be expected from a dilution effect. On the other hand briquettes made from the same coal mixed with an unactivated char

could not show a disproportionate reduction. It thus appears that the tar like pyrolysis products evolved during heating were cracked on the extensive surface of the activated charcoal. The surface area that would be accessible to the large molecules likely to be present in these volatile vapours would be about $200 \text{ m}^2/\text{gm}$, whereas the accessible surface area of the unactivated char would be less than $5 \text{ m}^2/\text{gm}$.

When mixtures of coal and activated charcoal or beds of coal overlaid with activated charcoal were heated in a slow stream of nitrogen, or at a reduced pressure to about 600°C , no tarry material was formed instead it was possible to collect in cooled traps an almost colourless liquid. This liquid was found, by infra red analysis, to be composed of simple organic molecules (the benzene and toluene yield was in the range 0.3–0.7 per cent of the dry coal weight, compared with 0.1 per cent from the coal alone).

Table 1 YIELDS OF PRODUCTS FROM THE CARBONIZATION TO 600° C OF A LOW-RANK COAL (N C B TYPE 902) OVERLAID WITH ACTIVATED CHARCOAL
(Percentages of dry coal weight)

| Ratio of charcoal to coal | Aldie aqueous liquor | Tar oil | | Combustible gas | | Carbon dioxide | Carbon deposited in the charcoal | Total |
|---------------------------|----------------------|---------|-------------------|-----------------|----------------------------|----------------|----------------------------------|-------|
| | | Total | Benzene + toluene | Total | Paraffin to hydrogen ratio | | | |
| 0 | 0.7 | 10.0 | 0.11 | 7.2 | 1.5 | 3.0 | 0 | 20.9 |
| 1 | 0.7 | 2.7 | 0.10 | 8.9 | 1.5 | 3.7 | 5.3 | 30.2 |
| 1 | 0.7 | 1.4 | 0.46 | 8.5 | 1.4 | 4.7 | 5.5 | 29.7 |
| 1 | 0.7 | 1.2 | 0.72 | 8.5 | 1.3 | 6.8 | 6.0 | 31.2 |

The gaseous material evolved from the bed was found to be different from that obtained from the carbonization of the coal alone and, further, it was deduced from weight balances for the system and from analysis of the charcoal after use that carbon had been deposited in the charcoal.

In Table 1 are compared the results obtained from the carbonization to 600° C of a low-rank coal (N C B type 902) with those from the same coal overlaid with an activated charcoal.

When smaller proportions of charcoal were used in the carbonization experiments it was found that the condensates became slightly coloured and their complexity was increased. The charcoal could be used again, provided the deposited carbon from the cracking process, which reduced the effectiveness of the charcoal, was removed by oxidation, for example, with steam at about 900° C. There seemed to be little doubt that to achieve the complete elimination of dark tarry material from the condensates it was necessary for the vapours of the pyrolysis products of the coal to encounter a substantial amount of carbon surface. The effect reported by Adams *et al* is not as great as that which we have observed, the reduction by only 1 per cent of the amount of tarry matter formed, and the slight increase in the amount of liquor, suggest that but little carbonaceous surface was available for cracking the coal 'volatiles'.

It could be concluded that if a large amount of a pre-carbonized char, sufficient to have the necessary available surface area, was overlaid upon a 'green' coal and the whole was heated, very little tar would be formed, although some benzene would be obtained together with a gas of useful calorific value.

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¹ *Nature*, 183, 33 (1959)

² *Brit. Coal Utilisation Res. Assoc. Ann. Rep.*, 38 (1959)

Smoke Emission from Coal and Low-Temperature Chars

Work by this Association in a laboratory apparatus¹⁻³ has confirmed the observations of Piersol⁴, afterwards verified by Adams, Gaines, Gregory and Pitt⁵, that volatile matter is not an adequate guide for the amount of smoke produced from chars. In Fig. 1 it will be seen in all cases that chars prepared from a low-rank coal produce less smoke than coals with equivalent volatile matter. Although Piersol⁴ claimed a straight-line relation between the amount of smoke liberated under standard conditions of testing and the percentage of volatile matter in a range of coals, we did not find a direct proportionality (Fig. 1). There is a general

tendency for smoke emission to decrease with decreasing volatile matter, but highly caking and swelling coals tend to mask this trend. McHugo, Shaw and Whittaker⁶, who burnt a range of coals in a domestic appliance, observed a similar effect.

We found a relation between tar-yields (Gray King assay at 600° C) and smoke emission for a number of samples, similar to that found by the Coal Research Establishment workers⁶. We decided to extend the investigation into the relation between the hydrogen content of coals and their smoke emission for the following reasons.

(1) Spooner⁷ maintained that the tar yield of bright coals was related to their hydrogen contents. Bradbury and Mott⁸ therefore stated that, since tar yield and smoke emission are related, either the hydrogen content or the tar yield should serve as a guide to the amount of smoke produced. We have also established a definite correlation between the tar yields (not given in this communication), and the hydrogen contents for the fuels which we examined (eighteen), the correlation coefficient being calculated as 0.93, which is found to be significant at the 0.001 level of probability.

(2) Smoke is probably related in some manner to the chemical constitution of the fuel, particularly to the size and stability of the condensed aromatic ring clusters and the number of edge groups, which in turn are related to hydrogen content.

(3) We have shown by statistical examination that when weight of smoke is plotted against volatile matter (Fig. 1) the high swelling coals follow a different relation from that for the low-swelling coals, the high-swelling coals producing more smoke than low-swelling coals with equivalent volatile matter.

Fig. 2 shows the general relation between the weights of smoke and the hydrogen contents of the coals and chars tested. Both high- and low-swelling coals appear to follow the same relation.

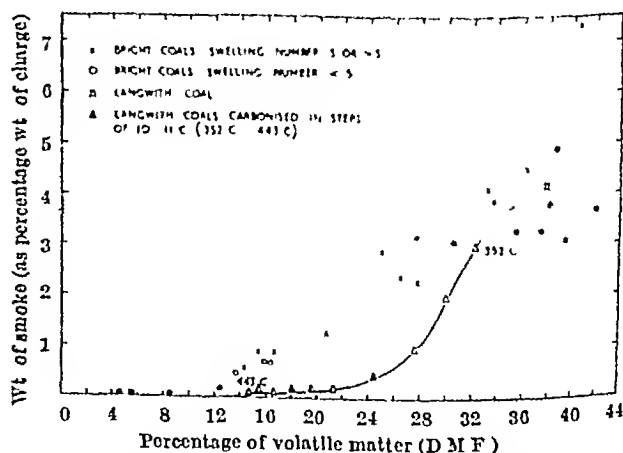


Fig. 1 Variation of smoke with volatile matter: comparison between a series of chars and a range of bright coals

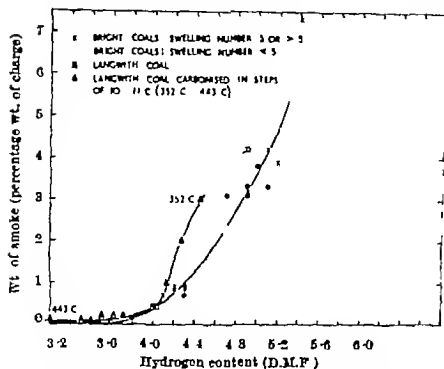


Fig. 2. Variation of smoke with hydrogen content: comparison between a series of chars and a range of bright coals

In Fig. 2 the smoke emission from chars prepared from a low rank coal is also plotted against their hydrogen contents and the curve obtained may be compared with that from the range of coals discussed above. At the lowest carbonizing temperatures (352–382°C) there is a rapid rate of decrease in smoke emission. As the carbonizing temperatures increase the rate of decrease decelerates. At about 382°C (4.2 per cent hydrogen content D.M.F.) the two curves meet. Below this point the differences between the weights of smoke emitted for corresponding hydrogen values are so small they may be ignored, and for the purpose of the subsequent discussion the lower parts of the two curves may be regarded as coincident.

From differential weight losses on Langwith coal¹⁰ it is known that its pyrolysis begins about 335°C and the decomposition reaches a maximum rate at about 410°C. Consequently, since chars produced at 400°C emit inappreciable amounts of smoke (Fig. 2) it would seem that the low boiling (low molecular weight) constituents which are first evolved are the main compounds responsible for smoke formation.

Using infra red techniques Brown¹¹ examined a weakly caking and a strongly caking coal. Between 440° and 550°C he found that hydrogen is lost by the removal of edge groups and the evaporation of small molecules followed by the loss of aromatic

hydrogen and some graphitization at higher temperatures.

The rank of coal¹¹ as well as the temperature of carbonization will affect the rate and type of decomposition and the structure of the residue. These factors will obviously influence the constitution of the residue and the composition and amount of smoke evolved from a particular char during combustion. The results with chars from Langwith coal may therefore be used only cautiously when coals of other rank are considered.

When volatile matter is the abscissa and smoke the ordinate (Fig. 1) then the curve for chars lies below that for coals, but when hydrogen content is the abscissa (Fig. 2) the positions of the two curves are reversed.

The explanation proposed is that although a char and a coal may yield the same volatile matter in the BS test, the constituents evolved may be quite different. The coals will evolve moisture and low molecular weight hydrocarbons which react and polymerize to form "tarry bodies", whereas the chars will evolve hydrogen and other gases which ignite more easily or react together and condense less readily than those from coals. Consequently, a coal with the same volatile matter as a char will produce more smoke. It is not clear why a char with a hydrogen content equivalent to that of a coal yields more smoke.

The laboratory work has suggested that either the tar yield or the hydrogen content provides a better indication of the amount of smoke emitted from coals than does the volatile matter. Other work now in progress in these laboratories should indicate how far such relations hold for domestic open fires during ignition and steady state combustion conditions.

D. FENCH

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TWO ENZYMIC MECHANISMS FOR HYDROGEN TRANSPORT BY PHENOLIC OESTROGENS

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OESTROGENIC steroids such as oestradiol 17 β can mediate the enzyme transfer of hydrogen between triphosphopyridine nucleotide and diphenylpyridine nucleotide^{1,2}. The same enzyme concerned with this oestrogen-dependent transhydrogenation also catalyses both the reduction of these two nucleotides by oestradiol 17 β , and the oxidation

of their reduced forms by oestrone. There is strong evidence^{3,4} that in the transhydrogenase reaction the steroid transports hydrogen by the change steroid alcohol \rightleftharpoons steroid ketone.

It has been suggested that this coenzymatic function of ovarian oestrogens is related to their mode of physiological action⁵. However, powerful oestro-

genic activity is exhibited by many phenolic compounds devoid of secondary alcoholic groups capable of reversible oxidation to ketone functions, and which fail (a) to act as coenzymes for hydrogen transfer in such systems^{1,4} and (b) to reduce pyridine nucleotides in the presence of the enzyme which catalyses the transhydrogenation. Examples of such substances are 17-deoxyoestradiol⁵, diethylstilboestrol and hexoestrol⁶, doisyonic and allenolic acids⁷, and isoflavones such as genistein⁸. Accordingly, it became of interest to examine model enzymic systems for the transport of hydrogen by phenolic oestrogens of this nature. Hochster and Quastel⁹ observed that, in the presence of manganese dioxide as a terminal hydrogen acceptor, diethylstilboestrol acts as a hydrogen carrier in a number of dehydrogenase systems. The quinone form of the oestrogen could be detected in the reaction mixture, and it was postulated to carry hydrogen in virtue of the reaction $\text{quinol} \rightleftharpoons \text{quinone}$. The present experiments show that both natural and synthetic phenolic oestrogens function as hydrogen carriers in two other types of enzymic reaction. The first of these is catalysed by certain phenolases and appears to involve an initial hydroxylation of the oestrogens to a corresponding *o*-diphenol, hydrogen is then transported by the change $\text{diphenol} \rightleftharpoons \text{quinone}$. The second type of reaction is catalysed by some peroxidases, accelerated by traces of manganous ions, and implicates a free-radical form of the oestrogen as a hydrogen carrier. It is well known that many simple non-oestrogenic phenols can carry hydrogen in both enzyme systems. However, the remarkable reactivity of many phenolic oestrogens in either type of reaction emphasizes that these substances can participate directly in hydrogen transport.

Warburg¹⁰ demonstrated that phenolases (polyphenol oxidases) are copper proteins, and that small amounts of *o*-diphenols which are oxidized by such enzymes mediate the oxidation of reduced pyridine nucleotides^{10,11}. We have found that phenolases purified from white potatoes and edible mushrooms oxidize reduced di- or tri-phosphopyridine nucleotides on the addition of trace amounts of many phenolic oestrogens. The oxidations proceed to completion with the consumption of one atom of oxygen per mole of reduced pyridine nucleotide oxidized. Fig. 1 shows that with oestradiol-17 β as carrier, a definite induction period occurs before the rate of oxidation of reduced diphosphopyridine nucleotide reaches a maximal value, whereas with the corresponding *o*-diphenol 1,3,5-oestratriene-3,4, 17 β -triol¹², no such lag is observed. Hexoestrol and 3-hydroxyhexoestrol behave in an analogous manner. The activity of the mushroom and potato enzymes in these reactions parallels their phenolase activity (measured by the oxidation of tyrosine plus 3,4-dihydroxyphenylalanine) during fractionation procedures which result in purifications of more than fifty-fold. The oestrogen-stimulated oxidation of reduced pyridine nucleotide is unaffected by catalase, but is abolished by heating the enzymes to 70° for 10 minutes, and by the addition of 0.001 *M* sodium cyanide. The cyanide-inhibited enzyme can be reactivated by cupric ions. Oestradiol-17 β did not mediate the oxidation of reduced diphosphopyridine nucleotide in the presence of haemocyanin, of copper sulphate (0.0001 *M*) or of the soluble phenolase of spinach leaves.

A free phenolic hydroxyl group is essential for both natural and synthetic oestrogens to transport hydrogen by these phenolase-catalysed reactions.

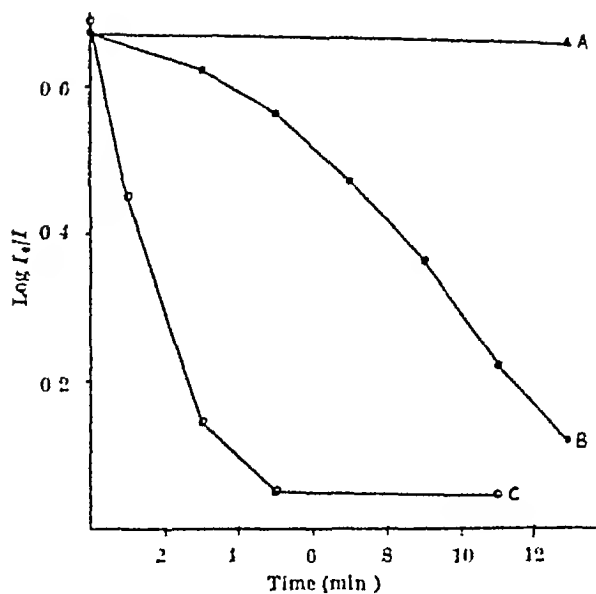


Fig. 1. Oxidation of reduced diphosphopyridine nucleotide by phenolase in the presence of potato phenolase. Sodium phosphate buffer pH 7.4 (0.05 *M*), 15 μ g/ml oestrogenic phenol in 0.01 ml dioxane, 200 μ g/ml potato phenolase, 0.3 μ moles DPNH. Total vol. 3 cc. Light path 1 cm. Wave length 340 m μ . 25° C in air. 4, no oestrogen; B, oestradiol 17 β ; C, 1,3,5-oestratriene 3,4, 17 β triol.

Thus, nearly equivalent carrier activity is found with oestradiol-17 α or -17 β , 17-deoxyoestradiol, oestrone and a triol, while 3-deoxyoestradiol-17 α or -17 β are completely inert. *bis*-Dehydrodoisyonic acid is a good hydrogen carrier, whereas the corresponding *O*-methyl ether is inactive. At least one phenolic hydroxyl group must be present in analogues of diethylstilboestrol and hexoestrol¹³ to exert this carrier function. The activity of natural and synthetic oestrogens is affected markedly by minor structural changes in the molecule. Thus, 1-methyloestradiol 17 β , 2-nitro oestrone and 4-nitro oestrone will not act as hydrogen carriers, and are without influence upon the action of oestradiol-17 β . 6 β -Hydroxyoestradiol-17 β (which does not mediate the oxidation of reduced diphosphopyridine nucleotide) and 7-keto-oestrone (which has approximately 10 per cent of the activity of oestradiol-17 β), both at equimolar concentrations, depress the hydrogen-transporting activity of oestradiol-17 β . The concentrations of oestrogens permitting 50 per cent of the maximal rate of oxidation of reduced diphosphopyridine nucleotide by potato phenolase were found to be 1×10^{-6} *M* for 1,3,5-oestratriene 3,4, 17 β triol, 3×10^{-6} *M* for oestradiol-17 β , oestrone, 17-deoxyoestradiol and hexoestrol, and 1×10^{-5} *M* for genistein.

Hydrogen transport by phenolic oestrogens under these conditions can be described as follows. The induction period with monophenolic oestrogens probably reflects the time required for the phenolase to catalyse hydroxylation to *o*-diphenol derivatives. The diphenol is oxidized by the phenolase to the corresponding quinone, and the quinone is then reduced by the reduced pyridine nucleotide. Although it is not known whether the latter reaction is enzymically catalysed or not, it may be mentioned that pyridine nucleotide-menadione¹⁴ and -quinone¹⁵ reductase activity is readily separable from the oestrogen-mediated reactions during purification of the phenolases. In accordance with this formulation it was found that, after aerobic incubation with potato phenolase, diphosphopyridine nucleotide, ethanol and crystalline yeast alcohol dehydrogenase,

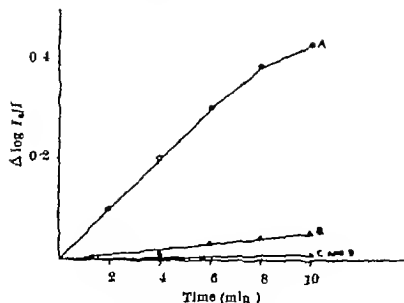


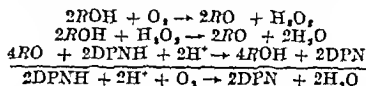
Fig. 2. Oxidation of reduced diphosphopyridine nucleotide by peroxidase in the presence of oestrogenic phenols. *Tris* (hydroxymethyl) amino methane buffer (0.05 M), pH 7.4, 0.5 μmole DPNH, 20 μgm. oestradiol-17β in 0.02 ml. ethanol, 0.03 μmole MnCl₂, 5 μgm. horseradish peroxidase. Total vol. 3 cc. Light path 1 cm. 25°C. in air. Wave-length 340 mμ. A, complete system; B, omit oestradiol 17β; C and D, omit MnCl₂ or oestradiol-17β and MnCl₂.

oestradiol 17β is converted to at least two other substances which migrate much more slowly than oestradiol 17β when chromatographed on paper with a heptane-methanol solvent.¹⁶

These findings are undoubtedly related to the reported inactivation of oestrogens by plant phenolases.¹⁷ It is possible that they have some bearing on the formation of hydroxylated derivatives of oestradiol 17β catalysed by liver microsomes in the presence of reduced triphosphopyridine nucleotide and oxygen¹⁸, the stimulation of formate incorporation into isolated uterus by the addition of a hydroxylated derivatives of oestradiol 17β *in vivo*¹⁹, and the urinary excretion of 2 methoxy forms of oestrone²⁰ and oestrone.²¹

An entirely different type of hydrogen transport mediated by phenolic oestrogens is catalysed by peroxidases purified from either horse radish or cow's milk. Fig. 2 shows that reduced diphosphopyridine nucleotide is oxidized upon the addition of peroxidase and low concentrations of oestradiol 17β, and that the reaction is stimulated by 10⁻⁴ M manganous chloride. Manometric experiments revealed that the oxidation of reduced diphosphopyridine nucleotide proceeds to completion with the consumption of one atom of oxygen per mole of reduced diphosphopyridine nucleotide oxidized. Reduced triphosphopyridine nucleotide and reduced nicotinamide mononucleotide are oxidized at the same rate as reduced diphosphopyridine nucleotide. This phenol-dependent oxidation of reduced pyridine nucleotide does not require the addition of hydrogen peroxide. Under these experimental conditions, hydrogen peroxide does not induce the oxidation of reduced diphosphopyridine nucleotide unless an appropriate phenol is present. With oestradiol 17β, or hexoestrone or diethylstilboestrol as co-factors, the oxidation of reduced diphosphopyridine nucleotide is abolished by 0.001 M sodium cyanide and by catalase. 50 per cent of the maximal rate of oxidation was found with a final concentration of oestradiol 17β of 8 × 10⁻⁶ M. A free phenolic hydroxyl group is required for oestrogens to exert a carrier function. In contrast to the phenolase-catalysed reactions described above, no induction period is observed when monophenolic oestrogens mediate the oxidation of reduced diphosphopyridine nucleotide in the peroxidase system. Moreover, many o-diphenols which act as hydrogen carriers in

the phenolase-dependent reactions are incapable of transporting hydrogen in the peroxidase system and inhibit the action of oestradiol 17β therein, for example, adrenalin, noradrenalin, and 3-hydroxytyramine. The behaviour of phenolic oestrogens under these conditions is similar to that described for a number of simple phenols by Akazawa and Conn.²² The latter authors have pointed out the similarity between such phenol-dependent reactions and the oxidation of dihydroxyfumaric acid catalysed by peroxidase.²³ They suggested that a ternary complex of peroxidase, Mn²⁺ and hydrogen peroxide catalyses the oxidation of the phenol (ROH) by oxygen to an oxidized form (RO), presumably of a free radical nature and hydrogen peroxide. The latter substance could then, by the action of peroxidase, oxidize another molecule of the phenol to the oxidized (free radical) form. Reduced diphosphopyridine nucleotide could further reduce the oxidized phenol. The process can be envisaged as



Our ability to recover oestradiol 17β unchanged from this peroxidase system is in agreement with this formulation.

These experiments suggest strongly that phenolic oestrogens can transport hydrogen in virtue of the reaction phenol \rightleftharpoons phenoxyl radical. Electron spin resonance studies by Roxroad and Gordy²⁴ have shown that hexoestrone can be converted to a free radical form(s) by irradiation. It is of interest that the injection of physiological doses of both natural and synthetic oestrogens into ovariectomized rats induces enormous increases in the activity of uterine peroxidase.²⁵

It is a pleasure to acknowledge many valuable discussions with Drs. Charles Huggins, Paul Talalay, Gerhard Closs and the generous gifts of compounds from Drs. G. C. Mueller and E. V. Jensen. This work was supported by grants from the American Cancer Society, Inc.

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ACTIVATION AND INHIBITION OF THE ARYLESTERASE OF HUMAN SERUM

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HUMAN blood plasma contains at least two different enzymes capable of hydrolysing phenylacetate^{1,2}. One of them is a cholinesterase, the other an aromatic esterase (arylesterase)³. The present studies deal with arylesterase and stem from our observation that the disodium ethylenediamine tetraacetate ('Sequestrene') added to prevent coagulation in blood samples inhibited arylesterase without affecting cholinesterase activity. Since human arylesterase has been reported to be remarkably resistant to many of the usual inhibitors³, we have supposed that further studies of the inhibition and acceleration of activity of arylesterase by selected agents would prove of interest. In particular, tests of the effects of metal ions and sequestering agents were indicated.

The activity of the enzyme was assayed with a modification of Zeller's⁴ method in a Cary recording spectrophotometer at a wave-length of 2800 Å. The instrument was equipped with an expanded scale (0-0.1) slide wire assembly, which greatly increased the extent of registration. The concentration of phenylacetate was 1×10^{-3} M. In the early runs of the investigation, the source of enzyme was pooled, heparinized human plasma. Later, pooled, normal human serum gave similar results. The serum was diluted 1:2,000 v/v, the absorption cells of the spectrophotometer contained 0.002 ml of serum in a *tris*-hydroxymethyl aminomethane (*tris*) buffer of pH 7.4. At this dilution the contribution of cholinesterase to the hydrolysis of phenylacetate was found to be negligible in the sera of healthy donors. In the experiments where the effects of inhibitors or activators were tested on the cholinesterase, the source of enzyme was purified human plasma cholinesterase preparation ('Cholase', Cutter Laboratories). This preparation was void of arylesterase activity. The temperature was kept constant at 27°C. In a few control studies, the usual Warburg manometric technique or an automatic recording titrator (Titri-graph, Radiometer) gave similar results. The effect of most of the compounds on the enzyme was tested after 5-min pre-incubation. All concentrations given in this report show the final dilution of the substance used.

It was found that the hydrolysis of phenylacetate by arylesterase increased in the presence of calcium chloride⁵. The sensitivity of the different serum samples toward calcium varied to a great extent. On the average, an 85 per cent acceleration was observed at 1×10^{-4} M concentration of calcium chloride. Ethylenediaminetetraacetate also enhances the activity of arylesterase in the lower concentration ranges. This activation changes sharply to inhibition at concentrations higher than 10^{-5} M. The enzyme was totally inhibited by 2.5×10^{-5} M ethylenediaminetetraacetate. When the sodium salt of the calcium-ethylenediaminetetraacetate complex ('Sequestrene Na₂Ca', calcium-ethylenediaminetetraacetate) was used instead of ethylenediaminetetraacetate, no inhibition was observed. On the other hand, the

magnesium-ethylenediaminetetraacetate complex inhibited similarly to ethylenediaminetetraacetate. This latter effect was probably due to the fact that calcium from the system replaced magnesium in the complex. The stability constant of ethylenediamine tetraacetate with Ca²⁺ is $\log K = 10.59$ and that of Mg²⁺, 8.69. Another ethylenediaminetetraacetate derivative, ethylenediamine di(o-hydroxyphenyl acetic acid) ('Chel DP'), which has little tendency to co-ordinate with calcium ($\log K$ for Ca²⁺ is 1.6), did not inhibit arylesterase. In some preliminary studies, swine serum arylesterase⁶ was also inhibited by ethylenediaminetetraacetate.

The results obtained with calcium prompted us to investigate the effect of other cations on the enzyme. Arylesterase was inhibited by a number of rare earth, alkaline earth and metal ions. The best inhibitor was GdCl₃, $I_{50} = 1 \times 10^{-4}$ M, the weakest, MgCl₂, $I_{50} = 4 \times 10^{-4}$ M. The inhibitory effect decreased in the following order: GdCl₃, CeCl₃, LaCl₃, Y(NO₃)₃, SmCl₃, CdSO₄, HgCl₂, AgNO₃, PbCl₂, ZnSO₄, NiSO₄, CoSO₄, CuCl₂, MnSO₄, BaCl₂, SrCl₂, MgCl₂.

Under the experimental conditions used, the most interesting feature of these series was the inhibition by low concentrations of the stable trivalent rare earth cations and by somewhat higher concentrations of heavy metals. Yttrium and the rare earth ions were about equally active, the I_{50} values falling in the 10^{-7} to 10^{-6} M range. *p*-chloromercuriphenyl sulphonic acid also inhibited the enzyme ($I_{50} = 3 \times 10^{-6}$ M). Thus, in addition to rabbit³, the human enzyme is also sensitive to sulphhydryl agents. Sodium citrate and an amino-oxidase inhibitor, 1-phenyl-2-hydrazinopropane (JB516), inhibited the enzyme in a relatively high concentration. The I_{50} values were 6×10^{-4} M and 2×10^{-4} M, respectively.

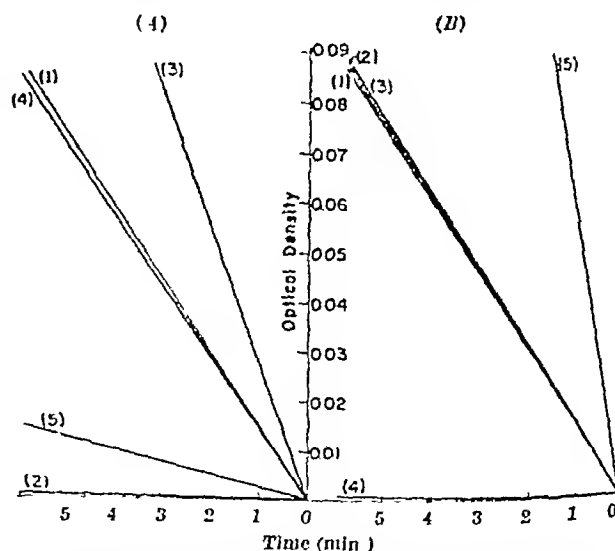


Fig. 1. Inhibition and acceleration of the hydrolysis of phenylacetate by human serum arylesterase (A) and by purified, concentrated human plasma cholinesterase (B). (1) control, (2) ethylenediaminetetraacetate 2.5×10^{-4} M, (3) calcium chloride, 1×10^{-4} M, (4) eserine, 2.5×10^{-4} M, (5) JB516, 1×10^{-4} M.

As indicated above $2.5 \times 10^{-4} M$ ethylenediamine tetraacetate inhibited the enzyme completely. Presumably this inhibition is due to removing the calcium from the enzyme molecule. The acceleration by low concentrations of ethylenediaminetetraacetate may reflect a hindering of an inhibitor present in the system. When a $10^{-4} M$ calcium chloride solution was added soon after $5 \times 10^{-4} M$ ethylenediaminetetraacetate to the enzyme, the inhibition gradually decreased and up to 70 per cent of the normal activity was restored. If, instead of calcium, magnesium was added, only a negligible decrease in inhibition was observed.

When a 1:10 v/v dilution of serum was dialysed against a *tris* buffer at $4^\circ C$, the activity of aryl esterases decreased 65 per cent within 17 hr., but it could be partially restored by adding calcium to the dialysed enzyme. If the enzyme solution contained ethylenediaminetetraacetate in the dialysis tube, 95 per cent of the activity disappeared during the dialysis and calcium did not reactivate the enzyme. This indicates that the removal of calcium from the arylesterase led to irreversible changes. When the enzyme solution contained calcium-ethylenediamine tetraacetate during the dialysis instead of ethylenediaminetetraacetate the enzyme activity remained the same as that of the dialysed control. Finally when the enzyme was dialysed against a *tris* buffer which contained $10^{-4} M$ calcium chloride, the activity did not diminish during dialysis.

Others have shown earlier that phenylacetate is hydrolysed by both arylesterase and the cholin

esterase of human serum or plasma. However Fig 1 summarizes some of the differences between the two enzymes. In this figure the increase in optical density is plotted against time in minutes. This increase is due to the amount of phenol liberated which in turn is a function of the enzymic activity. Part 4 shows that arylesterase was inhibited by ethylenediamine tetraacetate and JB516 activated by calcium and unaffected by eserine¹⁻³. Cholinase (part B) as expected was inhibited by eserine. The activity of cholinesterase with phenylacetate substrate was accelerated by JB516 and unaffected by $1 \times 10^{-4} M$ Ca²⁺ and ethylenediaminetetraacetate.

The results summarized in this report indicate the dependence on calcium of the arylesterase as well as the sensitivity of this enzyme toward several inhibitors. A detailed account of the work with arylesterase and on the effect of JB516 on cholinesterase will be published elsewhere.

Ethylenediaminetetraacetate, its derivatives and the technical data were kindly supplied by Geigy Industrial Chemicals, JB516 by Lakeside Laboratories.

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REDUCTION OF TOXICITY OF CATIONIC MACROMOLECULES BY COMPLEXING WITH ANIONIC DERIVATIVES OF SYNTHETIC POLYGLUCOSES

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ANIONIC derivatives of synthetic polyglucoses were found¹ to inhibit enzyme activity of cationic proteins in consequence of the formation *in vitro* of complexes through electrostatic forces. In the case of lysozyme, small amounts of salt prevented complex formation when added after complexing; salt caused dissociation accompanied by reversal of the inhibition. On the other hand, low salt concentration did not prevent complexing with ribonuclease, hyaluronidase and some other enzymes.

The present communication reports experiments designed to ascertain whether the toxicity of cationic drugs of high molecular weight can be effectively blocked by analogous complexing with anionic polyglucose derivatives in the living animal, where complex formation can be affected by the salt and by the competing cationic macromolecules which are present. It was found that the toxicity of a number of such materials could, indeed, be reduced. Our findings extend the recent report of Higginbotham² that heparin, a naturally occurring anionic polysaccharide, reduced the toxicity of polymyxin B in mice.

In the current experiments the compounds were employed in solution in pyrogen free water, the total volume of fluid administered was kept between 0.1 and 0.4 ml. per animal. Ten week old strain C

mice of both sexes, weighing 18-20 gm., were employed in groups of ten. The mice were observed for several hours after treatment, and 24 hr. survival was tabulated.

The cationic substances administered at toxic level were polymyxin B, protamine, streptomycin and neomycin. Toxic effects were found to be reduced by subsequent administration of the sodium salts and of the free acid forms of the sulphate and carboxyl derivatives of polyglucose. Two sulphated preparations were employed, both derived from a polyglucose with a number average molecular weight of about 20,000; the number of sulphate groups per anhydroglucose unit was 3 and 0.6 respectively. The former was preparation H⁴, $[\eta] = 0.04$; the latter was preparation D⁴, $[\eta] = 0.04$; the free acid form was obtained by treatment with a cation exchange resin. The carboxyl derivative contained 17 per cent carboxyl (preparation e)³.

Polymyxin B was given in a standard dose of 0.5 mgm./mouse. The mice reacted as follows: within 3 min. they were prostrated, respiratory embarrassment and severe convulsions developed in about 10 min., they began to die in about 20 min., those few that survived for 40 min. recovered and were still alive at 24 hr.

Table 1 COUNTERACTION OF TOXICITY OF CATIONIC MACROMOLECULES BY SUBSEQUENT ADMINISTRATION (5 MIN. LATER) OF ANIONIC POLYGLUCOSE DERIVATIVES

| Toxicity from | | Counter treatment | | 24 hr survival (10 mice per group) |
|--------------------|-------------|-------------------------|-------------|------------------------------------|
| Cationic substance | Mgm / mouse | Polyglucose derivative | Mgm / mouse | |
| Polymyxin B | 0.5 | — | — | 2 |
| | | Sulphate II (acid form) | 1 | 10 |
| | | Sulphate II | 0.5 | 10 |
| | | Sulphate II | 1 | 9* |
| | | Sulphate II | 1 | 8† |
| | | Sulphate II (Na salt) | 1 | 10 |
| | | Carboxyl (acid) | 1 | 10 |
| | | (acid) | 0.5 | 10 |
| | | (Na salt) | 0.5 | 10 |
| Protamine | 3 | Control | — | 0 |
| | | Sulphate II (acid) | 3 | 10 |
| Streptomycin | 8 | Control | — | 2 |
| | | Sulphate II (acid) | 8 | 8 |
| Neomycin | 3 | Control | — | 4 |
| | | Sulphate II (acid) | 6 | 8 |
| | | | 10 | 6 |

* 10 min. interval between injections

† 20 min. interval between injections two mice were already dead

When polyglucose sulphate was administered 5 min after this dose of polymyxin-B, all the mice recovered rapidly and behaved normally within 30 min., even when the counteracting dose was delayed for 10 or 20 min., at which time some of the mice were already dead, the moribund animals recovered. Similar counteraction of the toxicity of polymyxin was obtained with both the salt and the acid forms of the sulphate and carboxyl derivatives (Table 1). Analogous protection was obtained against the lethal effect of protamine. However, the toxicity of streptomycin and of neomycin was only partially reduced even when larger amounts of polyglucose sulphate were used. This is in line with the requirement for high molecular weight in the blocking² of enzyme activity.

In the second set of experiments (Table 2) the polyglucose derivative was injected first, subcutaneously at the nape, while the cationic substance was given intraperitoneally. In the experiments with polyglucose sulphate and polymyxin-B, protection against lethality and toxic manifestations was virtually complete when the interval between the injections was 2-90 min. The protective effect of the carboxyl derivative was of shorter duration. Polyglucose

Table 2 PROTECTION FROM LETHAL TOXICITY OF POLYMYXIN-B (0.5 Mgm/MOUSE) BY PRIOR INJECTION OF ANIONIC POLYGLUCOSE DERIVATIVES AT A DIFFERENT SITE

| Protective treatment | | Time between injections | 24 hr survival (10 mice per group) |
|-------------------------------------|-------------|-------------------------|------------------------------------|
| Polyglucose derivative (acid forms) | Mgm / mouse | | |
| None | — | — | 2 |
| Sulphate II | 1 | 1 day | 4 |
| " | 1 | 300 min | 3 |
| " | 1 | 180 " | 8 |
| " | 1 | 90 " | 10 |
| " | 1 | 60 " | 10 |
| " | 1 | 30 " | 10 |
| " | 1 | 5 " | 10 |
| " | 1 | 2 " | 9 |
| " | 0.5 | 30 " | 6 |
| " | 0.25 | 30 " | 5 |
| Carboxyl | 1 | 5 " | 10 |
| " | 1 | 10 " | 1 |
| " | 2 | 10 " | 8 |

sulphate (1 mgm.) yielded partial protection against the lethal dose of protamine (3 mgm.)

These experiments showed that polyglucose sulphate afforded protection promptly even when injected by a different route and at a site distant from that employed for the polymyxin. In addition to the direct action of the anionic derivative upon the cationic drug, it is possible that mobilized acid polysaccharide of tissue origin also may contribute to the blocking of the lethal effect⁶.

Synthetic polyglucose derivatives can provide molecular model systems suitable for the study of macromolecular interactions and of the consequent biological changes. Polyglucoses can be prepared different in molecular weight and in degree of branching⁷. They have a highly branched, spherical structure⁸, and possess numerous alcoholic hydroxyl groups suitable for graded substitution with dissociating groups. For example, polyglucose sulphates with different degrees of sulphonation⁴ can be used to study the effect of molecular parameters (size, charge density, etc.) on macromolecular interaction^{1,2}.

The effect of difference in charge density of polyglucose sulphates upon their potency in counteracting the lethal effect of polymyxin-B was also investigated. Preparations H and D of polyglucose sulphate sodium salt, described above, were given as in the experiments summarized in Table 1, that is, the anionic derivative was injected 5 min after the lethal dose of polymyxin-B (both given intraperitoneally). Table 3 shows that the polyglucose sulphate with the higher charge density gave greater protection, for example, at the 0.1 mgm level, preparation H gave complete protection while preparation D gave none.

Table 3 EFFECT OF CHARGE DENSITY OF POLYGLUCOSE SULPHATE ON COUNTERACTION OF TOXICITY OF POLYMYXIN-B (0.5 Mgm/MOUSE) INJECTED 5 MIN. EARLIER

| Polyglucose sulphate sodium salt | | | 24 hr survival (10 mice per group) |
|----------------------------------|---|-------------|------------------------------------|
| Preparation | SO ₃ /anhydrous glucose unit | Mgm / mouse | |
| — | — | — | 1 |
| H | 3 | 0.5 | 10 |
| D | 0.6 | 0.5 | 0 |
| H | 3 | 0.25 | 10 |
| D | 0.6 | 0.25 | 3 |
| H | 3 | 0.1 | 10 |
| D | 0.6 | 0.1 | 1 |
| H | 3 | 0.05 | 4 |

Thus it has been found that such anionic derivatives of polyglucose were capable of protecting mice against a lethal dose of cationic macromolecules not only when administered first, but also by counteracting toxicity in moribund animals. Furthermore, the greater their charge density the greater was their effectiveness.

Cationic polyglucose derivatives have now been synthesized. Their interaction with naturally occurring anionic macromolecules, and the effect of such interaction on the biological properties of the latter, are projected.

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QUANTITATIVE ASSAY OF COMPOUNDS IN ISOLATED, FRESH NERVE CELLS AND GLIAL CELLS FROM CONTROL AND STIMULATED ANIMALS

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FOR electrophysiological studies it is desirable to express results in amounts of biologically important substances per cell. The same trend seems now to exist in neurocytology for unicell analyses as in the case in electrophysiology. This article gives an account and applications of the methods used in our laboratory for the determination of substances expressed as $\mu\text{g}/\text{m}^3$ per fresh nerve cell or per volume of fresh glial cells.

Lowry¹ and his associates² have dissected nerve cells from thick, frozen and dried sections and have obtained excellent results. We prefer to dissect nerve cells from a cut surface through the desired locus of the fresh tissue, immersed in isotonic sucrose solution. The dissection is made free hand under a stereo microscope at a magnification of 64 or 100. A stainless thread 15 or 18 μ in diameter, and sharpened to $\sim 2\mu$ (manufactured by Kanthal AB, Hall

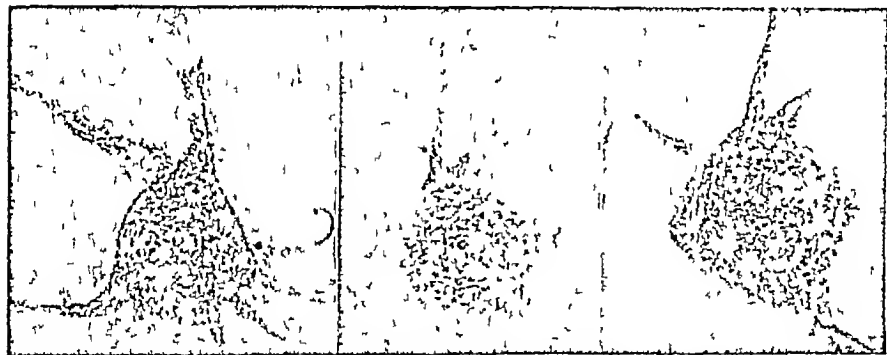


Fig 1 Fresh nerve cells dissected out free hand, photographed in the phase-contrast microscope. Slightly stained with methylene blue to show density of the synapses as small knobs on the surface ($\times c 200$)

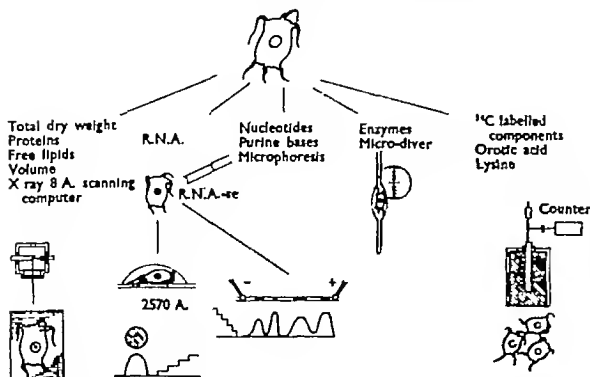


Fig 2 Survey of the methods used on the dissected out nerve cells and their glial cells

stadhammar Sweden), is used for lifting out the nerve cells into an isotonic sucrose solution. The main part of the dendrites comes with the coil (Fig 1). Usually a very small amount of methylene blue in sucrose solution is applied to the cut surface for some seconds. The stain is taken up by the synapses which are seen as a finely dotted border around the area occupied by the unstained nerve cell. The cell is removed before it takes up the dye and transferred to the substrate or to the sucrose solution, where it is freed from adhering glia by gentle manipulation. Note the density of synapses on the surface of the soma and dendrites of the fresh nerve cell (Fig 1). Nerve cells sampled in this way are used for the determination of the weight

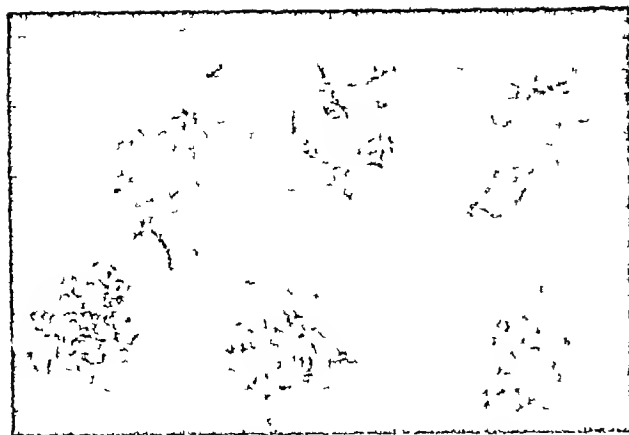


Fig 3 Fresh nerve cells plus the neuroglial cells originally closely surrounding each cell dissected free and trimmed to the same volume as that of their nerve cell and placed in a row below the nerve cells. The collection of glial cells slightly pressed against the glass. (Phase contrast, $\times 360$)

a protein and a free lipid fraction¹⁴, ribonucleic acid⁵, nucleotides¹⁷, of labelled substances such as ¹⁴C-crotic acid and ¹⁴C-L-lysine¹⁸, and of enzyme activities⁹ (Fig 2). The oligodendrocytes closely surrounding the nerve cell easily come off in the substrate and adhere to each other, and the collection may assume a spherical form. It can easily be trimmed to approximately the same volume as that of the nerve cell to which they belong (Fig 3). The collection of glial cells is freed from larger parts of axons or dendrites.

No method hitherto described is ideal for volume determination of such an irregular cell as the nerve cell, not even the interference microscope technique. The following method seems adequate. The total dry weight of a fresh nerve cell including the main part of the dendrites, precipitated with 1 N cold perchloric acid for 30 sec and washed and dried is determined by X-ray microradiography at 8-10 Å. The X-radiogram is evaluated by our scanning cell analyser, which gives the weight of the cell based on up to 12,000 measurements in 4 min. The dry weight per unit volume of the nerve cell is determined on a frozen and dried section prepared in the cryostat. The volume of the fresh cell irrespective of its irregular form is the total weight divided by the mass per μ^3 of the cell material. The value for the organic material in the nucleus has been found to be as high as that in the cytoplasm.

It was found that the mass per unit volume of fresh glial cells is $0.20 \mu\text{gm}/\mu^3$, which is the same as that of their nerve cells. Hence, it is possible to compare nerve cells and glial cells on the same volume basis.

Rabbits were subjected to mild rotation, through 120° horizontally and 30° vertically, 35 turns/min, for 25 min/day for 6 days. The results—

Table 3 EFFECT OF VESTIBULAR STIMULATION ON THE RESPIRATORY ENZYME ACTIVITY IN DIPPER'S CELLS AND IN THE SAME VOLUME OF THEIR GLIAL CELLS

Enzyme activity as $10^{-4} \mu\text{l O}_2/\text{hr}/\text{cell}$ at 37° . Cells measured one, two or three at a time in one micro-diver

| | Cytochrome oxidase | | | | Succinoxidase | | | |
|-------------------------|--------------------|------|----------|-------|---------------|------|----------|-------|
| | No. of cells | Mean | P | Ratio | No. of cells | Mean | P | Ratio |
| Nerve cells, stimulated | 25 | 7.0 | 0.01** | 1.8 | 57 | 6.0 | 0.001*** | 2.8 |
| Nerve cells, controls | 34 | 4.2 | | | 35 | 2.1 | | |
| Glial cells, stimulated | 36 | 3.0 | 0.001*** | 0.3 | 41 | 4.0 | 0.6 | 0.9 |
| Glial cells, controls | 34 | 11.5 | | | 33 | 4.5 | | |

those on the effect of stimulation on the nerve cells—will be published in detail elsewhere, in collaboration with Dr. A. Pigeon.

Table 1 DATA FROM 80 DIPPER'S NERVE CELLS, RABBIT. Values in μgm . Vol. averaged $93,200 \mu^3$. The dry weight as $\mu\text{gm}/\mu^3$ was 0.23

| Structure | Dry weight | Proteins | Lipids soluble in chloroform | Phosphonucleic acid | Ribonucleic acid, percent of dry protein |
|------------------|------------|----------|------------------------------|---------------------|--|
| Soma | 20,800 | 16,000 | 4,200 | 1,100-1,200 | 7 |
| Nucleoplasm | 800 | 670 | 200 | ~20 | |
| Nucleolus | 100 | | | | |
| Nerve cell total | 21,700 | 17,250 | 4,400 | | |

The ribonucleic acid content of the oligodendrocytes expressed per volume, equivalent to that of the nerve cell, was in 15 analyses found to be approximately $100 \mu\text{gm}$, that is, ten times less than the ribonucleic acid content of the nerve cell. This is noteworthy since the number of glial cells surpasses that of the neurons by a factor of probably more than ten. Thus, it is not possible to state that ribonucleic acid found in bulk analyses of the central nervous system is that of the nerve cells, as is stated in several papers.

Table 2 EFFECT OF VESTIBULAR STIMULATION ON THE DRY WEIGHT OF DIPPER'S CELLS, RABBIT. Values in μgm .

| Nerve cells | No. | Weight | Pt. (per cent) | P |
|----------------------------------|-----|--------|----------------|--------|
| Controls | 50 | | 19 | 0.01** |
| Stimulated 25 min/day for 6 days | 47 | 24,300 | 11 | |

1 V, variation coefficient

The effect of the vestibular stimulation on these cells, second in the neuronal chain, is thus a significant increase of the dry weight of organic material. The conclusion is that the increased functional demands cause a production of intraneuronal organic material, the proteins included. This fits with earlier findings using another type of technique¹⁰.

With measurements also on nerve cell plus same volume of glial cells altogether 500 cells have been measured.

In the controls, the respiratory enzyme activity is twice as high in the glial cells as in the nerve cell they belong to, measured on the same volume. This fits well with the results of the same enzyme activity in spinal ganglion cells and in their satellite cells¹.

and also with respect to other enzyme activities in this type of nerve cells¹¹

The vestibular stimulation for 25 min./day for 6 days increased the respiratory enzyme activity of the nerve cells, belonging to the second neuron of this pathway, to a higher level. Considering that the organic mass per nerve cell also increased, it may be assumed that the stimulation caused an increase in the enzyme concentration as well as activity. But, at the same time, the enzyme activity in the glial cell decreased, and significantly so in the case of cytochrome oxidase. It is impossible at present to interpret these results. The following tentative working hypothesis may be presented. Several observations support the view that the glial cells, especially the oligodendrocytes, are donors of energy or of food to the nerve cell they serve. It is also known that there occurs a shift in the substrate for the metabolism of the stimulated central nervous system compared with the non-stimulated. The central nervous system can furthermore burn substances other than glucose¹².

Therefore, when the nerve cells demand more energy at the increased activity, they are presumably given priority to the necessary substances by the

neuroglia. These cells may cut down their metabolism, which is reflected in the decreased cytochrome oxidase activity. There may be an inhibiting mechanism at that terminal step at increased neuronal activity and the glial cells may be the cellular parts of the central nervous system which have to resort to substances other than glucose.

These studies have been supported by the Rockefeller Foundation and by the Swedish Medical Research Council.

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VIRAL MULTIPLICATION AND CELLULAR HYPERPLASIA

By PROF COUNCILMAN MORGAN

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IN assessing the mechanisms whereby certain viruses cause either cellular proliferation or neoplasia, it is obviously important to determine whether replication of the virus augments or inhibits mitosis of the host cell. Data bearing directly on this problem are scant. Dawson¹, studying the histology of focal lesions in chicken chorioallantoic membranes infected with herpes simplex virus, reported necrosis and hyperplasia of the ectodermal cells but found that only "some of the cells show the characteristic intranuclear changes of infection". Burnet *et al.*² confirmed these observations and noted that the proliferation followed initial necrosis of the ectoderm. In addition, these authors described hyperplasia of the ectodermal cells without the nuclear swelling, margination of chromatin and formation of inclusion bodies which were believed to accompany viral infection. Later, Beveridge and Burnet³ found inclusion bodies "only with great difficulty" in some chorioallantoic lesions induced by herpes simplex virus. The foregoing observations, together with the fact that sterile broth, saline and omissions or filtrates prepared from animal tissue caused proliferation of the ectoderm at the site of inoculation, led the authors to suggest that in the case of viral infection "the cell is damaged, and in response to something diffusing from the damaged cell—either virus particles or, more probably, growth stimulating substances resulting from primary damage—neighboring ectodermal cells proliferate".

Regarding neoplasms it has been recognized that in the human skin some verrucae caused by viruses⁴ were characterized by the presence of intra-nuclear inclusion bodies⁵ and by the appearance in the electron microscope of intranuclear crystalline arrays of particles presumed to represent virus⁶.

Bunting *et al.*⁷ and Blank⁸, however, noted that the cells which contained the inclusion bodies were not seen in process of division. More recently Bloch and Godman⁹ reported that the bulk of these tumours was composed of "normal appearing cells" and suggested that "epidermal cells with morphological stigmata of infection, that is inclusion bodies, have lost their capacity for mitotic proliferation". These authors proposed either that the explanation by Beveridge and Burnet regarding growth promoting substances was correct or that the viral infection was present but morphologically and cytochemically unapparent in the light microscope.

The preceding studies by light microscopy were largely dependent upon the recognition of inclusion bodies as presumptive evidence for the presence of virus. It has not been definitely established, however, what relationship the inclusion bodies bear to the viral particles themselves, nor is it known whether viral development is invariably accompanied or followed by the appearance of an inclusion body in the host cell. Another approach to the problem of identifying virus in specific cells was provided by the fluorescent antibody technique. Neyes and Mellors¹⁰ examined sections of rabbit papillomas stained with fluorescent antibody to the antigen of the Shope papilloma virus. The antigen was found to be intra-nuclear and generally confined to cells of the superficial keratinohyaline or keratinized layers. It was surprising, the authors commented, "that practically all the cells in the proliferating layers of the papilloma contained no antigen, for the cells in these layers make the major contribution to the growth of the papilloma". They added that "there was failure to demonstrate any viral antigen in the mitotic figures of the proliferating layers". From these results the

authors advanced the postulate "that the virus is present in the germinal and the proliferating cells but exists there in an early stage of development, consisting mainly of nucleic acid and deficient in protein, and therefore non-antigenic and not demonstrable by fluorescent antibody." The possibility that virus was present but in insufficient amounts to produce fluorescence could not be excluded.

With the advent of techniques suited to the preparation of thin sections for electron microscopic examination, a method was at hand for visualizing viruses in host cells at sufficient resolution to detect stages in the differentiation of structural components. Of the viruses mentioned above, herpes simplex virus lends itself most readily to study in the electron microscope by virtue of the fact that it grows well both in tissue cultures and in the chorioallantoic membrane. Employing the latter cell system, it had been determined previously¹¹ that the virus develops in the nucleus where it differentiates within characteristic aggregates of granules and appears initially as a central body enclosed by a single membrane. Afterwards, a second membrane is formed. Particles with a central body and two peripheral membranes appear to be the completed, infectious unit. Once the stages in morphological development were recognized it became possible to identify an infected cell with considerable certainty simply by the presence of viral components, even though few in number and not fully assembled into complete virus, and by the accompanying alterations in fine structure. It was decided, therefore, to re-examine the relationship of herpes simplex virus to cellular hyperplasia. Accordingly, a recently isolated strain (JM)¹² of herpes simplex virus was transferred from tissue cultures directly to chorioallantoic membranes. Three and five days after inoculation the resulting focal lesions were fixed in osmium tetroxide, dehydrated in ethyl alcohol, embedded in methacrylate and cross sectioned at multiple levels for examination in the electron microscope. Thick sections were also cut and stained for orientation by light microscopy. At three days there was marked hyperplasia of the ectoderm with necrosis of the superficial cells toward the centre of the lesion. The mesoderm showed oedema and infiltration by inflammatory cells and there was moderate, but definite, hyperplasia of the underlying endoderm. The most striking feature revealed by the electron microscope was that only a small proportion of the ectodermal, epithelial cells contained viral components or, indeed, showed any of the characteristic changes in nuclear fine structure associated with viral multiplication. At five days more cells of the ectoderm were found to be infected and necrosis had extended. Contrary to expectation, however, many of the cells undergoing necrosis were devoid of virus. In no instance was an infected cell encountered within the hyperplastic endoderm. The foregoing suggests that under the conditions of these experiments hyperplasia is not dependent upon the intracellular presence of recognizable virus or viral components.

Recently, Stoker¹³, studying single HeLa cells in tissue cultures infected with herpes simplex virus, found that "none of the cells which yielded virus divided" and, further, that using tissue cultures in synchronous division it was possible to inhibit mitosis by the addition of virus even 1 hr before division was to occur. If it could be shown that the mode of viral development were similar both in tissue culture and in the chorioallantoic membrane, it would not be unreasonable to assume that Stoker's

observations regarding the inability of infected cells to divide would apply to the latter cell system as well. Consequently, detailed comparison was made by electron microscopy between the development of the JM strain in chorioallantoic membranes and its development in HeLa and human amnion cells grown in tissue culture. No basic differences either in the manner of viral evolution or in the morphological response of the host cell were encountered. Presumably, then, in the chorioallantoic membrane, as in tissue culture, herpes simplex virus prevents mitosis of the cells in which it differentiates. It would appear that some factor provided by the intact host is necessary for the hyperplasia to occur, for, as Stoker¹³ has pointed out, there is little evidence to suggest that this phenomenon is associated with the infection of tissue cultures by herpes simplex virus. There are insufficient data to determine whether virus also interferes with mitosis of host cells in the case of tumours, but the observations cited above regarding verrucae and the Shope papilloma are certainly consistent with such a concept. In this connexion, it is of interest that the virus encountered in the Lucke carcinoma of frogs¹⁴ closely resembles herpes simplex virus in morphology and intranuclear site of multiplication.

The purpose of this communication has been to indicate that the hypothesis advanced by Beveridge and Burnet regarding the hyperplasia associated with infections by herpes simplex virus is supported by electron microscopic examination and warrants further study with the techniques currently available. Although none of the observations herein reported exclude the possibility that a masked form of the virus is operative in neoplasia, it is equally possible that in certain neoplasms a cellular product other than the virus itself stimulates mitosis. The role, then, of the initiating viral infection would be to generate or liberate this product. If such were the case, it would explain the apparent contradiction presented by the suggestion that a virus may inhibit mitosis, on one hand, and stimulate cellular division, on the other, for the virus could multiply at a site removed from the region of cellular proliferation. Moreover, the wide variation encountered in viral assays of tumours¹⁵ could be accounted for if the stimulus for mitosis were mediated not by the virus *per se*, but by a cellular product resulting from viral infection. In these circumstances the titre of virus within the tumour would not necessarily bear a consistent relationship to the extent of mitotic activity.

This study was aided by a grant from the National Foundation.

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FORTHCOMING EVENTS

Saturday October 3

ASSOCIATION OF CLINICAL BIOCHEMISTS (Joint meeting with the Association of Clinical Pathologists at the Royal College of Surgeons, Lincoln's Inn Fields, London W.C.2) at 9.30 a.m.—Scientific Papers, 6 p.m.—Annual General Meeting

Monday October 5

SOCIETY OF CHEMICAL INDUSTRY LONDON SECTION (Joint meeting with the Plastics and Polymer Group) at the Royal Institution, Albemarle Street, London W.1, at 6.30 p.m.—Sir Robert Robinson O.M.F.R.S. The Polymerisation of Olefines Using Organo-metallic Catalysts

Wednesday October 7

SOCIETY FOR ANALYTICAL CHEMISTRY (at the Chemical Society Burlington House Piccadilly, London W.1) at 7 p.m.—Meeting on "Atmospheric Pollution Analysis"

Friday October 9

INSTITUTION OF ELECTRICAL ENGINEERS (at Savoy Place, London W.C.2) at 5.30 p.m.—Sir Willis Jackson F.R.S.—Presidential Address

SOCIETY FOR ANALYTICAL CHEMISTRY BIOLOGICAL METHODS GROUP (at The Peabody, Tudor Street, London E.C.4) at 6.30 p.m.—Discussion Meeting on "Routine Toxicity Tests in the Control of Pharmaceuticals" opened by Mr P. Andrews

Saturday October 10

NUTRITION SOCIETY (at Guy's Hospital Medical School, St Thomas's Street, London S.E.1) at 10.30 a.m.—Symposium on Nutrition and the Eye

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned

ASSISTANT LECTURER IN AGRICULTURE—The Principal, Yorkshire (W.R.) Institute of Agriculture, Askham Bryan near York (October 8)

HEAD OF THE DEPARTMENT OF PHYSICS AND APPLIED PHYSICS—The Registrar, Royal Technical College, Salford 5, Lancs (October 10)

SENIOR LECTURER IN MATHEMATICS or LECTURER IN MATHEMATICS and an ASSISTANT GRADUATE IN MATHEMATICS—The Registrar, Royal Technical College, Salford 5 (October 10)

SENIOR LECTURER (with particular interest in proteins or nucleic acids) in the DEPARTMENT OF MICROBIOLOGY—The Deputy Registrar, The University, Edgbaston, Birmingham 16 (October 14)

READER or SENIOR FELLOW IN GEOGRAPHY IN THE DEPARTMENT OF GEOGRAPHY, Research School of Pacific Studies, Australian National University, Canberra—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London W.C.1 (Australia, October 16)

LECTURER IN PSYCHOLOGICAL MEDICINE—The Secretary of University Court, The University, Glasgow (October 19)

CHAIR OF OPHTHALMOLOGY at the INSTITUTE OF OPHTHALMOLOGY—The Academic Reading Office, University of London, Senate House, London W.C.1 (October 21)

VANDERVELT CHAIR OF PHARMACOLOGY at the INSTITUTE OF MEDICAL SCIENCES—The Academic Registrar, University of London, Senate House, London W.C.1 (October 22)

LECTURER IN CIVIL ENGINEERING at the University of Western Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London W.C.1 (Australia, October 30)

CHAIR OF INORGANIC and PHYSICAL CHEMISTRY in the University of Tasmania—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London W.C.1 (Australia, November 10)

CHAIR of a new Institute in the Academic Division of the University—The Registrar, University Office, 40 North Bailey, Durham (November 21)

LECTURERS (2) IN GEOGRAPHY and a LECTURER IN GEOLOGY at the University of Hong Kong—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London W.C.1 (New Zealand, December 15)

TECHNICIAN in the Department of Physiological Chemistry to cut sections and apply standard histochemical tests in relation to a programme of research which is just being started—The Assistant Bursar, The University, Reading (October 31)

FELLOW or SENIOR FELLOW IN PHILOSOPHY within the Department of Social Philosophy, Australian National University, Canberra—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London W.C.1 (Australia, November 10)

CHAIR of a new Institute in the Academic Division of the University—The Registrar, University Office, 40 North Bailey, Durham (November 21)

CHAIR OF GEOGRAPHY in the University of Otago, Dunedin, New Zealand—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London W.C.1 (New Zealand, December 15)

HEAD OF THE DEPARTMENT OF MATHEMATICS—The Registrar, The College of Technology, Ashley Down, Bristol 7

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplements)

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Philosophical Transactions of the Royal Society of London. Series A. Mathematical and Physical Sciences. No 957, Vol. 251 (11 June 1959). The Propagation of Plane Irrotational Waves Through an Elastoplastic Medium. By L. W. Morland. Pp. 341-383. 13s. 6d.

No 958, Vol. 251 (11 June 1959). The Rational Characterization of Certain Sets of Relatively Abelian Extensions. By A. Fröhlich. Pp. 333-355. 13s. 6d. (London: Royal Society, 1959) 1s. 6d.

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Other Countries

Laboratoire d'Astronomie du Lill. Astronomical News Letter. No. 94. Pp. 1+46. (Lille: Laboratoire d'Astronomie, 1959) 1s. net.

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Chicago Natural History Museum Fieldiana Geology Vol 12, No 6 Pennsylvanian Invertebrates of the Mazon Creek Area, Illinois By Eugene S Richardson, Jr Pp 1+70-82 30 cents Fieldiana Zoology Vol 33, No 6 Philippine Zoological Expedition, 1946-1947 Tabanidae (Diptera) By Cornelius B Philip Pp 1+643-626 2 dollars Vol 39, No 26 Ticks (Ixodidae) of Arabia, with special reference to the Yemen By Harry Hoogstraal and Makram N Kaiser Pp 207-322 65 cents Vol 39, No 29 Deep Sea Fishes from the Gulf of Mexico, *Squalogadus intermedius* (Macrouridae) By Marlon Grev Pp 323-346 50 cents (Chicago Chicago Natural History Museum, 1959) [186]

Annals of the New York Academy of Sciences Vol 78 Article 1. Germfree Vertebrates Present Status By James A Reynolds and 30 other authors Pp 1-400 (New York New York Academy of Sciences 1959) 5 dollars [186]

California Department of Fish and Game Forty-fifth Biennial Report July 1, 1956 through June 30, 1959 Pp 95 (Sacramento State of California, Department of Fish and Game, 1959) [186]

European Organization for Nuclear Research Annual Report 1959 Pp 87 (24 plates) (Geneva CERN, 1959) [186]

United States Department of the Interior Geological Survey Bulletin 1042-S Geology and Fluorspar Deposits, Big Four Fault System, Crittenden County Kentucky By George C Hardin Jr. and Robert D Trace Pp III+699-734+plates G1 and G2 Bulletin 1045-D Core Logs from Bristol Cidly and Draby Dry Lakes, San Bernardino County California By A M Bassett, D H Kupfer and F C Barstow Pp I+415-486+plates 45-48 Bulletin 1060-C Geology and Construction-Material Resources of Pottawatomie County, Kansas By Glenn R Scott, Frank W Foster and Carl F Crompton Pp I+07-178+plate 5 Bulletin 1072-D Quartz Crystal Deposits of Southwestern Virginia and Western North Carolina By John H Mertle, Jr Pp I+233-298 30 cents Bulletin 1082-B Radioactive Rare Earth Deposit at Scrub Oak Mine, Morris County, New Jersey By Harry Klemle, A V Hlevi, Jr A R Taylor and Jerome Stone Pp I+20-59+plate 1 60 cents Bulletin 1084-B Rapid Analysis of Chromite and Chrome Ore By Joseph I Dinin Pp I+31-68 20 cents (Washington, D C Government Printing Office, 1959) [186]

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LETTERS TO THE EDITORS

ASTROPHYSICS

The Upper Boundary of the Van Allen Radiation Belts

THREE measurements have now been made of the intensity and extent of the Earth's upper radiation belt and of the primary cosmic ray intensity beyond. These were made by (1) the American space probe *Pioneer III* (December 6-7 1958, ref 1) (2) the Russian cosmic rocket, *Mechta* (January 2-4 1959, ref 2) and (3) the American space probe *Pioneer IV* (March 3-6 1959 ref 3). Since the radiation belts vary with time the three experiments gave different results for the intensity of the belts but the measurements of cosmic ray intensity beyond the belts ought to be comparable. Nevertheless preliminary results of the *Pioneer* tests seemed to indicate a difference in cosmic ray intensity of almost a factor of 2. This communication discusses the resolution of this discrepancy and some new data bearing on the spatial extent of the trapped radiation.

On *Pioneer IV* the counting rate was observed to be a constant 1.00 counts/sec beyond a range of 91 000 km (measured from the centre of the Earth). Since this rate persisted for 86.9 hr during which the range of the probe increased by 564 000 km it is clearly characteristic of the interplanetary particle flux.

Pioneer III on the other hand never reached a region where the counting rate ceased to vary with altitude. Van Allen¹ suggested that the upper boundary of the radiation belt might reasonably be considered to be 64 000 km since the rate of decrease of counting rate with increasing range is very small above this altitude (see Fig 1). Actually however, when the Goldstone tracking station lost radio contact with the probe at a range of 107 600 km, the counting rate had dropped to only 2.25 counts/sec and appeared to be still dropping at approximately 0.01 counts/sec per 1 000 km.

It was reasonable to assume as Van Allen did that the 2.25 counts/sec rate was near the asymptotic value and that the trapped radiation contributed negligibly to the counting rate. It will be shown here that these assumptions are not valid; that the counting rate actually dropped considerably lower and that therefore the puzzling discrepancy between the measurements of *Pioneers III* and *IV* probably does not indicate a change in the primary cosmic ray flux as has been suggested².

The Goldstone tracking station lost contact with *Pioneer III* at 22 16 30 τ about 16.6 hr after launch and 2.5 hr before it reached apogee. It was expected to rise over the horizon at Puerto Rico about 13 hr later at a range of 87 000 km and the tracking station there attempted to re-acquire its signal. At first, only occasional momentary phase lock-ons were obtained but their duration and frequency increased steadily, and after 15 20 τ the telemetry data were, to use Van Allen's phrase "solid". They continued to be solid until the probe set over Puerto

Rico's eastern horizon at 19 29 τ about 3 300 km over the central Atlantic. During solid telemetry the counting rate rose rapidly, as shown by the solid curve in Fig 1, from about 3.3 counts/sec to very high rates in the radiation belts.

Even without reading the doubtful region of the telemetry record it can be shown as follows that the rate of 2.25 counts/sec cannot correspond to the cosmic ray counting rate alone.

The 17 stage scaling circuit was provided with three output taps so that distinctive signals (which we call down flips) occur at intervals of 2^0 , 2^1 , and 2^2 counts and up flips halfway between. At low counting rates all six different kinds of scaler flips are distinguishable. Thus, between the last stage 17 up flip on the Goldstone record at 21 55 57 τ , and the first one on the Puerto Rico re-entry record, at 16 17 24 τ the next day the counter must have recorded $2^{17} n = 131\,072 n$ counts (where n is an integer). Between these times 35 stage-9 cycles corresponding to 17 820 counts, appear on the solid telemetry record, and hence we can calculate the number of counts which the probe detected when we were not watching it. Thus

$$\begin{aligned} \text{Interval of missing telemetry} & 22.14.32 \text{ to } 16.21.30 \\ \text{Time interval} & 61\,64 \text{ sec} \\ \text{Counts} & 131\,072 n - 17\,820 \\ \text{Mean counting rate (counts/sec)} & 1\,836 \pm 127 (n-1) \end{aligned}$$

Thus, the mean counting rate in the interval of missing telemetry was either (1) 1 836 counts/sec if $n = 1$, in which case the minimum counting rate was considerably lower or (2) 3 063 or 0 000 counts/sec or some higher value if $n > 1$ in which case the probe must have run into a region of radiation of high intensity near its apogee and would probably never have recorded cosmic ray background.

Further evidence is obtained by a re-examination of the telemetered data. The telemetry was recorded on magnetic tape. By playing the Puerto Rico tape back into a pen recorder using a compressed time scale and an expanded frequency scale, it is possible to obtain a graph which cannot be read accurately but on which the pattern of scaler flips is clearly discernible back to about 13 00 τ fairly readable back to 12 30 τ and possibly distinguishable as early as 12 00 τ . With the time-compressed record as a guide it is possible to locate some of the scaler flips on the original record to within a few seconds and to obtain reliable data well before 15 20 τ .

In Fig 1 the solid curve shows the counting rate where it is well known from solid telemetry and the experimental points are our best estimate of the data in the region where phase lock is intermittent. The data shown as circles were obtained by reading flip times from the original record and are essentially as reliable as the solid data. Each point represents 768 counts and times can be read to a few seconds. The data marked as triangles were obtained by reading the played back time-compressed record with an accuracy of about a minute; their reliability is increasingly doubtful at earlier times. Each point represents 512 counts. It appears clear that the counting rate dropped to as low as approximately 1.4 counts/sec and that even this value probably

does not correspond to cosmic-ray background, since it was observed at a range of only 65,000 km, below a region of higher intensity.

The two dashed curves in Fig 1 show the implications of assuming different values of n . The lower one corresponds to $n = 1$ and the upper to $n = 2$. Their exact shape is arbitrary, but they are adjusted so that the area under each corresponds to the proper number of counts in the interval of absent or intermittent telemetry, while still making the curves as simple as possible. It is, of course, possible that the curves should show additional peaks and valleys, such as were seen by *Pioneer IV*.

The lack of symmetry about apogee of the high-altitude portion of the counting-rate curve could indicate a spatial or a temporal variation of the radiation itself or could result from the directional response of the counter. The first explanation seems most reasonable, since the probe was considerably farther south on descent than on ascent. An altitude-versus-latitude plot of the trajectory is given in ref 1,

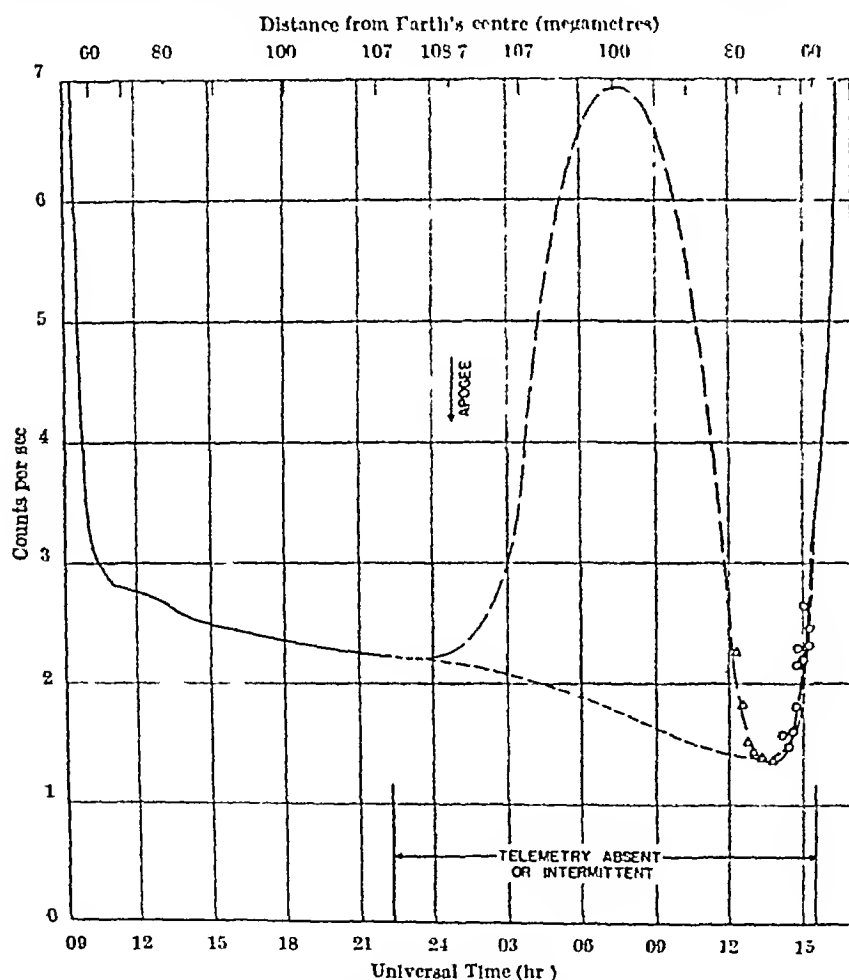


Fig 1 Radiation counting rate observed by *Pioneer III* in the region near apogee. The solid curve shows the rate at times when telemetry was continuous. Experimental points show the rate when telemetry was intermittent. Dashed curves, illustrating possible rates when telemetry was absent, are adjusted to have the proper area on the assumption that the 17-stage binary scaler went through one (lower) or two (upper) cycles in the interval.

and the detailed co-ordinates of four points are listed in Table 1. These are the two points at a range of 65,000 km, the apogee, and the point of most southerly magnetic latitude. Positions are believed to be accurate to about 10 km. The magnetic co-ordinates are based on the eccentric dipole of 1922 (ref 4), using the formulae of Shelton⁵. The distance

Table 1 CALCULATED POSITION CO-ORDINATES OF *Pioneer III* AT SELECTED TIMES

| Position co-ordinates | Universal time | | | |
|-------------------------|----------------|--------------|--------------|--------------|
| | Dec 6, 10 48 | Dec 7, 00 45 | Dec 7, 03 15 | Dec 7, 14 43 |
| Range (km) | 65,000 | 109,700 | 106,950 | 65,000 |
| Longitude (deg) | 26 5 W | 146 5 J | 105 1 E | 38 4 W |
| Latitude (deg) | 15 3 S | 23 7 S | 21 7 S | 28 4 S |
| Right Ascension (deg) | 210 1 | 233 0 | 236 8 | 258 3 |
| Declination (deg) | -15 3 | -23 7 | -24 7 | -28 4 |
| Magnetic range (km) | 64,670 | 109,900 | 107,100 | 64,720 |
| Magnetic latitude (deg) | 6 6 S | 32 8 S | 36 2 S | 18 4 S |

between the two points at 65,000 km range is 46° or about 51,000 km.

Vernov *et al*² state that the upper boundary of the radiation belt as seen by *Mechta* was at a range of 55,000 km near the magnetic equator. *Pioneer IV* detected numerous narrow peaks of radiation intensity between 47,000 and 91,000 km, but the rapid drop in intensity beyond the main peak of the radiation belt appears to end at about 60,000 km. The curve of Fig 1 for *Pioneer III* is fairly accurately symmetrical about apogee between 40,000 and 60,000 km. These three facts strongly point to the region of 9-10 Earth radii as being the upper boundary of the radiation belts. This accords well with the theoretical considerations of Hoyle⁶ and the magnetometer measurements of *Pioneer I* (ref 7), which place the upper boundary of the Earth's magnetic dipole field in the same region. Probably the radiation above cosmic ray background at greater ranges than this is trapped on magnetic field lines which are still attached to the Sun. The amount of such radiation observed by the three probes which have penetrated the region correlates well with the amount of solar activity in the few days preceding their launching.

This communication presents the results of one phase of research carried out at the Jet Propulsion Laboratory, California Institute of Technology, under Contract No NASw-6, sponsored by the National Aeronautics and Space Administration.

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Formation of Stellar Associations from Galactic Gas

GALACTIC gas is present in three types of regions. According to Schlüter¹ these are (1) cold dense H I clouds of temperature of the order of 100° K and density of 10 atoms/cm³ occupying about 5 per cent of space (2) these are surrounded by a hot transparent continuous gas at 10,000° K density 0.1 atom/cm³ and pressure 10⁻¹² dyne/cm² (3) in addition about 0.5 per cent of space contains hot dense rapidly expanding H II regions, heated by nuclear energy derived from embedded O or B type stars, supernovae and novae. The temperature of 10,000° K of the main continuous component is probably maintained by turbulent and viscous dissipation of rotational galactic shear which can supply 10⁻¹¹ erg/cm² sec for 6×10^8 years, and by absorption of stellar radiation. The energy sink is provided by radiation into intergalactic space. The H I regions must have a comparatively short life of some 10⁷ years and must be replenished. Steady population of all ages must develop in which condensations are born from the hot continuous component by Jeans type instability based on strong dependence of cooling of ionized gas on density. Denser eddies of ionized gas continue losing internal pressure by excessive radiative cooling and collapse from the excess pressure of the surround hot gas. After recombination, cooling rate slows down but shear energy supply disappears. An ideal spherical region would deform under galactic shear first into an ellipsoid, which would then continue to collapse into an elongated disk of very small thickness. Collisions of H I regions and turbulence of the continuous component combined with galactic shear would tend to disperse such sheets and return their contents to the hot gas closing thus their cycle of evolution.

The hot component is turbulent at Mach number or order 0.5 as a consequence of large Reynolds number. However, the galaxy is stable against large scale turbulence. There must therefore be a maximum size of an eddy, which cannot exceed 3,000 parsecs, as then the Rayleigh stability criterion $d(v)/dr > 0$ begins to work. This probably accounts for the observed peculiar velocities, sizes and masses of the H I regions, whereas the large-scale appearance of spiral arms is laminar.

The life-cycle of the larger H I regions may be modified by gravitational self-attraction. Gravitational effects in thin sheets are much stronger than in three-dimensional regions of the same total mass and lateral extension. Forces similar to surface tension of liquids appear although gravitation is a long range force whereas in liquids only short-range forces contribute to the surface tension. These tend to keep the sheets infinitely thin and planar. Local condensations of the type suggested by Jeans may form which may account for some stars and clusters especially at the galactic rim. However, a more efficient process has been found, similar to bursting of a membrane under surface tension. When a thin sheet of self-gravitating matter is pierced by a hole, for example by an accidental presence of a hot star, the hole will begin to expand by the appearance of radial forces at the rim. An expanding ring will form, which will increase its mass as it sweeps up the material of the sheet. Instability may arise along the ring, leading to the formation of a chain of stars, located on an expanding circle.

Galactic shear and magnetic fields may modify this process, causing anisotropy of expansion. Magnetic lines of force may become drawn along parts of the ring and the resulting stars would assume magnetic dipoles directed along the ring.

Search of stellar photographs reveals many elliptical chains of stars, which may be identified with stellar associations. When searching photographs, very elongated ellipses become more clearly visible to the eye when the photographs are viewed obliquely so that the ellipses become foreshortened into circles.

Some star chains so observed appear to be double with a dark lane running in between the two parallel ellipses. This phenomenon can readily be explained by the present theory. If the ring is fed by a sufficiently planar sheet two vortices of opposite circulation may form one above and one below the sheet. They will hydrodynamically repel each other. The rings may disintegrate into two parallel chains of stars spinning with their axes parallel to the local tangents to the rings. Corresponding pairs of stars above and below the sheet would rotate in opposite directions. Trapped magnetic fields will generally be parallel to the rotation axes. In the outermost layers of the protostars angular momentum would be available for planet formation, whereas inner portions of stars would tend to rotate but slowly. Planetary systems should be common.

Rough order-of-magnitude calculation suggests that a ring 10 parsecs in diameter formed in a sheet 0.01 parsec thick and of surface density 3×10^{-5} gm./cm² would have radial expansion velocity 5 km./sec and mass of 10,000 solar masses. Much thinner sheets would produce comparable expansion velocities at lower surface densities and masses.

I wish to express my thanks to Prof G. Gamow for helpful discussion. This work has been done when under appointment as a visiting professor in the Chemistry Department, University of Colorado.

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¹ Schlüter Internat. Astro. Union Symposium No. 2, p. 144 (North Holland Pub. Co. Amsterdam 1955).

An Error in the Determination of ΔT from the Lunar Ephemeris and the Frequency of Caesium in Terms of $UT + \Delta T$

THE ellipticity of the Earth causes perturbations of the elements of the Moon's orbit with a period of 18.6 years. The value of the ellipticity used in Brown's "Tables of the Motion of the Moon" and in the "Improved Lunar Ephemeris" is 1/294. As has been pointed out elsewhere¹, the correction to be applied to the tabular longitude of the Moon in order to reduce it to ellipticity 1/297 is equal to $-0.149^\circ \sin \Omega$ where Ω is the longitude of the Moon's node. This is equivalent to a correction of $+0.271 \text{ s} \sin \Omega$ to ΔT as defined by the International Astronomical Union². Recent observations of artificial Earth satellites indicate that the true value of the ellipticity may be nearer 1/298 (ref. 3) in which case the correction to be applied to ΔT is $+0.36 \text{ s} \sin \Omega$.

A value for the frequency of caesium in terms of $UT + \Delta T$ has been published by Murkowitz and

others⁴ based on the change of ΔT in the interval 1955 50–1958 25. The corrections which should be applied to ΔT at these epochs, on the assumption that the true value of the ellipticity is $1/298$, are -0.36 s and -0.19 s, respectively, and the corresponding correction to this particular determination of the frequency is -18 c/s.

More generally, if e is the true value of the ellipticity, then the correction to be applied to an observed frequency of caesium in terms of $UT + \Delta T'$, where ΔT has been determined from the lunar ephemeris, is $+8.8 (e^{-1} - 294) \cos \Omega$ c/s.

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GEOPHYSICS

Geophysical Effects of High-Altitude Nuclear Explosions

RECENT observations of geophysical effects of high-altitude nuclear explosion¹ have indicated that such blasts give rise to signals similar to solar flares when recorded in the 27 kc/s range. A re-examination of the 27 kc/s record of August 12, 1958, obtained in Pittsburgh, Pa., shows a striking similarity to the integrated atmospherics obtained in Japan, but delayed by about 1 hr.

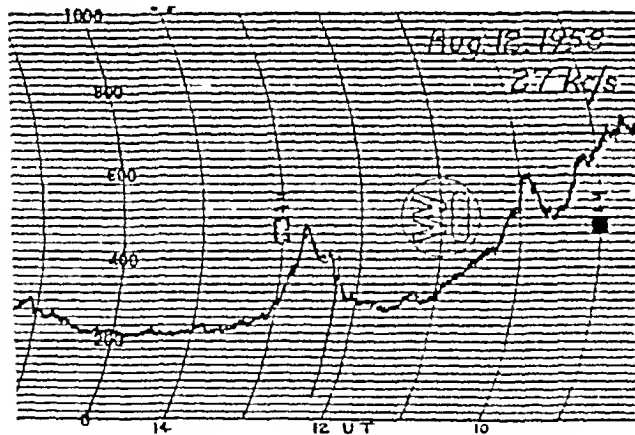


Fig. 1

The accompanying graph (Fig. 1) shows the enhancement between 12 and 13 hr UT. The line at 12 15 (8 15 EDT) is a time check mark. Local sunrise was at 10 UT and is shown by the characteristic sunrise hump. This sunrise effect is present on all records previous to and following August 12. The local weather report for August 12 indicates clear skies at sunrise, followed by fog later in the morning and thunderstorms in the late afternoon. There was no major solar activity at the time of enhancement.

While these results are not entirely unambiguous, they may add interesting speculation on the detectability of high-altitude nuclear blasts.

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¹ Obayashi, Coroniti and Pierce, *Nature*, **183**, 1476 (1959)

PHYSICS

Quadrupole Anti-Shielding Factor in Copper

RECENT measurements of the nuclear magnetic resonance absorption line in heavily deformed copper sheet¹ showed that, although the plastic deformation caused some reduction in the intensity of the line, this reduction was only one third of that predicted by Bloembergen² on the basis of nuclear quadrupole interactions; furthermore, there was no apparent broadening of the line.

Assuming a value of $\gamma = 60$ for the quadrupole anti-shielding factor in the copper lattice (see below), Bloembergen showed by an approximate calculation that a dislocation density of 3×10^8 lines/cm² would be sufficient to render unobservable the satellite components of the resonance line, and thus cause a reduction of 60 per cent in the intensity of the observed line. In the specimens of rolled sheet referred to above, which had undergone 25 per cent–90 per cent reduction in thickness by rolling, the dislocation density was probably³ of the order of 10^{11} lines/cm²; and the reduction in intensity compared with the annealed material was only 20 per cent, it therefore appears that the estimate of $\gamma = 60$, which is deduced indirectly from measurements on copper-zinc alloys, may be too high.

In the present investigation a series of experiments has been performed with the object of determining γ directly from measurements of the broadening of the resonance line in specimens of copper subjected to elastic strain. The maximum strains available are of the same order of magnitude as those to be expected, on the basis of a simple model, in the main part of the strain field due to a random array of dislocations with a density of 10^{10} lines/cm².

The specimens were made from the same sample of electrolytic copper that was used in the earlier experiments on plastic deformation: a preliminary experiment on annealed films showed that the intensity of the resonance line was the same as that from an annealed sample of spectroscopically pure copper. Each specimen was a strip $2.0 \times 0.6 \times 0.0045$ cm which had been annealed for 2½ minutes at a temperature of 300° after 97 per cent reduction in thickness by rolling. Metallographic examination revealed that the material had fully recrystallized and had a grain size of 5–10 μ . The strip was in the shape of a spiral of 1½ turns with an air space of 0.1 cm between adjacent surfaces; this was mounted in a special holder in which the spiral could be 'wound up' like a clock spring while remaining in the specimen coil of the spectrometer. It was found that after the centre had been rotated in either sense through an angle of 45° there was less than 5° change in the equilibrium position, from which it was assumed that this deformation was predominantly within the elastic range, it corresponds to a maximum strain of approximately 9×10^{-4} .

The nuclear magnetic resonance absorption line was observed by means of a Colpitts marginal oscillator operating at a frequency of 5.5 Mc/s, with the specimen in the equilibrium position and in the deformed positions. About 50 lines were recorded from 5 specimens. The result was that no difference could be detected, either in width or intensity, between the lines obtained in the two states. The signal-noise ratio was reasonably high (about 5:1 with an inte-

grating time of 5 sec) and, in view of the fact that a homogeneous type of broadening would be expected it was estimated that a change of 20 per cent in the mean square line width would have been easily observable. Since the normal mean square line width is about $(3 \text{ kc/s})^2$, the following upper limit can be placed on the contribution of quadrupolar strain broadening to the width of the satellite components

$$\overline{\Delta\nu_Q^2} < (1.0 \text{ ko/s})^2 \quad (1)$$

The quadrupolar perturbation of the nuclear magnetic resonance at a given site depends on the electric field gradient grad grad ϕ which is connected with the strain at the site by a fourth-order tensor which may be written by the use of the Voigt notation, in terms of components F_{ij} . An estimate F_{ij}^* of these components may be obtained if it is assumed that the field gradient is due to single electronic charges e located at the lattice sites in a uniformly deformed crystal for the twelve nearest neighbours in a face-centred cubic lattice with nearest neighbour distance a these components are

$$F_{11} = -2F_{22} = 6ea^{-3}, \quad F_{33} = F_{11} \quad (2)$$

and the anti shielding factor λ may be defined by the equation

$$\lambda = F_{11}/F_{33} \quad (3)$$

It must be emphasized that λ is not in general, the same as the Sternheimer factor $(1 + \gamma_\infty)^4$.

In first order quadrupolar interaction the only operative component of grad grad ϕ is $\partial^2\phi/\partial z^2$ where z is the direction of the applied magnetic field. The effect of a simple compressional strain ϵ in polycrystalline material may be estimated by calculating $\partial^2\phi/\partial z^2$ in terms of the components of F as a function of crystal orientation and averaging over all possible orientations to find the mean square value; the result (assuming that $F_{44} = F_{11}$) is

$$\left(\frac{\partial^2\phi}{\partial z^2}\right)^2 = \epsilon^2 F_{11}^2 \frac{1}{84} (3 + \cos^2 A)^2 \quad (4)$$

where A is the angle between the strain and the z axis.

An upper limit can now be set on the value of λ . Using equations 1-4 in conjunction with the well known formulae for first-order quadrupole interaction⁵, and averaging over all values of A and ϵ , the result is $\lambda < 7$.

In this calculation the usual assumption has been made that the satellite components make their full contribution to the nuclear magnetic resonance in pure annealed copper. However the possibility cannot be excluded that λ has a very high value and that the satellite components do not contribute even in the annealed state.

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Solid State Rheological Study of the Mechanism of Paraffin Detergent Interactions in Aqueous Systems

THE generation of new surfaces in a solid by rheological means affords the opportunity of studying the behaviour of these clean surfaces in respect to specific surface reactions. Thus a sensitive stress-strain record of the slow plastic deformation of a solid is somewhat akin to the Heyrovsky dropping mercury polarograph in the respect of fresh surfaces being available for analytical (chemical, physical or electrochemical) studies. As a part of a fundamental Instron¹ precision tension apparatus study of first and second-order transitions in some solid paraffins we made a number of stress strain tests of the mechanism of paraffin detergent interactions in aqueous solutions. We wished to see whether the new surfaces produced by a slow (0.50 in./min.) plastic extension would interact to a measurable degree with two detergent solutions. Four representative specimens were tested in each of three environments distilled water, a 0.4 per cent solution of technical grade sodium lauryl sulphate in distilled water, and a 0.4 per cent solution of technical grade sodium dodecyl benzene sulphonate in hard water. (The approximate composition of this Ponca City hard water was calcium 110 magnesium 34, sodium, 180 potassium 4 chloride 284 sulphate, 107, bicarbonate 320 p.p.m., the total solids being 888 p.p.m.) The hard water solution was used according to a suggestion of Dr W. H. Harwood of our Research Department who indicated (this was easily proved by simple beaker dipping tests) that a greater paraffin wetting action might be expected in waters containing the divalent ions of calcium and magnesium these forming the corresponding detergent salts of decreased solubilities. The tensile specimens were prepared from a thin paraffin sheet formed by pouring liquid paraffin upon a clean hot water surface.

There were found pronounced effects upon both the surface of the paraffin was tensile specimens and upon their elongations. With the detergent molecules present there were myriads of surface cracks which had a tendency to be normal to the surface and normal to the longitudinal axis of the specimen. We interpreted and expected that the preferred orientation of the paraffin crystals controlled this particular rheological response. Table 1 illustrates the results.

TABLE 1. ELONGATION MEASURES OF DETERGENT-PARAFFIN INTERACTIONS (using an Instron precision tension test instrument)

| Condition | Test Results | |
|---|---|-------------------------|
| | Elongation Average of Four Specimens Each | Elongation Ratio (%) |
| 1. Distilled water elongation | 1.77 in. | 100 |
| 2. With 0.4 per cent solution of sodium lauryl sulphate | 1.210 in. | 68.2 |
| 3. With 0.4 per cent solution (hard water) of sodium dodecyl benzene sulphonate | 0.036 in. (3 specimens) | 52.6 |

* The surface cracking effects of Run No. 3 were sharper and deeper than with No. 2. Here also were the best geometric indications upon the surface of the tensile specimens of the direct relation of the paraffin structural orientation to the crack form and orientations. Specimens 0.5 in. long, 1/8 in. thick, 1 in. wide at shoulder; 1/8 in. wide at waist, 1/8 in. shoulder-to-shoulder length. Tensile strength, 125 lb. per sq. in. (not seriously affected by detergent solution contacts) the average of eight specimens tested at 22° C.

obtained. No special strength effects were noted. We interpret this to mean that strength is primarily a volume property, whereas elongation is a strongly surface limited property. It will be noted that the detergent paraffin system of the sodium dodecylben-

zene sulphonate in hard water was the most damaging to the elongation. Four specimens were employed for each data point. One specimen was tested in sodium lauryl sulphate at a concentration of 0.01 per cent, but the elongation thereof was such as to fall within the scatter range of the distilled water data.

We conclude that the wetting effects caused by the detergent molecules cause a serious elongation reduction, that the mechanism of this is probably due to the no repair possibility of extremely fine surface cracks in the paraffin by the wetting action of the detergent solution. If the second point be true, then it would appear that there are many surface cracks or microfissures which are at least partly healed during tensile flows under ordinary circumstances. From the data it also can be seen how important the testing environment is. To the extent of our data (four separate runs 0 per cent, 0.01 per cent and 0.4 per cent sodium lauryl sulphate in distilled water and 0.4 per cent sodium dodecyl benzenesulphonate in hard water), the elongation impairment is in a direct relation to the observed wetting action.

These data have a multiplicity of possibilities, as they not only show the rheological consequences of the paraffin-detergent surface interactions but they also indicate how paraffinic or other solids could be studied for use in extraction or for chromatographic purposes. Perhaps the data afford the explanation possibly of why it is that the commercial detergent product, as 'Tide', happens to be a good chromatographic column material for various hydrocarbon gases—herein again is the detergent-paraffin system but in an inverted relation as to the solid and the dilute (gaseous) states. The paraffin-detergent interactions also have at least two significant industrial aspects. One is that some of the solid long-chain hydrocarbons are in widespread use for milk cartons, wax paper and various food packaging applications. The other is in the field of plastics testing there exists a standard stress-corrosion cracking test of polyethylenes in a certain nonionic detergent solution. This elongation test may be a supplement to or a substitution for the above stress corrosion cracking system. Finally, whereas it had been shown that aqueous proteins and milks of various fat contents were capable of oluting certain complex hydrocarbons from wax surfaces, we are unaware of studies of the reverse system.¹

We are indebted to Dr. William H. Harwood for his comments and interest in these studies.

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¹H. L. Falk, P. Kottin, A. Miller, *Nature*, 183, 1184 (1959)

Action of Mixed Solvents on Wool

DURING the course of another investigation¹ it was observed that the resistance of wool fibres to extension in water is greater than in butanol saturated with water. This surprising result, which has an important bearing on methods of determining the accessibility of wool to different reagents², led to a study of the behaviour of wool fibres in mixtures of other primary alcohols and water, as well as in mixed solvents generally. Among the more interesting results so far obtained are those for *n*-propanol and water. After

being calibrated by 30 per cent extension in distilled water at 22.2°C, merino wool fibres (5 cm lengths) were released and allowed to stand in distilled water for 24 hr, before transference to the propanol-water mixture for 18 hr, followed by re-extension in the mixture at 22.2°C. The percentage change in resistance to 30 per cent extension (C.R.E.) was calculated from the two load/extension curves for each fibre, and each of the results in Table 1 is the average of the values for 10 fibres.

TABLE 1

| Propanol in mixture (per cent w/w) | C.R.E. (per cent) | Propanol in mixture (per cent w/w) | C.R.E. (per cent) |
|---------------------------------------|----------------------|---------------------------------------|----------------------|
| 0 | -1.5 | 50 | -10.9 |
| 10 | -5.5 | 60 | -7.6 |
| 20 | -8.7 | 70 | -5.7 |
| 30 | -8.8 | 80 | +2.5 |
| 40 | -10.7 | 90 | -52.2 |

Maximum weakening is obtained with the mixture containing 45 per cent (w/w) propanol, and in this mixture the diameter of Lincoln wool fibres was found to be 3.4 per cent greater than in water. The weakening is thus accompanied by swelling which is greater than that of wool fibres in hydrochloric acid at pH 1 (ref. 3), and it seems probable that this is one of the causes of the success of solvent assisted dyeing processes.⁴

The form of the curve showing the C.R.E. as a function of the propanol content of the mixture is similar to that of corresponding curves for the turbidity temperature of solutions of zein and gliadin.⁵ In addition, there are many similarities between the action of aqueous solutions of different primary alcohols in modifying the elastic properties of wool and in dissolving zein. It seems probable, therefore, that amide and inert side chains of keratin are grouped in such a way that some sections of the chain molecules resemble those of zein, and that cohesion between such sections is weakened by the same solvent action which leads to the ready dissolution of zein in aqueous propanol.

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Polynomial Representation of Thermodynamic Tables

IN a recent communication Berry, Black and Enderby¹ describe an interesting use of the Teichmüller polynomials to represent the thermodynamic steam tables of Keenan and Keyes. This was a preliminary description which will presumably be followed by more details and a tabulation of the actual expansion coefficients. However, based on this initial communication, it is apparent that these authors have done a particularly elegant job of reducing a lengthy tabulation to a relatively small number of expansion coefficients. It is the purpose of this communication to point out the possibility of even further reduction in the number of coefficients required to represent the thermodynamic data.²

For the gas phase the tables of Keenan and Keyes actually present values of specific volume, specific enthalpy and specific entropy, with temperature and pressure as the independent variables. Berry *et al* actually regarded the curve fitting as three separate problems: volume, enthalpy and entropy were each represented by orthogonal polynomial expansions in temperature and pressure. This is somewhat redundant thermodynamically. The expansion of volume as a function of temperature and pressure plus an expansion of the isobaric heat capacity as a function only of temperature at zero pressure would provide the necessary and sufficient information to compute explicitly values of enthalpy, entropy and other thermodynamic quantities.

These thermodynamic computations require differentiations and integrations of the volumetric and heat capacity data. One advantage of the Tchebichef polynomials is the availability of a set of relations which reduce integration and differentiation operations to simple algebraic operations. Lanczos² describes the integration identity. A differentiation identity which is perhaps less known is as follows:

$$T^{n+1}(x) = \frac{n}{2(1-x^2)} [T^{n-1}(x) - T^{n+1}(x)]$$

Berry *et al* reverted their Tchebichef polynomial expansion to a conventional integer power polynomial expansion. There may be substantial advantage in using the equation of state directly in the Tchebichef form. First, there exists a recursion formula which makes it feasible to generate values of the Tchebichef polynomials very rapidly, especially if the computations are being performed with a digital computer. Secondly the availability of the differentiation and integration formulae mentioned above make it possible to obtain values of all thermodynamic quantities by simple matrix operations on the volumetric and heat capacity expansions. Thirdly in the Tchebichef form the expansion coefficients are independent entities, which makes it possible to truncate the expansion arbitrarily if a lower order approximation is required; this is in contrast to the power polynomial coefficients which form a decidedly interdependent set for which truncation is disastrous.

A fuller description³ of the use of orthogonal polynomials for representation of thermodynamic tables will be available shortly.

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RADIOCHEMISTRY

Thermal Decomposition of Irradiated Lead Oxalate

In a previous communication¹ it was suggested that the thermal decomposition of a solid would be affected by pre irradiation if the decomposition of the unirradiated substance proceeds by a branching chain mechanism, and if a simple metal cation is

present. Lead oxalate satisfies these requirements², and we report here some preliminary results on the effects of pre irradiation by gamma rays on the subsequent thermal decomposition of this substance in the range 300–325°C.

The study of pre irradiation effects necessitates a high degree of reproducibility of the decomposition of the irradiated and unirradiated material. The decompositions of the permanganates so far studied and silver oxide, satisfied this requirement. However when using lead oxalate prepared by the method formerly used² the decompositions were not sufficiently reproducible. This difficulty was overcome by precipitating the lead oxalate from N/600 sodium oxalate by the very slow addition of N/5 lead nitrate. The specimen was crystalline with particles approximately 4.2×10^{-3} cm in diameter. The induction period prior to the main acceleration of the decomposition reaction was preceded by the rapid evolution of gas liberated during the decomposition of a surface layer of the oxalate. This conclusion was supported by the fact that immediately after this rapid reaction the particles were visibly coated with product. Pre irradiations were carried out at room temperature in the spent fuel irradiation facility at Harwell. The γ ray dose rate was 4×10^6 rads hr⁻¹. The effects of pre irradiation doses of 70 Mrad and 250 Mrad on the decomposition are shown in Fig. 1. In all cases for a constant mass of irradiated and unirradiated lead oxalate the final gas pressure was the same within experimental error, showing that no measurable decomposition takes place during irradiation.

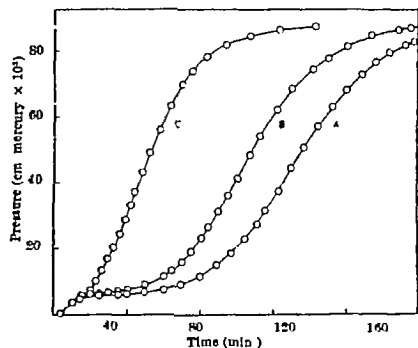
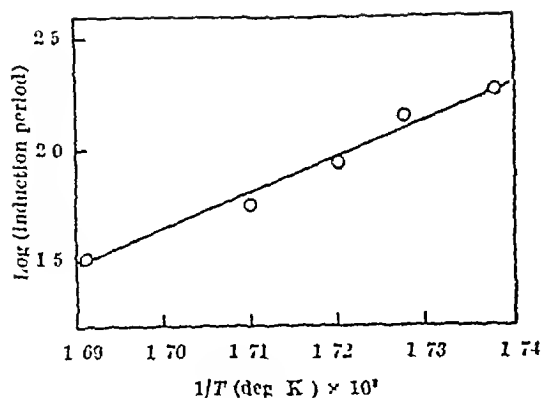


Fig. 1. Curves showing the effects of pre irradiation by gamma rays on the decomposition at 325°C. A. Unirradiated. B. 70 Mrad. C. 250 Mrad.

The effects of pre irradiation are similar to those found for potassium permanganate³ and silver permanganate⁴ in that the induction period is progressively shortened with an increasing dose of gamma rays, and the acceleration of the reaction is increased. In the studies of potassium and silver permanganates it was suggested that the dependence of the length of the induction period on temperature for a fixed irradiation dose, could be used to obtain values of the activation energy for the migration of point defects. The plot of \log_{10} (induction period) against $1/T$ (deg. K.) for a gamma ray dose of 70 Mrad on lead oxalate is shown in Fig. 2. The activation energy calculated from the slope of the line is 3.3 eV. The reported⁵ activation energy for the



decomposition of unirradiated lead oxalate is 36.0 kcal/mole

A more detailed account of this work, together with further observations, will be published elsewhere. We wish to thank the South African Council for Scientific and Industrial Research for a grant towards irradiation costs and for a scholarship held by one of us (P. J. H.).

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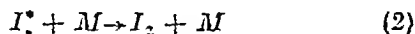
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CHEMISTRY

Mechanism of Atom Recombination

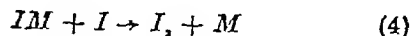
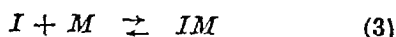
THE RECOMBINATION of two atoms requires the intervention of a third body—a chaperon¹—which stabilizes the diatomic complex by reducing its energy below that of the two separate atoms. One plausible kinetic representation of this process is



where I are atoms, M is the chaperon and I_2^* represents a collision complex which is iso-energetic with the separate atoms.

This scheme does not give a satisfactory account of the principal features of atom recombination reactions which have been observed experimentally. The most accurate data are those derived from flash photolysis studies of halogen atom recombinations which have established that (a) rates of recombination of iodine atoms in the five inert gases are in inverse order to those calculated for reaction (2) by means of collision theory², (b) rates in many other gases, for example, mesitylene³ and iodine⁴ are much greater than would be predicted simply on the basis of increased collision diameters or additional degrees of freedom, (c) temperature coefficients are negative⁵.

An alternative mechanism which has been widely discussed for some time (see, for example, refs 5, 6) is the following



In order to explain the negative temperature coefficients and to account for the efficiencies of the atomic gases, it is necessary to assume that IM is a collision-stabilized complex in thermal equilibrium. The overall termolecular rate constant of recombination k , then becomes equal to $k_1 K$, where K is the equilibrium constant of IM formation. The rate constant can then be expressed in the form

$$k = AT^2 e^{-\Delta E/RT} \quad (5)$$

where ΔE is the increase in internal energy accompanying reaction (3) and A is a factor which is nearly independent of temperature. Detailed calculation by statistical mechanical and collisional theory methods shows that the relative rates with the various chaperons will then be determined principally by the magnitude of ΔE .

Previous experimental work has not supported this conclusion. The only extensive work on temperature coefficients in a number of gases indicated that these coefficients were nearly constant for all chaperons². Only in the case of iodine as the chaperon molecule is there clear evidence for a higher temperature coefficient, but this was thought to be a special case of chemical compound formation². A further serious difficulty is that energies of formation of complexes IM calculated from second virial coefficients are too small in absolute magnitude and in relative variation to account for the observed rates.

In order to test the complex theory of recombination we have recently carried out an investigation of the temperature coefficients of iodine atom recombination in a number of gases and our results are now sufficient to establish that there is a definite correlation between the rate of recombination and the magnitude of the negative temperature coefficient. The values of A and ΔE defined by equation (5), and the rate constant of recombination at 20° C are given for iodine atom recombination in nine different gases in the accompanying table, ΔE for iodine being taken from ref. 7. The value of A varies in a random manner by a factor of about ten whilst the rate varies over a factor of 10³. Some variation in A is to be expected and absolute calculations of A require a rather empirical choice of collisional diameters and statistical weight factors.

TABLE 1

| Chaperon | k_{20} (ml ² molecules ² sec. ⁻¹) $\times 10^{22}$ | A (ml ² molecules ² sec. ⁻¹) $\times 10^{26}$ | $-\Delta E$ (k cal/mole) |
|----------------|--|---|--------------------------|
| Helium | 0.84 | 2.6 | 1.4 |
| Argon | 1.64 | 1.8 | 2.0 |
| Oxygen | 3.72 | 2.0 | 2.2 |
| Carbon dioxide | 7.41 | 4.1 | 2.4 |
| Benzene | 43.9 | 24 | 2.4 |
| Toluene | 107 | 11 | 3.4 |
| Ethyl iodide | 144 | 24 | 3.1 |
| Mesitylene | 223 | 2.0 | 4.8 |
| Iodine | 764 | 2.9 | 5.3 |

but a not unreasonable selection of such parameters can lead to agreement with the experimental values⁹.

If this evidence is regarded as sufficient to establish the theory outlined we must conclude that the iodine atom forms complexes with other gases whose energies of formation vary from 1.4 kcal for helium to about 5 kcal for mesitylene and iodine. These values are considerably greater than the usual estimates of Van der Waals type interactions between such species.

Absolute calculations based on such interactions can lead to correct rate constants in some cases⁷ but they depend on a fortuitous choice of various

quantities and are of far less significance than the fact that neither the correct magnitude of temperature coefficients nor the correct relative magnitude of the rate constants are predicted. Calculations of *IM* energies from second virial coefficients are carried through on the assumption that the iodine atom has the same properties as xenon and use of the geometrical mean combining rule. The absolute magnitude of the calculated interaction energy could be increased by assuming that the iodine atom has a much higher polarisability than xenon but no matter what properties of iodine are assumed the observed relative values of *IM* interaction energies cannot be reproduced.

The phenomena are too general to be interpreted in terms of specific chemical forces and we believe that the explanation is to be found in terms of a charge transfer complex between the iodine atom and the chaperon. No satisfactory quantitative theory of charge transfer forces has yet been developed but the theory of Matsen *et al.*, and the limited experimental results on charge transfer complexes involving the iodine molecule in solution indicate that energies between one and five kcal are not unreasonable for charge transfer complexes between the gases studied and a species with high electron affinity such as the iodine atom.

The question as to whether the complex mechanism and the charge transfer theory are generally applicable to other atom recombination reactions and perhaps to some radical recombination reactions must wait further experimental data. Although the energy of formation of charge transfer complexes by other atoms will generally be less than those of iodine, we shall expect that in many other cases the complex mechanism of recombination will play a significant part.

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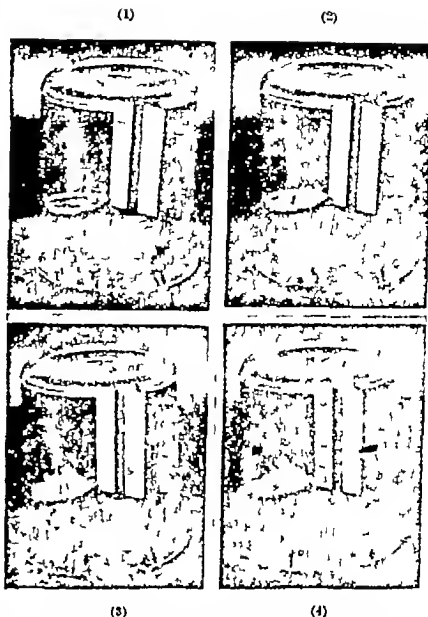
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Primer Explosion Triggers Reaction

RECENTLY, when making certain experiments with the furnace for trondhi mortar shells, a thin (0.1 mm) disk of pure aluminium was placed between the primer and the detonator. It was noticed that, immediately after this disk was pierced by the gases of the exploding primer, a white mass started to grow on the aluminium surface around the hole, and this growth continued to expand most vigorously for about 12-15 min.

Figs 1-4 show consecutive stages of this reaction. After about 10 min (Fig 4) the fragile structure started to collapse under its own weight.

The disk was placed under an inverted beaker to protect the delicate growth from air currents. In some cases these 'feathers' reached a height of



about 20 mm. before collapsing and resembled greatly in shape the delicate sea anemones. The primer charge consisted of approximately, 50 mgm. of the usual priming mixture containing mercury fulminate, potassium chlorate and antimony sulphide.

The mechanism of this reaction is apparently, as follows: vapours of mercury formed at the moment of explosion ($\text{Hg}(\text{CNO})_2 = \text{Hg} + 2\text{CO} + \text{N}_2$), are condensed as tiny droplets on the cold aluminium surface in presence of the moisture of air an energetic electrochemical action starts at those points where two metals are in intimate contact and aluminium is readily converted into its hydroxide— $\text{Al}(\text{OH})_3$.

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A New Approach to Carbon Gasification

TERMS such as 'active sites' and 'active centres' have long been used in describing the reactions of carbons with gases, without any specific knowledge of either the real nature or real function of such 'sites'. Recent work in these Laboratories has thrown some light on both nature and action of at least one common type of reactive centre.

A series of chars was produced from *Eucalyptus marginata*. These samples contained varying amounts of oxygen depending on the temperature of charring. When this oxygen was determined by heating the char in a stream of purified nitrogen at 1,250° C it was liberated partly as carbon dioxide and partly as carbon monoxide. The greater part of the oxygen, liberated as carbon monoxide, represents oxygen groupings in

which only one atom of oxygen is attached to a carbon atom. These groups show both oxidizing and reducing characteristics and may possibly be the semiquinone type or the chromene groups described by Garten and Weiss^{1,2}.

When reacted with hydrogen, carbon dioxide or water vapour, to form methane, carbon monoxide and carbon monoxide plus hydrogen respectively, under the usual conditions of temperature and pressure applying in gasification practice, the rates of reaction measured by the number of gm moles of product formed per min per gm of carbon, were found to follow, in every case, the type of curve shown in Fig. 1.

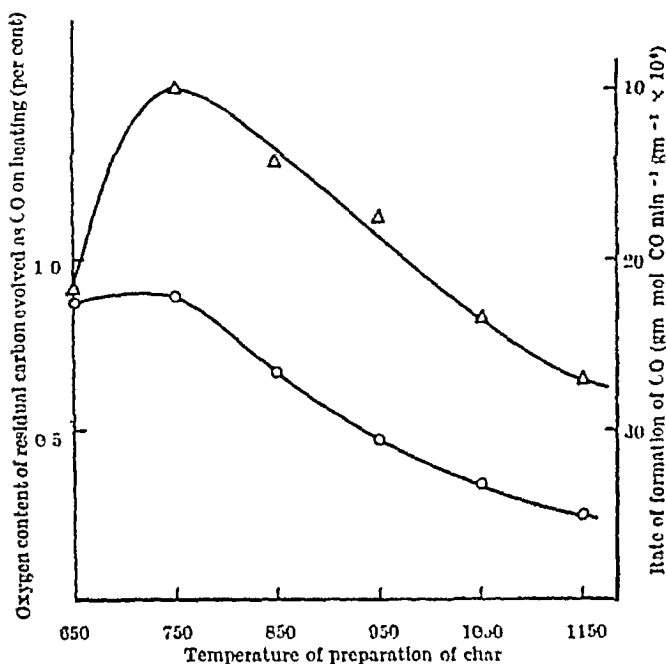


Fig. 1 Showing relationship between residual oxygen bound as $\text{C}=\text{O}$ — and reaction rate O , Oxygen content of char residues Δ , reaction rate of carbon when gasified by water vapour dissociated in a radio frequency field

This pointed to the oxygen-containing groups as being the rate determining agents.

The same chars were also reacted in an apparatus³ in which the gases were first passed at a pressure of about 0.3 mm mercury through a high-frequency field. The effect of the field was to produce high concentrations of hydrogen atoms from hydrogen, oxygen atoms and carbon monoxide from carbon dioxide, and hydrogen atoms and hydroxyl radicals from water vapour. In the experiments with hydrogen and carbon dioxide the atomic species reacted very readily with the carbon at room temperature and the rate of each reaction was the same for all the chars, thus indicating that atoms of hydrogen or oxygen were reacting with the carbon independently of the active sites. However, for water vapour the reaction-rates showed the same variation as for the various gases at high temperatures and pressures in the absence of the radio-frequency field.

It is deduced from this evidence that the role of the oxygen groups is to split the molecular species involved to atoms, which then react with the carbon either at the site or nearby. In the cases of hydrogen and carbon dioxide in the high-frequency field the production of atoms of hydrogen and oxygen is brought about by the field and the oxygen groups are therefore not involved. However, for water vapour in the field splitting of the hydroxyl radicals must still be brought about before oxidation can occur, and this is again effected by the oxygen groups.

A more detailed account of this work will be presented elsewhere.

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Polyethylene Absorption Cells for Infra-Red Spectrophotometry

THE infra red spectroscopy of aqueous solutions has been hampered not only by the infra-red absorption of water itself, but also by the difficulty of finding material for absorption cell windows which would be insoluble in water and still sufficiently transparent in the desired region. This problem is particularly irksome to biochemists who are primarily interested in aqueous solutions. Several groups of workers¹⁻⁴ have been successful in observing infra red spectra in water solution by using cells sufficiently thin for absorption by water not to be excessive and by choosing materials such as silver chloride, barium fluoride, thallium bromide, etc., for windows. The expense and inconvenience of these special windows has prevented many from benefiting by this powerful technique, so that we have been led to consider the possibility of using polyethylene as a window material for aqueous solutions.

All measurements have been made using the Perkin-Elmer 'Infracord', Model 137 Spectrophotometer. Two pieces of polyethylene sheet were heat-sealed around three sides to form bags of a size that would fit in the regular sample cell holders. A few drops of liquid to be analysed were added and the excess squeezed out to remove air bubbles and leave a capillary film.

Fig. 1 gives the absorption spectrum of polyethylene showing that large transparent bands are available between the hydrocarbon absorption bands. For comparison a spectrum of 'Nujol' is included since 'Nujol' is frequently used as a mulling medium in spectral determinations. Polyethylene is clearly as transparent as 'Nujol' in the regions of most interest.

Fig. 2 compares the absorption spectra of capillary films of nitrobenzene on sodium chloride and polyethylene windows. Except for the narrow bands of polyethylene absorption, the two spectra are identical, so that because of its negligible cost, polyethylene may be preferred even for some compounds which can be run on sodium chloride. No cleaning of polyethylene windows is ever necessary, fresh ones can be used for each determination.

Fig. 3 gives the absorption spectra of sodium acetate as a 'Nujol' mull and in aqueous solution. In the region around 3 microns 'Nujol' appears superior because of the large water absorption. If desired, deuterium oxide rather than water may be used as a solvent⁵ so that only the narrow polyethylene band would interfere. In the carboxyl absorption region better resolution was obtained in solution than in 'Nujol' since 'Nujol' has two absorption bands here while polyethylene has one narrow band which falls at 6.8 μ , just between the carboxyl bands at 6.4 and 7.1 μ . Throughout the remainder of the

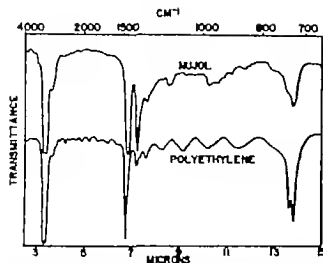


Fig 1 Infrared absorption spectra of Nujol in a capillary film on sodium chloride windows and of polyethylene film in two layers each of 0.002 in. thick

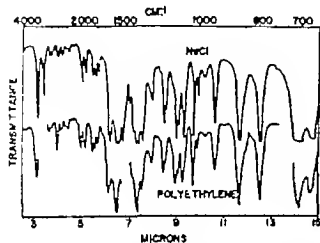


Fig 2 Infrared absorption spectrum of nitrobenzene as a capillary film either between sodium chloride windows or between two layers of 0.002 in. polyethylene film. In the latter case a similar thickness of polyethylene was in the reference beam. Breaks in the bottom curve indicate regions which are not usable because of polyethylene absorption

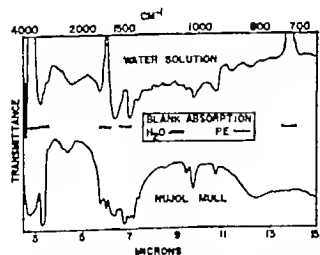


Fig 3 Infrared absorption spectrum of sodium acetate trihydrate as a Nujol mull between sodium chloride windows or in saturated aqueous solution as a capillary film between polyethylene sheets. In the latter case the reference beam passed through a capillary film of water in polyethylene. Dashed lines indicate regions where high absorption by water or polyethylene makes sample spectrum indistinguishable

spectrum there is little of interest but the two techniques appear to give similar bands. Both polyethylene and Nujol show strong absorption at 13.6–14.0 μ . The difference appears because for polyethylene this was compensated by a reference sample.

The major objection to the polyethylene technique arises from the difficulty of controlling sample thickness. The flexibility of thin polyethylene prevents

spacers being used with any accuracy. However, for qualitative applications with aqueous solutions polyethylene seems in many ways preferable to the other cell materials which are available.

Thanks are expressed to the Kordite Corporation, Macedon, New York, for supplying the polyethylene sheet used in these experiments.

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Stability of Metal Complexes of Oxine and its Sulphonic Acid

THE STABILITY constants for the complexes of 8-hydroxyquinoline-5-sulphonic acid (oxine sulphonic acid) have recently been compared with those for 8-hydroxyquinoline (oxine). For any given metal the reported difference between corresponding constants was large (up to 10,000 fold) and a plausible explanation was offered.¹ However the comparison is not valid because the values for the sulphonic acid were determined in water and those of the 8-hydroxyquinoline in 70 per cent dioxan.²

When a comparison is made between results obtained in the same solvent it is seen that the presence of the sulphonic acid group has only a small effect on the stability constants. This is clearly shown by the typical values (Table 1), all of which were obtained in water at 20–25°.

TABLE 1

| Cation | Oxine (ref. 3) | Oxine sulphonic acid (ref. 3) | Oxine (ref. 4) | Oxine sulphonic acid (ref. 5) |
|------------------|----------------|-------------------------------|----------------|-------------------------------|
| | log K_1 | log K_1 | log K_1 | log K_1 |
| Cu ²⁺ | 12.7 | 12.5 | 12.6 | 11.5 |
| Ni ²⁺ | 9.0 | 10.0 | 9.1 | 8.8 |
| Co ²⁺ | 0.1 | 0.2 | 8.7 | 8.8 |
| Zn ²⁺ | — | 8.4 | 8.6 | 8.7 |
| Fe ²⁺ | 8.0 | 8.4 | — | — |
| Mn ²⁺ | 6.8 | 6.6 | — | 6.0 |
| Mg ²⁺ | 4.5 | 4.4 | 4.7 | 4.8 |

Method: Potentiometry, Ionic strength: 0.01

Potentiometry, Ionic strength: 0.01

Spectrometry, $\lambda \rightarrow 0$

Spectrometry, $\lambda \rightarrow 0$

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BIOCHEMISTRY

Rivanol, Resin and the Isolation of Thrombins

HUMAN, cow, and horse thrombins were quickly fractionated from citrate- or bio-activated prothrombin preparations by precipitation of residual prothrombin and inert protein(s) with the cationic dye 6,9-diamino-2-oxoacridine lactate (often referred to as rivanol, available under the trade name 'Ethodin' from the Winthrop Laboratories, New York, New York). This is a general procedure previously applied in purifying γ -globulin¹, β 1-metal-combining globulin², and ceruloplasmin³. A more efficient yet rapid fractionation, however, was achieved by the adsorption of preparations containing thrombin on filter cakes or short columns of 'IRC-50' ('XE-64-Rivanol'), this resin form being prepared by stirring 'XE-64-Na⁺' with an excess of rivanol. After the impurities, including other rivanol-soluble proteins, were washed off, the thrombins were eluted with 0.15 M calcium chloride. The thrombins were recovered from all eluates by acetone precipitation.

As thrombin sources, prothrombin preparations from the plasmas of various species⁴ were activated both autocatalytically⁵ and with bioactivators prepared by special treatment of acetone powders of brain tissue from the species to be studied. Five hundred mgm of the brain powders⁶ were first incubated with 10.0 ml of serum from the same species for 30 min at 25° C. They were then washed twice with 0.15 M magnesium chloride and finally suspended in 10.0 ml of 0.15 M calcium chloride. Within 30 min one volume of the suspensions completely activated 5 vol of prothrombin solutions containing about 4,000–5,000 units/ml. After activation the thromboplastin was removed by high speed centrifugation and the proteins were precipitated with cold acetone.

The batch purification of these thrombin preparations by precipitation of impurities with rivanol was studied in various solutions. Maximum purification was obtained over a broad range of conditions. Rivanol concentrations of 0.1–1.0 per cent, ionic strengths of 0.1 to 0.5, and pH's between 7.0 and 9.5 did not affect the degree of purification. Anion type did not influence the fractionation. The only important variable was the protein concentration. Quantitative recoveries of thrombin were obtained when the protein concentrations were held in the range of 1–5 mgm/ml, whereas some losses occurred with more dilute or concentrated solutions. The results in Table 1 demonstrate changes in the specific

potassium citrate, pH 8.5, which was 0.3 per cent with respect to rivanol. After centrifugation to remove the insoluble impurities, the thrombins were precipitated by adding two volumes of cold (–10° C) acetone and the precipitates were dissolved in dilute magnesium chloride solutions. The most proteins were recovered from the dye protein precipitate by dissolving the material in 0.5 M trisodium citrate and then adsorbing the rivanol on 'XE-64-Na⁺'.

Subsequent to these preliminary batch experiments, a highly efficient and rapid fractionation technique was devised by superimposing the rivanol precipitation phenomenon on the very effective ion exchange chromatography of thrombin first accomplished by Rasmussen⁷. Up to 12 fold purifications were achieved. 'XE-64-Rivanol' was washed repeatedly with 0.1 M sodium acetate. Filter cakes or columns of the resin 5–7 cm high were prepared and the thrombin preparations were applied and washed with 0.1 M sodium acetate until the effluents were protein free. The thrombins were then eluted with 0.15 M calcium chloride, and the effluent fractions were collected with an automatic device. Only 2–3 hr were required for the entire procedure, including activation of the prothrombin, separation of the thrombin on 'XE-64-Rivanol', and, finally, precipitation of the thrombin fraction with acetone. Data indicating the degree of purification of several species of thrombin by this method appear in Table 1. Samples of the horse thrombin containing 8,200 units/mgm tyrosine, which in quantitative yield was purified to 30,800 units/mgm tyrosine on the 'XE-64-Rivanol' column, were also purified independently by the batch rivanol treatment and by ion exchange chromatography⁷. The batch technique gave an increase in specific activity to only 16,800 units/mgm tyrosine, while chromatography produced a product with only 22,500 units/mgm tyrosine. To emphasize the great efficiency of the purification method, the activated prothrombin preparations selected for this study were purposely of a very low activity compared to their theoretical maxima⁴. However, except for its rapidity, the author doubts that the 'XE-64-Rivanol' technique is superior to ion exchange chromatography in the isolation of thrombin prepared from completely activated, homogeneous prothrombin preparations⁸. Preliminary studies indicate that the horse and cow thrombins isolated using short 'XE-64-Rivanol' columns approach homogeneity. If this should be true, it is noteworthy that a twofold difference in specific activities exists between the isolated thrombins of the two species just as between the respective prothrombins⁴.

The 'XE-64-Rivanol' fractionation method is being applied to other protein mixtures, and the several factors governing the separation process are under study.

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Table 1 PURIFICATION OF THROMBINS WITH RIVANOL AND 'XE-64 RIVANOL'

| Method | Species | Type activation | Specific Activity* | |
|---------------|---------|-----------------|---------------------|--------------------|
| | | | Before purification | After purification |
| Batch Rivanol | Horse | Autocat- | 12,000 | 23,500 |
| | Horse | Bio- | 10,700 | 19,400 |
| | Cow | Autocat- | 17,700 | 28,000 |
| | Human | Bio- | 6,900 | 12,100 |
| XE-64-Rivanol | Horse | Bio- | 8,200 | 30,800 |
| | Cow | Bio- | 5,100 | 61,100 |
| | Human | Bio- | 6,900 | 42,000 |

* Iowa units/mgm. tyrosine (Folin Cloacaltea)

activities of some citrate- and bio-activated horse, cow, and human prothrombins brought about by the batch precipitation of impurities with rivanol. These fractionations were carried out at 0° C in 0.05 M

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Identification of Phenazocine, a Potent New Analgesic

THE synthesis of a new analgesic of remarkable potency, phenazocine (2-hydroxy 5,9-dimethyl 2-phenethyl 6,7-benzomorphane), has recently been announced¹. This compound of which the (-) isomer has an analgesic effect twenty times as great as that of morphine, is now undergoing clinical trials in the United States.

The absolute identification of a compound of this type is of considerable importance, as all synthetic analgesics previously described have been shown to be habit forming, and have therefore been placed under international control. Phenazocine may be identified by both colour and crystal tests². It gives a brown colour with the formaldehyde/sulphuric acid reagent (Marquis) and a bright blue turning to yellow green with the ammonium molybdate/sulphuric acid reagent. It resembles the morphine alkaloids in giving a yellow colour followed by orange with Vital's test, while with the micro-diazo test³, when coupled with diazotized *p*-nitroaniline, it gives a brown colour, turning to bluish grey as the test drop dries. These tests however do not serve to differentiate between the racemic and the optically active forms of phenazocine nor to distinguish this compound from 2-hydroxy 2,5,9-trimethyl 6,7-benzomorphane, which also has analgesic properties⁴. Nevertheless, this may readily be done by means of crystal tests. With potassium iodide solution (\pm) phenazocine gives oily rosettes, the (-) isomer an oily amorphous precipitate, and the trimethyl compound no precipitate at all. With sodium carbonate solution they give hummocks of irregular prisms, fans of oily needles, and dense rosettes of prisms respectively. The first two crystallize slowly and incompletely, while crystals of the last form in a few minutes. With picric acid (\pm) phenazocine gives an oily precipitate, (-) phenazocine shell-like rosettes, and the trimethyl compound curving blades that are highly characteristic.

Run as a paper chromatogram, using the butanol citric acid system described by Curry and Powell⁵, phenazocine has an *R_F* value of 0.80 and 2-hydroxy 2,5,9-trimethyl 6,7-benzomorphane a value of 0.45.

I am grateful to Dr N B Eddy and Dr E L May of the National Institutes of Health, Bethesda, for a gift of the above compounds.

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Corticosterone Inhibition of Pyridine Nucleotide Oxidase from Heart Sarcosomes

It has recently been found in this laboratory that corticosterone is present in higher concentrations in heart tissue than in plasma¹. Since steroid hormones are known to interfere with tissue oxidations, presumably at the level of the flavine enzymes², the relative abundance of corticosterone in heart tissue suggested a study of the effect of this steroid on heart tissue oxidations *in vitro*. Reduced diphosphopyridine nucleotide was chosen as substrate in order to get the flavine enzymes involved as directly as possible. The

enzyme preparation used in the experiments was made from isolated pig heart sarcosomes. These were ground with alumina oxide, suspended in dilute tris buffer pH 7.4 and centrifuged for 20 min at 25,000 *g*. The opalescent supernatant contained an active reduced diphosphopyridine nucleotide-oxidase³ with a specific activity of about 0.1 μ mole reduced diphosphopyridine nucleotide oxidized per min per mgm protein at 25° C.

The time course of the oxidation of reduced diphosphopyridine nucleotide is presented in Fig. 1. Addition of corticosterone to a final concentration of 10^{-4} M produces an instantaneous fall in the rate of oxidation as measured by the decrease in optical density at 340 m μ of the reaction mixture. The reaction product was diphosphopyridine nucleotide also when corticosterone was present. This could be shown by the restoration of optical density to the initial value following addition of the diphosphopyridine nucleotide-specific alcohol dehydrogenase and ethanol.

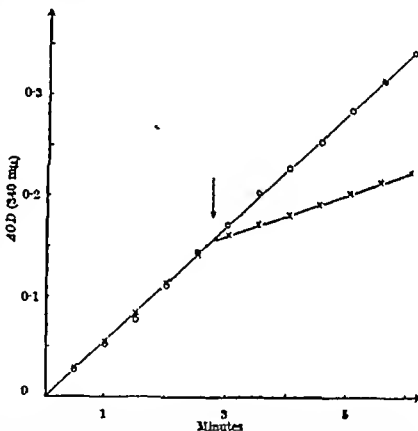


Fig. 1. Corticosterone inhibition of reduced diphosphopyridine nucleotide-oxidase. Each cuvette contained 25 μ mole trihydrochloric acid, 0.25 μ mole reduced diphosphopyridine nucleotide and enzyme in a total volume of 2.5 ml pH 7.4, 25° C. The reaction was started by addition of the enzyme. The arrow indicates addition of 0.25 μ mole corticosterone dissolved in 10 μ l. dioxane to the experimental, and of 10 μ l. dioxane to the control cuvette. Each point represents the mean of changes in optical density recorded in two separate runs. O—O control, X—X, corticosterone.

Cytochrome *c* is commonly agreed to be a component of the reduced diphosphopyridine nucleotide oxidase system⁴, linked with the dehydrogenation of reduced diphosphopyridine nucleotide by the cytochrome *c* reductase. The effect of corticosterone on the reduction of cytochrome *c* was therefore compared with the effect on the complete oxidase system. A comparison was also made with the effect of corticosterone on the diaphorase activity of the enzyme preparation. The results are given in Table 1. They show that cytochrome *c* reductase is inhibited to about the same extent as the reduced diphosphopyridine nucleotide oxidase within the range of corticosterone concentrations used. The diaphorase activity, however, is almost unimpaired by the addition of the steroid. These results thus agree with the above mentioned suggestion that the site of action of the steroid hormones in the respiratory chain lies between the flavo proteins and cytochrome *c*.

Table 1 EFFECT OF CORTICOSTEROIDS ON REDUCED DIPHOSPHOPYRIDINE NUCLEOTIDE OXIDASE, CYTOCHROME *c* REDUCTASE AND DIAPHORASE

| Corticosterone conc (M) | Activity as ΔOD per min | | |
|-------------------------|---------------------------------|---|----------------------------|
| | DPNH oxidase* (110 m μ) | Cytochrome <i>c</i> reductase† (550 m μ) | Diaphorase‡ (600 m μ) |
| 0 | 0.125 — | 0.111 — | 0.182 — |
| 5×10^{-4} | 0.103 (14) | 0.103 (7) | 0.178 (2) |
| 5×10^{-4} | 0.067 (46) | 0.057 (40) | 0.161 (10) |
| 5×10^{-4} | 0.017 (87) | 0.033 (70) | 0.163 (10) |

* Experimental conditions as stated in legend to figure except that corticosterone/dioxane was present from the start of the reaction

† Same as for reduced diphosphopyridine nucleotide-oxidase with the addition of 2 μ mole potassium cyanide and 1 mmol cytochrome *c*

‡ Same as for reduced diphosphopyridine nucleotide-oxidase with the addition of 2.5 μ mole potassium cyanide and 0.1 μ mole 2,6-dichlorophenol indophenol

Table 2 EFFECT OF CORTICOSTEROIDS ON REDUCED DIPHOSPHOPYRIDINE NUCLEOTIDE OXIDASE

| Corticosteroid added (final conc 10^{-4} M) | Activity ΔOD per min (Figures in brackets are % inhibition) |
|--|---|
| Corticosterone | 0.110 — |
| 17-hydroxy corticosterone (cortisol) | 0.045 (59) |
| 11-desoxycorticosterone | 0.070 (36) |
| 17-hydroxy, 11-desoxycorticosterone | 0.015 (87) |
| 17-hydroxy, 11-dehydrocorticosterone (cortisone) | 0.075 (32) |

Experimental conditions as stated in legends to Fig. 1 and Table 1

Table 2 lists the effect of five different corticosteroids on the oxidation of reduced diphosphopyridine nucleotide. Corticosterone and desoxycorticosterone inhibit the reaction to the same extent. The corresponding 17-hydroxy compounds are less potent inhibitors, and cortisone is the least effective. Mahler *et al.*⁵ found that a purified and soluble cytochrome *c* reductase from pig heart was inhibited to 70 per cent after 25-min preincubation with desoxycorticosterone (3×10^{-3} M) but found no effect of cortisone under the same conditions. Both steroids were ineffective in concentrations of 3×10^{-4} M. The difference between this purified preparation and the preparation used in the present experiments with respect to steroid sensitivity may be explained by the particulate nature of the latter, an explanation offered⁵ to account for the difference in sensitivity to British anti-lewisite and antimony between the purified preparation of Mahler and a particulate preparation of Slater⁴ similar to the one described here.

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Interferon produced by Cultures of Calf Kidney Cells

CERTAIN influenza A viruses multiply readily in bovine kidney cells.¹ Calf kidney cells infected with the influenza A strain WS produce virus continuously for about 2 days and then cease to do so. Few cells degenerate. After a few more days influenza virus begins to appear again (Fig. 1). Periods in which the amount of virus formed rises and falls may alternate

in this way for up to three months. Cultures, infected 6–12 days previously, which were yielding no detectable influenza virus haemagglutinins, were found to be resistant to superinfection with Sendai virus. No haemagglutinin was produced and no degeneration occurred.

The development of this state of interference was studied further. It was found that medium collected between 24 and 48 hr after infection with about 1 haemagglutinating (HA) unit of live influenza A contained a substance resembling the interferon of Isaacs and Lindenmann.² An experiment demonstrating this is shown in the first column of Table 1. Roller-tube cultures of calf kidney cells maintained in Hanks' saline were infected with approximately 2 haemagglutinating units of influenza A (1947) strain Kunz. Two days later the medium was collected and dialysed for 4 hr against 0.1 M citric acid-citrate buffer pH 2.1 and then against three changes of buffered saline.³ This treated medium did not haemagglutinate and was non-infectious. It was inoculated in volumes of 1 ml to each of a further set of calf kidney cultures. After 24 hr the medium in these was completely changed and 0.3 haemagglutinating units of Sendai virus was inoculated. The medium was titrated 3 days later and the results are given in Table 1. They show a reduction in the amount of virus produced by cells treated with the interferon preparation. The activity of interferon was not eliminated by immune serum against the virus strain used but was destroyed by boiling.

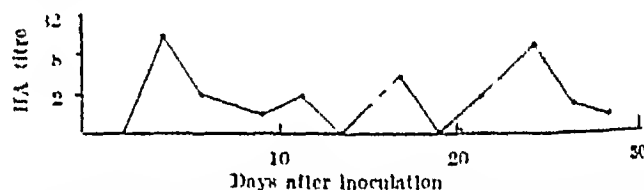


Fig. 1. Titre of haemagglutinin in a culture tube of calf kidney cells infected with 0.02 haemagglutinating unit of WS virus. The medium contained 5 per cent horse serum and 0.5 per cent lactalbumin hydrolysate and was changed and titrated on the days indicated by the points on the graph.

It was found that interferon could be demonstrated after infection of pieces of chorioallantoic membrane with living Kunz virus using the same technique as in the experiments with calf kidney (column 2 of Table 1). Isaacs and Lindenmann¹ used inactivated virus when they first demonstrated interferon but Burke and Isaacs² have since used live virus as described here. However, Table 1 shows that interferon made in cultures of chorioallantoic membrane has much less activity when assayed in calf kidney cells than when assayed in chorioallantoic membrane. Similarly, interferon made in calf kidney cells is relatively more active in homologous than in heterologous cells. It has previously been shown that interferon made with inactivated virus in chorioallantoic membrane has a little activity when assayed in monkey kidney cell cultures.

In view of these results any theory of the nature of interferon should now include an explanation of why it carries some of the specificity of the cell type from

Table 1 INTERFERON ASSAYS ON FLUIDS FROM CULTURES INFECTED WITH INFLUENZA A VIRUS

| Culture used as source of Interferon | Log ₂ mean haemagglutinin titre in assays using culture of Calf kidney cells | Chorioallantoic membrane |
|--------------------------------------|---|--------------------------|
| Calf kidney cells | 0.3 | 4.7 |
| Chorioallantoic membrane | 5.0 | —1 |
| Saline control | 4.0 | 5.0 |

which it was formed although it is produced as a response to virus infection. Also, interferon production should be considered a possible mechanism by which active virus and cell populations may coexist over long periods of time.

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PHYSIOLOGY

Resistance to Flow in Vascular Beds

CARILLI'S attempt¹ to dispel confusion in the use of the Ohm's law analogy in blood circulation theory requires further clarification since it is only the incorrect application of this analogy that needs to be abandoned not the analogy itself but it raises an important point. This is confirmed by Burton² when he insists that for vascular circuits

Resistance to flow (R) =

Pressure drop across the bed (P)

Flow (F)

For a definition consistent with the electrical analogy we must have $R = (P-p)/F$ where p is the critical closing pressure as referred to by Carillil. This gives $F = P/R - p/R$ which is of the form $y = mx - c$ since p/R is constant for any angle one of the lines in Carillil's Fig. 1 and gives the same result for dF/dP as in Burton's equation (4) derived from his incomplete expression of form $y = mx$.

The usage of the term 'dynamic resistance' is well defined in electrical fields, as is the term 'ohmic resistance' and it is desirable that analogous applications of such terms in physiological fields should be equivalent to the electrical ones. If conventional practice in electrical analysis (that is analytical symbols represent pure properties, for example, of voltage resistance, rectification as distinct from practical components which usually combine several properties) be used to interpret Carillil's Fig. 1, it can be seen that the lines showing pressure intercepts have characteristics given, in electrical analogy, by a direct current source or battery, in series with a resistance obeying Ohm's law and a rectifier. This equivalent circuit is shown in Fig. 1 between points A and D.

For current flow to occur (in fashion comparable with the vascular case) an electrical (hydraulic) energy source (of magnitude P), as shown between X and Y, must be acting across AD (or the vascular bed). The voltage between A and B (equivalent to the critical closing pressure p of the vascular bed,

and of magnitude specified by Carillil's pressure intercept) opposes the flow of electricity (or of blood or perfusion fluid). The term 'dynamic resistance' then refers to measurements made across AC or AD using a number of applied voltages (or pressures), which could involve alternating current (pulsating flow) and is obtained as a single value, the reciprocal slope of a straight line so long as resistance BC is ohmic. If resistance BC is non-ohmic, say having a partly curved characteristic as instanced by Burton, then a number of values of dynamic resistance must be chosen for parts of the curve each of which is regarded as approximating to a straight line. Carillil only considers the case where resistance BC does follow Ohm's law. Clearly the Ohm's law analogy is applicable to specify the resistance component of the vascular beds considered by him and is very helpful, if not essential in explaining and defining the term 'dynamic resistance'. A more extensive discussion of this type of electrical analysis and of the term 'dynamic resistance' is given by Richter³. It shows how the confusion in physiological theory, to which Carillil draws attention can arise in electrical theory in precisely analogous fashion.

Carillil proposes only the use of pressure and resistance components as represented between A and C. However connecting A to C would give a current flow. Also a reduction of pressure to negative values that is application of a suction, cannot produce a reversal of flow in the vascular bed. This 'valve' effect in a vascular bed must be represented electrically as the rectifier shown between C and D. The analogy with the effect of a single rectifier is virtually complete for vascular beds containing veins with competent valves, which permit blood flow in only one direction under positive pressures in addition to the valve effect of the closed vessels under negative pressures or small positive ones.

For vascular beds without vein valves, or with incompetent ones, an analogous electrical circuit may be obtained by adding in parallel with the circuit between A and D in Fig. 1, its own mirror image making contact D with A and A' with D or by drawing a full wave rectifier bridge with a battery and resistance in series across its output.

In the above equivalent circuits an ohmic resistance component can be said to be involved although the characteristic of the complete circuit over the range giving analogy with vascular phenomena, as far as it goes, departs from Ohm's law.

In practice the circuit between A and D in Fig. 1 can be replaced by an appropriately designed triode valve having mutual characteristics corresponding with the pressure flow lines of Carillil's Fig. 1. The magnitude of the pressure intercept for any of the pressure-flow lines is then determined in the triode analogy by the grid bias voltage. Other practical analogues can also be found.

The above analysis does not cover all details of the non-ohmic properties found in vascular circuits, some of which were dealt with by Burton, but is confined to those arising from the phenomena which Carillil is concerned to analyse. It has been necessary to assume simplified vascular circuits corresponding with the electrical circuits mentioned, in order to achieve the necessary link with his treatment. A comprehensive treatment could usefully lead to the design of practical analogue circuits giving models of the circulation or of parts of it, impossible to achieve by mechanical means.

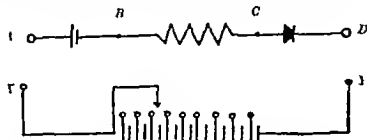


Fig. 1. This shows between A and C a voltage and resistance as electrical analogues of the two components proposed by Carillil to specify resistance to flow in the vascular beds related to his Fig. 1 namely pressure intercept and dynamic resistance. The rectifier between C and D is necessary to complete the analysis of Carillil's lines showing pressure intercepts. Between X and Y is a variable voltage source, the electrical analogue of the hydraulic energy source which must be applied across a vascular bed to determine its critical closing pressure and dynamic resistance.

The crux of this problem seems to lie in the different levels of advancement of analytical theory in the fields of electronics and physiology of the circulation. The development of physiological concepts now taking place should follow analogous practice in electrical or other fields where prior development has occurred, if circulatory physiology is to benefit from the possible uses of electrical analogues.

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Interrelations between the Blood Coagulating System and the Physiological Anticoagulating System

PREVIOUS publications^{1,2} attest to the existence of a physiological anticoagulating system in some animals. Moreover, a surmise was made concerning the presence in blood vessels of chemoreceptors reacting to the appearance of thrombin in the blood, and through the reflex are calling into play a neuro-humoral mechanism which prevents the coagulation of the circulating blood.

In subsequent experiments carried out by Kalshovsky and me, the physiological anticoagulating system was found to exist not only in the organism of mammals, but also in that of amphibians.

After injecting into the ventricular cavity of the frog's heart a moderate dose of thrombin (0.35–0.40 ml clotting an equal volume of the frog's blood at 37° in 7–9 sec), the circulation of blood was maintained and no clots were formed. Blood taken from the hearts of such animals completely lost its coagulating capacity *in vitro* in the presence of thromboplastin obtained from the tissue of the frog's lungs. At the same time, in frogs with a preliminarily destroyed spinal cord the injection of the same dose of thrombin in all cases resulted in an immediate total coagulation of blood in the vascular system. The destruction or extirpation of the brain as distinct from destruction of the spinal cord did not have the same effect; the anticoagulating system of such animals remaining in its functional condition. This suggests that the centre of the frog's reflex are receiving the signal of the appearance of thrombin in the circulating blood is connected with the spinal cord.

In previous communications^{1,2} it was shown that in response to a signal of thrombin formation in the circulating blood transmitted by chemoreceptors present in the vascular system, certain agents are immediately given off into the blood to prevent its coagulation, namely, fibrinolytic and heparin-like substances.

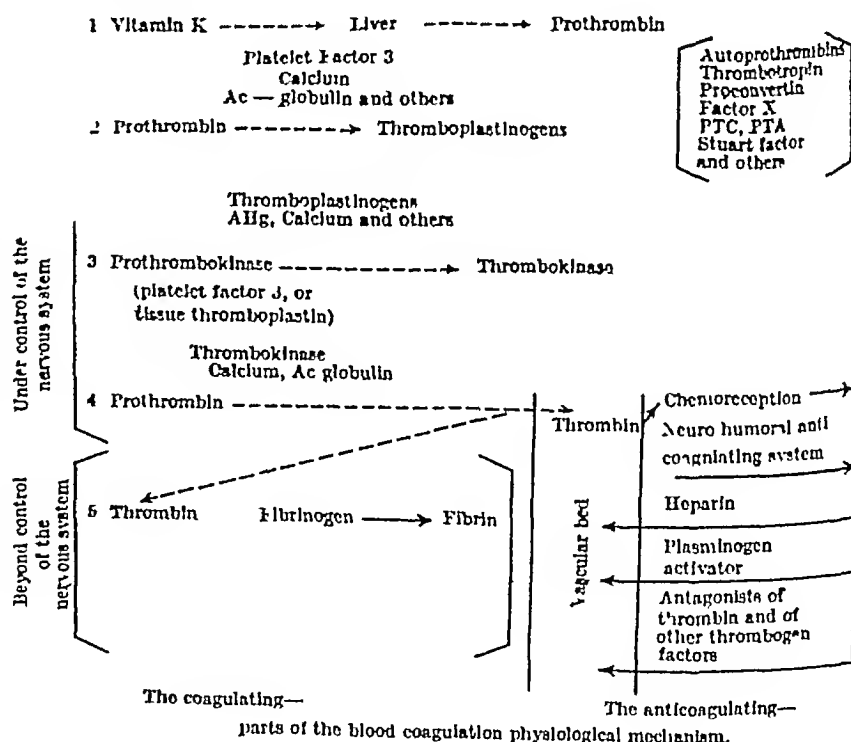
In experiments carried out on frogs, it was established that a preliminary injection of heparin (0.1 ml in concentration of 1/100,000) into the blood of frogs with destroyed spinal cords fully protected these animals against an intravascular blood clotting after a subsequent injection of thrombin solution into their heart cavities.

Under the same conditions the blood of normal frogs was found to possess the same protective property after thrombin injection into it. Thus, 0.9 ml of such a blood saved a frog the spinal cord of which had been destroyed from thrombin formation, when followed by an injection into its heart of 0.35 ml of thrombin solution clotting *in vitro* the normal frog's blood in 9 sec at 37°.

Experiments made in collaboration with Pastorova have shown the blood of rats to become greatly enriched with active plasmin after an intravenous infusion of tissue thromboplastin or thrombin, due to which a sharply accelerated fibrinolysis is seen to occur in distinction from the normal control animal blood. These results serve to prove that in a reflex act induced by the appearance of thrombin in the circulating blood, an activator of plasminogen together with other substances, is produced in the blood. This fact causes the formation of an excess of plasmin which removes fibrinogen.

The various schemes already put forward with the aim of interpreting the biochemical mechanism of blood coagulation without taking into account the existing neuro-humoral regulation, are, to a greater or lesser degree, correct for the process occurring *in vitro* or outside a normal vascular bed. The foregoing results show that the appearance of thrombin in the blood may lead to diametrically opposite reactions depending upon the presence or absence of the nervous system control. If thrombin appears in the circulating blood under physiological neuro-humoral control, it does not produce coagulation, but on the contrary

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its presence results in 'switching off' the clotting mechanism. When thrombin is formed in the blood which is beyond the control of the mechanism indicated, a conversion of fibrinogen to fibrin is seen to occur. That process may occur on the surface of the wound or in a test-tube as well as in the vascular system in pathological cases inducing a dysfunction of the physiological anticoagulating system.

The conglutination and the anticoagulating physiological mechanisms should be considered as two opposite but inseparably connected parts of a single clotting system of blood. This may be illustrated by the accompanying scheme.

The scheme indicates only some essential steps in the clotting process and of its regulation. To avoid unnecessary complication the actually existing two-stage slow and rapid form of thrombin production³ is omitted. At the appearance of thrombin the regulatory mechanism of the neurohumoral anticoagulating system already seems to act during the former slow stage, thus preventing an excessive thrombin content being present in the circulating blood. The scheme is based partly on Seegers results^{4,5} on transformation of prothrombin into autoprothrombins that is into agents stimulating the conversion of prothrombin to thrombin. The scheme indicates natural coagulants stabilizing the liquid condition of the circulating blood as a dynamic system in contradistinction to suggestions that there is a static balance between coagulating and anti-coagulating components.

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Response of a Single Retinula Cell to Polarized Light

It appears to be a well established fact that some arthropods use polarized light as a kind of light compass. von Frisch¹ has shown clearly that honey bee workers utilize polarized light from the blue sky to identify the direction of a food source. Wollington² reported that adult flies can also exhibit orientation relative to the direction of vibration of polarized light. These reports suggest that the arthropod photoreceptor, both the compound eye and the ocelli, has a kind of polarizer in the visual organ. Wulff³ has reviewed the many attempts that have been made to localize the possible polarizer in the compound eye and to find the physiological mechanism involved in the reception of polarized light in the compound eye, but no conclusion on this problem seems to have been reached.

Kuwabara and Naka⁴ have recorded an intracellular action potential from the compound eye of the fly and conclude that the response was obtained from a retinula cell. In our experiments the effects of stimulation by polarized light on the intracellularly recorded action potential were observed.

The fly *Lucilia caesar* reared in this laboratory was used. As shown in Fig. 1 the stimulating apparatus consisted of a 260 watt projector lamp a

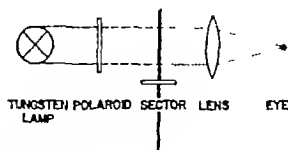


Fig. 1. Schematic representation of the optical apparatus to give intermittent polarized light. The polaroid was rotated at 15 r.p.m. while the sector interrupted the polarized light to give intermittent stimulation at 3 cycles per second.

Mitsubishi 'Diachrom' polaroid, and a turning sector to give an intermittent stimulation of about 3 cycles per second. In the experiment the polaroid was continuously rotated at about 15 r.p.m. while the turning sector interrupted the polarized light to take a continuous recording of responses. Other experimental procedures were the same as described elsewhere.⁵

In Fig. 2 intra- and extra cellular responses to the stimulation of 3 cycles per second are shown. The former were monophasic waves with an amplitude of more than 40 mV while the latter were biphasic with amplitude of about 5 mV. This figure also shows that the intracellularly recorded response completely followed stimulation of 3 cycles per second. The response to polarized light is shown in Fig. 3A and the record in Fig. 3B is a control taken without the polaroid. From these records it is clear that the amplitudes of the action potentials varied synchronously with rotation of the polaroid whereas in the control these amplitudes remained the same throughout the stimulation. The amplitude of the action potential decreased about 20 per cent when the plane of polarized light was rotated through 90°.

As these records were obtained intracellularly from the receptor layer the response to polarized light in Fig. 3 appears to represent the response of a single receptor cell that is the retinula cell.

The recent electron microscopic studies on the microstructure of the insect compound eye have revealed that the rhabdomere is composed of many regularly arranged honeycomb like microvilli and that the direction of the arrangement of the honeycomb like structure is different in each rhabdomere.⁶ In an ommatidium of the fly there are seven retinula cells.

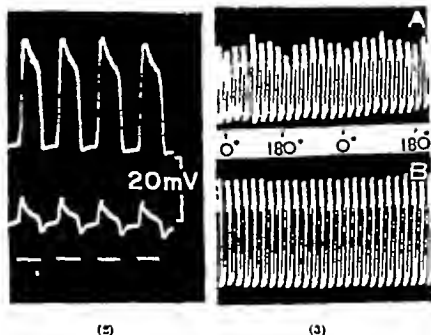


Fig. 2. Intracellular (upper record) and extracellular (lower record) responses to intermittent stimulation at 3 cycles per second.
Fig. 3. A. Intracellularly recorded responses to the stimulation by polarized light. B. control recorded without polaroid. Amplification is the same as in Fig. 2.

and each retinula cell has a rhabdomere, indicating that any stimulation of a retinula cell is mediated by the rhabdomere attached to the cell. Thus the electron-microscopic studies and the results of the present experiment favour the view that the rhabdomere acts as a polarizer in the compound eye.

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A Low Concentration of Certain Blood Constituents observed in Offspring of Alloxan-Diabetic Rabbits

THE purpose of this communication is to report our observation of low levels of plasma cholesterol, albumin and protein-bound hexose in offspring of alloxan-diabetic rabbits on the first day of life.

Four female rabbits of no particular strain weighing approximately 3,500 gm were rendered diabetic by injecting alloxan monohydrate intravenously in an amount of 200 mgm/kgm body-weight. The animals were given protamine zinc insulin and, when the metabolic condition was stabilized and no signs of albuminuria were present, they were mated with normal males. The rabbits were fed commercial chow *ad libitum* and supplements of carrots and lettuce were provided. Once a month a multiple vitamin preparation was administered intramuscularly. On this regimen the blood sugar levels fluctuated about the 250 mgm per cent level and the glycosuria seldom exceeded 10 gm a day. This was the best control which we were able to achieve without encountering the danger of hypoglycaemic attacks. Under these conditions demands for exogenous insulin fluctuated widely in pregnant as well as non-pregnant animals. Four normal rabbits were bred and maintained under the same experimental conditions.

The length of pregnancy and the weights of new-borns are recorded in Table 1. Two or more animals from each litter were killed within the first 18 hr of life by severing the carotid arteries, and blood was collected using heparin. Results of chemical analyses are presented in Table 2. The remaining animals of each litter were killed in the same fashion on the second and third day of life, but results of chemical analyses are not presented. Offspring of diabetic as well as of normal females appeared equally lively and well developed on the first day of life, and the stomachs of all autopsied new-borns were filled with milk. It is therefore unlikely that the differences observed between new-borns of diabetic and normal mothers would be the result of inadequate dietary intake in the postnatal period. On the second and third day of life, many new-borns of the diabetic animals deteriorated rapidly. Their stomachs were found empty, and lack of maternal care was evident in many other ways. This invalidated further comparisons between offspring of normal and diabetic mothers after the first day of life.

Blood sugar was determined on whole blood by King's

method¹. Plasma cholesterol was estimated by the Bloor, Pelkan and Allen procedure² and protein bound hexose by Lustig and Langer's method³ with minor modifications. Total plasma protein was determined with the biuret reagent by Weichselbaum's method⁴. Fractionation of plasma proteins was carried out by paper electrophoresis by Kunkel's method⁵. Paper strips were stained with bromophenol blue and cut into appropriate segments. The dye was eluted and the intensity measured in a photoelectric colorimeter. The carbohydrate components were visualized by staining paper strips with a modified periodic acid Schiff reagent, following Kôw and Grönwall⁶.

It is noteworthy that a high incidence of still birth and intra uterine death observed by Miller⁷ has not been encountered under our controlled experimental conditions. The length of pregnancy in our diabetic animals was not different from that observed in the normals, but the offspring of the former weighed less. At the same time there was statistically a highly significant difference between corresponding levels of total cholesterol, protein bound hexose and albumin in the two groups of new-borns. The lowering of the total levels of plasma protein was probably a reflexion of low albumin levels in offspring of diabetic rabbits because no appreciable differences were found in the three globulin fractions. Similarly no appreciable differences were found in blood sugar levels between the two groups of new-borns. No corrections were made on the basis of haematocrit readings, but it was obvious that the pronounced tendency toward haemoconcentration in the offspring of diabetic females made the observed differences even more significant.

Table 1 RESULTS OF PREGNANCIES IN NORMAL AND DIABETIC RABBITS

| Observation | Normal | Diabetic | P value | Significance |
|---|-----------------|----------------|---------|--------------|
| No. of animals | 4 | 4 | — | — |
| No. of pregnancies | 4 | 4 | — | — |
| Length of pregnancy (mean \pm S.D.) | 32.0 \pm 0.9 | 31.8 \pm 1.0 | > 0.5 | No |
| Total No. of live new-borns | 35 | 31 | — | — |
| Dead | 2 | 1 | — | — |
| Weights of live new-borns (mean \pm S.D.) | 53.8 \pm 13.0 | 43.6 \pm 6.1 | < 0.01 | Yes |

Table 2 OFFSPRING OF NORMAL AND DIABETIC RABBITS BLOOD CHEMISTRY ON FIRST DAY OF LIFE

| Constituent | Mean \pm S.D. (No. of observations) | | P value | Significance |
|--|--|-------------------------|---------|--------------|
| | Normal | Diabetic | | |
| Blood sugar (mgm/100 ml) | 54.4 \pm 35.1 (9) | 61.3 \pm 37.5 (11) | > 0.5 | No |
| Total protein (gm/100 ml) | 3.99 \pm 0.27 (9) | 3.44 \pm 0.23 (11) | < 0.01 | Yes |
| Albumin (gm/100 ml) | 2.32 \pm 0.28 (9) | 1.94 \pm 0.28 (8) | < 0.01 | Yes |
| Cholesterol (mgm/100 ml) | 134 \pm 31 (8) | 101 \pm 20 (10) | < 0.02 | Yes |
| Protein bound hexose (mgm/100 ml) | 53.5 \pm 5.0 (8) | 43.4 \pm 4.4 (6) | < 0.01 | Yes |
| Haematocrit, (per cent formed element) | 46.4 \pm 5.8 (13) | 51.0 \pm 6.7 (23) | < 0.05 | Yes* |

* Significant at a 5 per cent level only after enlarging the series of animals tested.

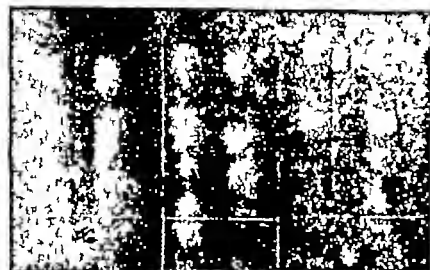


Fig. 1. Electrophoretic patterns of plasma proteins stained for carbohydrate. *Re*, Offspring of a normal rabbit; *DR*, offspring of a diabetic rabbit.

Fig. 1 is a photograph of a few representative plasma protein patterns stained for carbohydrate. It can be seen that the amounts of stainable material were diminished in all fractions from new-borns of diabetic females.

The low concentration of certain blood constituents and the low body weights are presumably reflexions of the pathological maternal environment to which these animals were exposed during the foetal life. Further work is in progress.

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Saliva-Serum Ratios of Deuterium Oxide after Administration of Heavy Water

TOTAL body water may be estimated by admixing a known weight of deuterium oxide and, after equilibration has occurred, determining its concentration in water obtained from some body fluid. Faller *et al.* have shown that within the limits of experimental error the same values are obtained for total body water whether the deuterium oxide is administered orally or intravenously. Serum is the usual source of body water containing the equilibrium concentration of deuterium oxide. If however urine or saliva could be used, the whole procedure could be carried out without venipuncture, this would be an advantage when serial estimations are to be made or when other investigations involving venipuncture are undertaken in the same subject.

Urine formed during the period 3-6 hr after administration of deuterium oxide yields water with a deuterium oxide concentration equal to that of a serum sample obtained during the same period. Unfortunately the method of Schloerb *et al.* for estimation of deuterium oxide cannot be applied directly to urine, which contains 'oxidisable impurities' that are not removed by simple vacuum distillation. The modified distillation procedure of Faller *et al.* enables samples of urine instead of serum to be used, but is longer and more laborious.

Within about 2 hr after administration, deuterium

| Subject | Weeks of gestation | Time interval (hr.) between D ₂ O administration and removal of samples | Serum conc., gm D ₂ O/100 ml Serum conc. | Saliva conc. |
|---------|---------------------|--|---|--------------|
| A | 8 | 3 | 0.154 | 1.05 |
| | 24 | 3 | 0.218 | 1.05 |
| | 30 | 3 | 0.211 | 1.22 |
| B | 12 | 3 | 0.136 | 1.14 |
| | 36 | 6 | 0.140 | 1.23 |
| | 36 | 24 | 0.136 | 1.39 |
| C | 11 | 3 | 0.144 | 1.20 |
| D | 12 | 3 | 0.124 | 1.17 |
| IL | 14 | 3 | 0.157 | 1.12 |
| K | 22 | 3 | 0.175 | 1.00 |
| | 31 | 3 | 0.226 | 1.00 |
| VL | 11 | 3 | 0.161 | 1.34 |
| P | 31 | 3 | 0.162 | 1.26 |
| | 10 days post partum | 3 | 0.230 | 1.37 |
| | 2 weeks post partum | 3 | 0.240 | 1.20 |
| K | 21 | 3 | 0.140 | 1.12 |
| Sp | 15 | 3 | 0.150 | 1.20 |
| | | | | Mean 1.19 |

oxide is distributed uniformly throughout many body fluids, including arterial and venous blood, urine, liver water, gastric juice and intestinal fluid. No report comparing salivary concentrations of deuterium oxide with those in blood has been found. Tritium apparently equilibrates in body water so that its concentration is similar in serum, urine, saliva, sweat, faeces and insensible perspiration within the limits of sensitivity of the method used, the concentrations of tritium involved are extremely low.

The subjects were normal pregnant women. Sufficient deuterium oxide was given orally, to bring the equilibrium serum concentration within the range 0.100 to 0.250 gm deuterium oxide per 100 ml of serum water. Immediately afterwards patients had breakfast. Three hours after administration of deuterium oxide, and approximately 24 hr after breakfast, samples of venous blood and of saliva were taken. For the saliva sample, the women were encouraged to salivate and swallow the saliva for a few minutes before providing the sample thus ensuring that it was recent secretion. Water was obtained from the serum and saliva by double vacuum distillation and the deuterium oxide concentration in the water was estimated by a modification of the falling-drop method described by Schloerb *et al.*

In one subject samples of blood and of saliva were taken 6 hr and 24 hr after administration of deuterium oxide. In all, 17 pairs of estimations were made.

Table 1 shows the ratios of saliva concentration to serum concentration of deuterium oxide together with the corresponding serum concentrations. The ratios are all greater than unity the mean being 1.19 and the range 1.05-1.39. Absolute serum concentration of deuterium oxide has no effect on the ratio but two women A and K tend to have ratios only slightly above unity.

Although the possibility exists that some substance in saliva distils across with the water and

affects the density of the drops, there is no reason to suspect this, and the results indicate that the salivary glands concentrate deuterium oxide above the level in serum, at least at the low levels of concentration in these experiments. Salivary gland appears to be unique among human tissues so far investigated in this ability.

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Effect of Cell-Free Extracts from *Mycobacterium tuberculosis* $H_{37}Rv$ on Lung Succinoxidase

SEGAL AND BLOCH showed that non-proliferating suspensions of human tubercle bacilli grown *in vivo* (LRv) exhibited different biochemical properties as compared with the same strain of tubercle bacilli grown *in vitro* (a) they had a lower hydrogen transfer capacity, (b) glucose and its intermediates failed to cause an increase over their endogenous respiration¹.

The experiments reported here were concerned with the electron transfer capacity of cell-free extracts from tubercle bacilli grown *in vivo* and *in vitro* and with the effect of these extracts on the respiration of lung homogenates.

The bacilli grown *in vivo* were obtained from the lungs of moribund or dead mice infected intravenously with the human strain of *M. tuberculosis* $H_{37}Rv$. To obtain a good yield each mouse was given intramuscular injections of 1.2 mgm cortisone acetate every second day starting from the fourteenth day after infection. The bacilli were isolated from the lungs by the method employed by Segal and Bloch¹. The *in vitro* grown tubercle bacilli strains $H_{37}Rv$ and BCG were obtained from 10–20 days cultures on 'Tween' albumin medium. The cells were separated from the culture media by centrifugation and washed twice in 0.1 M phosphate buffer pH 7.1. Cell-free extracts were obtained by disrupting of the cells in a 9 KC Raytheon sonic oscillator for 30 min and the debris removed by centrifugation at 9,000 r.p.m. for 10 min at 5° C.

The hydrogen transfer capacity of the extracts was examined by the reduction of triphenyltetrazolium chloride in the presence of different substrates. The cell-free extracts of BCG and $H_{37}Rv$ reduce tetrazolium in the presence of lactate, malate and succinate whereas the cell free extracts of $H_{37}Rv$ grown *in vivo* (LRv) did not show any activity in this respect. Since it was difficult to believe that LRv extracts would be entirely devoid of hydrogen transfer capacity, the assumption was tested that their inactivity was due to the presence of an inhibitor. LRv extracts were incubated with active BCG preparations in the presence of lactate. As seen from the experiment summarized in Table 1, this assumption proved to be correct. The cell-free extracts from LRv inhibited the lactic dehydrogenase of BCG extracts from 50 up to 100 per cent.

Table 1 INHIBITION OF LACTIC DEHYDROGENASE OF BCG CELL-FREE EXTRACTS BY CELL-FREE EXTRACTS OF LRv

| | O.D. of formazan formed in the presence of lactate by the extracts from | | | Inhibition (per cent) |
|-------|---|-------|-------------|-----------------------|
| | LRv | BCG | $BCG + LRv$ | |
| Exp 1 | 0.00 | 2.44 | 1.22 | 50 |
| Exp 2 | 0.00 | 3.20 | 0.00 | 100 |
| Exp 3 | 0.00 | 2.20 | 0.21 | 89 |

System: Cell free extracts (equivalent to 6.5 mgm protein) 0.5 ml in 0.1 M phosphate buffer pH 7.1, lactate, 0.3 M, 0.3 ml, 1 per cent solution of triphenyltetrazolium chloride 0.2 ml. Time of incubation 1 hr. Temperature, 37° C. The formazan was extracted with *iso*-butanol and read at 495 mμ in a Coleman Jr. spectrophotometer.

This result prompted us to test the action of LRv extracts on normal lung tissue homogenates. For this purpose lungs of normal mice were homogenized in 0.25 M sucrose and their oxygen uptake was measured by the conventional Warburg method in the presence of the extracts. Table 2 shows that the extracts of

Table 2 EFFECT OF MYCOBACTERIAL EXTRACTS ON SUCCINOXIDASE OF NORMAL MICE LUNG HOMOGENATES

| Source of enzyme | μl oxygen per hour* | | | |
|------------------------------|---------------------|-------|-------|--------------------------------------|
| | Exp 1 | Exp 2 | Exp 3 | Exp 4 |
| Lung homogenate | 27.2 | 50.4 | 33.0 | 36.1 |
| $BCG +$ lung homogenate | 27.2 | 53.2 | 33.0 | not examined not examined 20.0 |
| $H_{37}Rv +$ lung homogenate | 27.3 | 43.2 | 34.3 | |
| $LRv +$ lung homogenate | 15.2 | 31.1 | 15.5 | |

The Warburg vessel contained 1.0 per cent suspension of lung homogenate in 0.25 M sucrose, 0.4 ml where present bacterial extracts, 0.5 ml, 0.3 M succinate, 0.3 ml tipped from side arm after 15 min equilibration, phosphate buffer 0.1 M, 0.5 ml (pH 7.1), 15 per cent solution of potassium hydroxide, 0.2 ml in centre well. The final volume 2.2 ml. Temperature 37° C.

* The values are corrected for oxygen uptake of bacterial extracts.

LRv inhibited the succinoxidase of lung tissue from 31.1 up to 53 per cent. The extracts of $H_{37}Rv$ and BCG were without any effect except for one experiment in which $H_{37}Rv$ extract inhibited the oxidation of succinate by 14 per cent.

A detailed report will be given later.

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Seasonal Changes in the Oestrous Response by the Ovariectomized Ewe to Progesterone and Oestrogen

ROBINSON *et al.*¹ have presented results of the quantitative requirements of progesterone and oestrogen for oestrous behaviour in the spayed Merino cross-bred ewe. These results were derived mainly from experiments conducted over short periods (2–3 months) and within the normal oestrous season of that ewe. We have noted² that the oestrous response of the spayed Romney ewe following progesterone oestrogen treatment during November and December (months within the anoestrous season) was less than during the oestrous season. This difference could have resulted from the vasectomized rams exhibiting reduced libido during the summer and so failing to mark all ewes in oestrous³. However, our observations suggest that rams in this district will detect ewes in oestrous as we have seen following treatment of ewes

with progesterone and pregnant mares' serum during the anoestrous season. Also, ewes have been marked at this time following administration of greater quantities of oestrogen, than previously*. Therefore we have investigated further the response to progesterone and oestrogen in the spayed ewe.

Trials were conducted with spayed Romney ewes during January 1957–May 1959. The 12 spayed ewes previously mentioned* were used during January–July 1967. For the remaining trials these ewes and an additional 8 spayed animals of similar age and breeding were treated. In each trial three groups of ewes were injected for three consecutive days with progesterone (10 mgm/day) followed 40 hr later by oestradiol benzoate. The groups of ewes in a trial received either 10, 20 or 40 μ gm or 20, 40 or 80 μ gm oestradiol benzoate. The trials were conducted at 14-day intervals, but after each three consecutive trials a 3–6 week control period was allowed to elapse before further hormone treatment. The animals were run as one flock with one or two vasectomized rams and observations were made for mating marks. Mucus from the cervix was also collected on the three days following treatment with oestradiol benzoate and examined for crystallization patterns*. As well, random collections were made during the control periods and on some days of progesterone treatment.

Oestrus did not occur after an injection with 10 μ gm oestradiol benzoate. The oestrous response following injection with the higher quantities of oestrogen is given in Fig. 1. We noted previously* that similar progesterone treatment and 40 μ gm oestradiol benzoate resulted in one ewe of twelve treated being marked by the ram during November–December 1956. We have again found this to be the case during the two following anoestrous seasons. However during the oestrous season this same treatment has caused a greater oestrous response. A similar seasonal relationship appears to exist after treatment with 80 μ gm oestradiol benzoate.

Crystallization patterns in cervical mucus were found in practically all ewes treated. Even after the lowest levels of oestrogen (that is 10 and 20 μ gm oestradiol benzoate) the response of cervical mucus has been similar throughout the experiment. In contrast cervical mucus collected and examined during the control periods has shown in most cases little or no characteristic crystallization patterns. Thus although in some of the target organs associated with oestrous behaviour the sensitivity to progesterone and oestrogen may be reduced during anoestrus, the response of cervical mucus appears unaffected by seasonal changes.

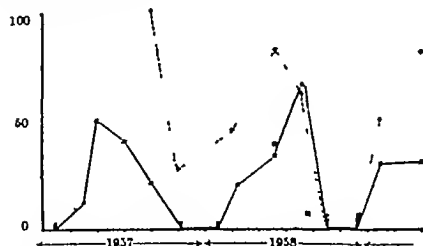


Fig. 1 Oestrous response in ovariectomized ewes following progesterone-oestrogen treatment.

Each point represents the percentage of ewes in oestrus for a series of three trials and plotted at the mean date for each series. Values obtained during December 1958 represent one trial only.
+ 60 μ gm, x—x 40 μ gm, □ 20 μ gm, ova.

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Uraemia and Its Treatment by Arginase Inhibitor

UREMIA is retention of urea in the body, and is due to renal insufficiency. It has been proved beyond doubt that the kidney is the only organ through which urea can be eliminated from the body*. Therefore renal insufficiency of an organic or a functional type will reverse the clearance of urea from the body with consequent retention. The methods involving intratinal and peritoneal dialysis, artificial kidney, and possibilities of a successful kidney homotransplant for the treatment of uraemia are mainly based on the principle of eliminating urea from the body. The problem becomes very much simplified if technique can be evolved checking the synthesis of urea which obviously could cause least damage to the patient.

In order to explore this possibility, experiments were performed involving the application of L-lysine monohydrochloride the most powerful arginase inhibitor on dogs in an artificially created state of athenic uraemia. It may be noted that arginase activity is essential in the synthesis of urea according to the classical work of Krebs*. The results so far noted are so consistently encouraging that an immediate announcement has been thought desirable in the interests of the medical practitioner in general and urologists in particular.

In spite of the fact that a number of arginase inhibitors* 4 such as quinones, buffers, different amino acids and some protein denaturants are known, L-lysine monohydrochloride was chosen in order to eliminate the different factors exerting harmful influence on the patients.

Control dogs (average weight of 10 kgm) were induced to a state of athenic uraemia by bilateral nephrectomy under a general anaesthetic. The level of blood urea (N) was recorded before and every 24 hr after the operation. The urea (N) percentage was found to increase at an average rate of 15–16 mgm every 24 hr. The animals died 80–84 hr after operation at urea (N) level of 67–70 mgm due to uraemia. During the period following operation the animals were kept on a protein free diet and received 50 gm. of glucose in 25 per cent solution intravenously daily in order to meet the basic calorie requirements and prevention of endogenous protein breakdown.

In another set of animals operations were performed. In this set, however, a dose of 1 gm. of L-lysine monohydrochloride in 10 per cent solution was injected intravenously daily after the operation. It was noted that the urea (N) percentage in the blood was found to increase only at the rate of 3–4 mgm. every 24 hr. In strong contrast to the control where it was 15–16 mgm during the same period. The animals survived for 274–278 hr after the operation at a urea (N) level of 68–70 mgm per cent at the time

of death, whereas in no case in the control preparations the animals survived more than 84 hr

In order to find out whether the survival period can be prolonged with an increased dose of L-lysine monohydrochloride in another set of experiments 1.5 gm of L-lysine monohydrochloride in 10 per cent solution was injected intravenously daily. The result was found to be similar to the previous one. This indicates that activity-level of L-lysine monohydrochloride in inhibiting synthesis of urea reaches its optimum with a dose of only 1 gm per every 24 hr.

It is worth pointing out that in normal animals, where bilateral nephrectomy was not performed, injections of L-lysine monohydrochloride no doubt caused a fall in the urea-level of the blood, but in all cases at least a level of 18 mgm per cent of urea (N) was maintained in the blood indicating thereby that a minimum level of urea in the blood is always kept by normal animals, if necessary through extra-hepatic urea formation⁵. The latter process can also explain the steady and slight rise in urea level in bilaterally nephrectomized animals treated with L-lysine monohydrochloride.

It is obvious that if urea synthesis can be minimized in a state of asthenic uræmia, the results of treatment with L-lysine monohydrochloride are expected to be very satisfactory when the kidneys are functioning at least partially.

I acknowledge with thanks the help received from the authorities of the Bengal Veterinary College, Calcutta and specially Prof P. C. Sen Gupta for allowing me to work in their laboratory. I am also grateful to Emsons Pharmaceuticals Ltd for the supply of L-lysine monohydrochloride.

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Enhanced Synaptic Function due to Excess Use

THE aim of the present investigation has been to give, in cats, excess use to the synapses of some monosynaptic pathways through the spinal cord, keeping other monosynaptic pathways as controls. In an initial aseptic operation the nerves to some muscles of a synergic extensor group in one hind limb have been severed and capped to prevent regeneration. Since the remaining muscles of such a synergic group have to substitute for the whole group in supporting the weight of the animal, it can be expected that there will be an excess of stress on them, consequently there will be an increased discharge from their stretch receptors along the group Ia afferent fibres, so giving an increased activation of the excitatory synapses on their motoneurons.

The nerves to the medial gastrocnemius, plantaris, tibialis posterior and flexor hallucis longus were severed and capped, leaving intact only the nerves to the lateral gastrocnemius, and flexor digitorum longus from the two groups of synergic extensor muscles. A dummy operation identical in all respects except for cutting and capping the nerves was performed on the other leg. The reflex pathways used as controls were from the biceps semitendinosus nerve and the deep peroneal nerve in both hind-limbs. They are particu-

larly suitable for controls because they give large monosynaptic reflexes, and, since they subserve flexor muscles, they should be little affected by the extensor asymmetry induced in the hind-limbs by the operation.

After recovery for a few days the animals were exercised in a treadmill for 40 min daily over 3-4 weeks, and appeared to spare the affected side very slightly, although compensating to some degree by overting that foot at the time of stepping off. At the final acute experiment under nembutal anaesthesia, all test and control nerves in both hind-limbs were prepared and placed on stimulating electrodes. The central cut ends of ventral roots S1, L7 and L6 on both sides were used for monophasic recording. Both legs and the back were made into pools of paraffin maintained at a constant temperature of 36-37° C. The stimulus strengths of the testing volleys at a frequency of 0.5 per sec were always at least twice maximal for activation of the group Ia afferent fibres, and the standard repetitive (tetanic) stimulation employed for post-tetanic conditioning in all experiments was 400 per sec for 15 sec. Corresponding reflexes were investigated in quick succession on the two sides in order to eliminate temporal inequalities of temperature or depth of anaesthesia.

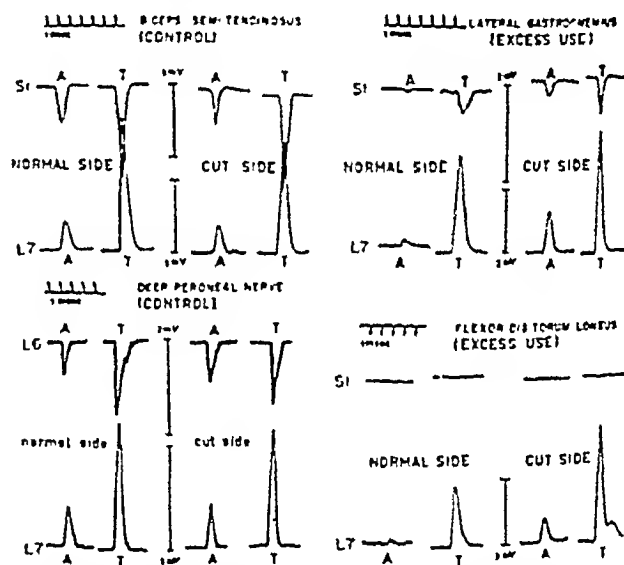


Fig. 1. All reflexes in this figure were taken from one typical experiment in which the monosynaptic reflexes for each nerve were displayed simultaneously from two ventral roots. Reflex heights t before, post-tetanic potentiation; T , after post-tetanic potentiation are shown for each nerve tested in both limbs.

On the left side of Fig. 1 the reflexes evoked by the biceps semitendinosus and the deep peroneal volleys before and after post-tetanic potentiation indicate a symmetry of monosynaptic reflexes into both L7 and S1 ventral roots. In contrast on the right side of Fig. 1 there is asymmetry for all monosynaptic reflexes evoked by lateral gastrocnemius and flexor digitorum longus volleys, invariably the reflexes were larger for the side on which these muscles were presumed to have been subjected to a prolonged excess stress on account of the denervation of their synergists. In each of 14 cats, up to four series of reflexes before and after post-tetanic potentiation were recorded with intervals of 1-2 hr between series. There were slight increases, not statistically significant, for biceps semitendinosus and deep peroneal reflexes on the cut side, but marked increases, which averaged more than 50 per cent, in the reflexes from the lateral gastrocnemius and

flexor digitorum longus nerves when compared to the corresponding reflexes from the control side. These increases are statistically significant $P < 0.001$ except lateral gastrocnemius into SIVR for which $P < 0.05$. There were no changes of statistical significance in the conduction velocity of the afferent fibres or the absolute refractory periods for any nerve on the two sides; nor were there any significant differences between the fibre counts or distribution of fibre diameters for the lateral gastrocnemius and flexor digitorum longus nerves on the two sides. Muscle wet weights did not show any significant differences between the two sides except a wasting of approximately 40 per cent in the denervated muscles.

In the absence of demonstrable changes in the afferent fibres we assume that the site of changes in excitability leading to the increased lateral gastrocnemius and flexor digitorum longus monosynaptic reflexes was either at the presynaptic terminals of the group Ia fibres or the post synaptic motoneurone membrane that is, at the excitatory synapse. Possible mechanisms by which the presumed excess use could render synaptic action more efficient include increased size of presynaptic terminals or alterations in the numbers and/or disposition of the synaptic vesicles at the presynaptic terminals. With synaptic potency thus increased, more motoneurons in the pool would be activated by each testing volley, the monosynaptic reflex being correspondingly greater than on the control side. Past evidence that prolonged disuse adversely affects synaptic function^{1,2} together with this new evidence that excess use leads to an enduring increase of synaptic efficacy provide strong support for the postulate that learning and conditioning are due to the enhancement of synaptic efficacy by excess use.

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Effect of Sulphanilamide on Citric Acid Production by *Aspergillus niger*

It has been shown that the mechanism of resistance to sulphanilamide toxicity in *E. coli* involves the enhanced formation of coenzyme A which is required for the acetylation of the drug.¹ A similar increase in the coenzyme A levels of the cells has been observed in *S. cerevisiae* subjected to sulphanilamide toxicity.² An interesting observation made in the experiments with *S. cerevisiae* was that concomitant with the increase in the coenzyme A levels of the cells, there was an enhancement in the levels of ergosterol as well.² In view of the known role of coenzyme A in sterol biosynthesis it was considered of interest to investigate the effect of sulphanilamide toxicity on other biosynthetic processes involving the action of coenzyme A. Accordingly the effect of the drug on citric acid production by a citric acid accumulating strain of *Aspergillus niger* was investigated. The results presented here show that the production of citric acid by the mould is markedly inhibited by sulphanilamide.

The basal medium used in these studies was glucose 140 gm ammonium nitrate, 2.5 gm potassium dihydrogen phosphate, 2.5 gm crystalline magnesium sulphate, 0.25 gm crystalline manganese sulphate, 100 mgm crystalline zinc sulphate, 1.25 gm distilled water to 1,000 ml. The pH of the medium was adjusted to 2.0-2.5 in all cases. All experiments were carried out in 250 ml Erlenmeyer or flasks containing 25 ml culture medium.

The effect of sulphanilamide on accumulation of citric acid by growing cultures of *A. niger* as well as by resting mycelial pads was investigated. In the former case sulphanilamide was introduced into the culture medium of growing cells of the organism and the incubation continued for a further specified period. The contents of each flask were analysed for dry weight of mycelia, total acids produced, citric acid formed and the amount of sugar consumed. Total acids were determined by titration of an aliquot of culture medium against 0.1 N sodium hydroxide. A colorimetric method³ was employed for citric acid determination while reducing sugar determinations were carried out by a method involving the use of Somogyi's high alkali copper sulphate reagent.⁴ The results are given in Table 1.

Table 1. EFFECT OF SULPHANILAMIDE ON GROWING CULTURES OF *Aspergillus niger*

| Period of Sulpha incubation (days) | Alkali added (mM) | Dry weight (mgm.) | Total acids (mM) | Glucose consumed (mM) | Citric acid formed (mM) | Percent molar yield (%) |
|---------------------------------------|-------------------------|-------------------------|------------------------|-----------------------------|-------------------------------|----------------------------------|
| after addition (days) | (mM) | (mgm.) | (mM) | (mM) | (mM) | (%) |
| 3 | 0 | 144 | 54.6 | 1565 | 179.0 | 11.39 |
| | 50 | 101 | 9.2 | 1479 | 35.4 | 1.92 |
| | 75 | 103 | 8.0 | 1409 | 3.8 | 1.93 |
| 6 | 0 | 183 | 91.0 | 1279 | 244.0 | 17.02 |
| | 50 | 112 | 20.6 | 1090 | 5.1 | 2.68 |
| | 5 | 104 | 11.3 | 1022 | 3.1 | 2.04 |
| | 100 | 109 | 8.2 | 1056 | 1.0 | 0.97 |

The organism was initially grown for 48 hr. in 15 ml medium at a concentration equivalent to 25 ml. single strength medium. 10 ml of sterile distilled water was then added to each of the control flasks and 10 ml sulphanilamide solution in appropriate concentration to the remaining flasks under aseptic conditions. Incubation was continued for 3 or 6 days after which the flasks were sterilized and the content analysed. All values represent averages of duplicate determinations.

In experiments with resting mycelia of *Aspergillus niger* the replacement technique of Chuglioti and Walker⁵ was adopted. The organism was initially grown for 4 days to form strong and integrated pads of mycelia. The culture medium was then withdrawn and replaced aseptically by an equal volume of sterile basal medium devoid of glucose. After incubation overnight the medium was again withdrawn and replaced with sterile 10 per cent glucose solution (w/v) containing added sulphanilamide where required. The incubation was continued for a further period of 3 or 6 days and then the contents of each flask analysed as before. The results are given in Table 2.

Table 2. EFFECT OF SULPHANILAMIDE ON CITRIC ACID FORMATION BY RESTING MYCELIA OF *Aspergillus niger*

| Sulphanilamide added (mM) | Weight of mycelia (mgm. dry weight) | Glucose used (mM/100 mgm. dry mycelium) | Citric acid formed (mM/100 mgm. dry mycelium) | Percent molar yield (%) |
|---------------------------------|--|--|--|----------------------------------|
| per flask | | | | (B/A × 100) |
| 0 | 215 | 490 | 94.0 | 17.5 |
| 5 | 213 | 451 | 31.9 | 6.0 |
| 50 | 222 | 456 | 22.9 | 4.4 |
| 100 | 210 | 483 | 5.6 | 1.0 |
| 125 | 250 | 518 | 5.4 | 0.9 |

Mycelial pads of the organism were incubated aseptically under resting conditions in 25-ml. lots of 10 per cent glucose solution, with addition of sulphanilamide as specified. The contents of each flask were analysed after 8 days incubation in the replacement medium. All values represent averages of duplicate determinations.

It is seen from the results given in Tables 1 and 2 that sulphanilamide produces a profound inhibitory effect on the production of citric acid by *A. niger* under growing, as well as resting, conditions. That this inhibition is not caused by an impairment in carbohydrate utilization is obvious from the fact that there is no decrease in the relative amounts of glucose consumed. In another set of experiments it has been found that the addition of *p*-aminobenzoic acid to the medium reverses the effect of the drug on the final weight of the mycelia under growing conditions but does not have any effect on citric acid formation. Indeed, it can be expected that the vitamin will have the same effect on the acetylating system as sulphanilamide and hence it is not surprising that it does not antagonize the effect of the drug on citric acid formation. Again, the inclusion in the medium of a mixture containing adenine, guanine and uracil and the amino-acids methionine and serine, compounds the biosynthesis of which involves the action of *p*-aminobenzoic acid, reverses the inhibition of growth but not the inhibitory effect on citric acid production.

It would seem that the inhibitory effect of sulphanilamide on formation of citric acid in *A. niger* is the result of the stress produced by the drug on the acetylase system. The present results, therefore, emphasize the importance of acetate in citric acid synthesis by the mould.

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A Chemical Effect of Ethylene during the Storage of Peas

In recent work¹ the author and others found that the crude lipid extracted from raw peas held in the pods in frozen storage (-17.8°C) for periods of time, consistently developed much larger peroxide values than that extracted from raw peas of the same variety, harvested from the same plots at the same time, which were vined previous to placing in storage.

It occurred to me that this difference might be caused by ethylene in the atmosphere inside the pods.

The present experiment was designed to test this hypothesis. The peas used in this work were harvested from the same plot at the same time, and were of the Perfected Freezer variety. Raw peas were carefully shelled by hand to avoid injury and were packed in glass bottles filled with glass lead-in and exit tubes so that the bottles could be flushed with an atmosphere of known composition. These tubes were so constructed so that they could easily be sealed with a flame as soon as the flushing with the controlled atmosphere was completed. The following atmospheres were used for this purpose:

- Gas I, 5 per cent carbon dioxide, 3 per cent oxygen, 92 per cent nitrogen
Gas II, 5 per cent carbon dioxide, 3 per cent oxygen, 91.98 per cent nitrogen, 0.02 per cent ethylene

Controls were run with raw peas held in the pods. A 7-month storage period at -17.8°C was employed for the results presented here.

The crude lipid was extracted and the peroxide numbers were determined as previously reported^{2,3} (Table 1).

Table 1. PEROXIDE VALUES* OF EXTRACTED CRUDE LIPID
Storage conditions Gas I Gas II Held in pods

| Peroxide value | 50 | 101 | 204 |
|----------------|----|-----|-----|
|----------------|----|-----|-----|

* Millimoles of peroxide oxygen per kgm. of lipid, average of determinations in triplicate.

It seems, therefore, that ethylene has an action on the lipid matter of peas stored in the presence of this gas. The peas stored in the atmosphere containing ethylene yielded crude lipid which gave a high peroxide value. It is interesting to note that the peroxide value of the lipid extracted from the peas held in the controlled atmosphere containing ethylene was almost identical with that obtained from the lipid extracted from the peas stored in the pods.

Since it was found in previous work¹ that storage in the pods retards the deterioration in flavour, it may be suspected that ethylene and possibly other gases have a part in bringing about this result.

It is possible, therefore, that the lipid fraction, small as it is, may be involved in the biochemistry of the normal ripening of fruits and certain vegetables.

The results of this work will be published in detail elsewhere.

I acknowledge with thanks the technical assistance of Miss Kathleen Thomas.

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Isolation of Fatty Alcohols with Plant-Growth Promoting Activity from Maryland Mammoth Tobacco

It has been reported previously that 3-indoleacetic acid could not be detected in leaves or apical tissues of Maryland Mammoth tobacco¹. Consequently, further attempts have been made to define more clearly the chemical factors responsible for the growth and development of this variety.

Leaves and apical tissues of two-month-old Maryland Mammoth tobacco plants were harvested, frozen rapidly in solid carbon dioxide, and ground in absolute ethanol. The subsequent extraction procedure was as described previously¹. The final extracts were chromatographed on a Gryksbo chromatographic filter paper column (type LKD-3391) with a steady flow of solvent consisting of isopropanol ammonium hydroxide water (80:5:15 v/v/v). Successive 100-ml fractions of percolate were removed at the bottom of the column until a total of three litres had been collected, and each fraction was stored at -20°C .

A light-coloured, oily precipitate separated in fractions 25-28 after a few days. This material was collected by centrifugation and dried over calcium chloride. The dry, tan solid then was subjected to a process of fractional crystallization from absolute ether which afforded finally several mgm. of a waxy solid exhibiting growth-promoting activity in the bio assay mentioned below.

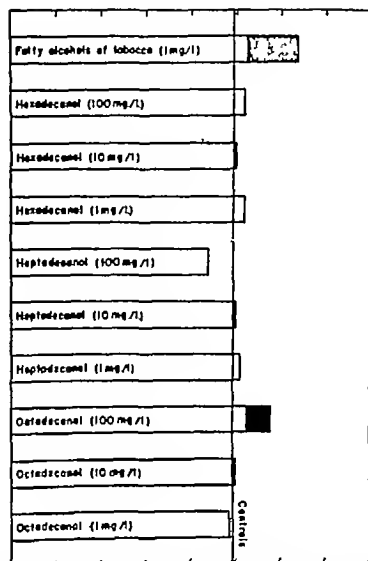


Fig. 1. Final mean lengths for ten *Avena* first-internode sections floated for 22 hr in buffer (with sucrose) containing the fatty alcohols isolated from tobacco, hexadecanol, heptadecanol, and octadecanol. Shaded areas represent statistically significant differences ($P = 0.01$).

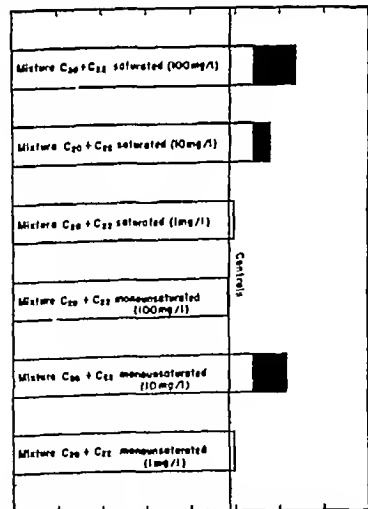


Fig. 2. Final mean lengths for ten *Avena* first-internode sections floated for 22 hr in buffer (with sucrose) containing $C_{20} + C_{22}$ saturated alcohols and $C_{20} + C_{22}$ monounsaturated alcohols. Shaded areas represent statistically significant differences ($P = 0.01$).

The white crystals were soluble in ether, ethanol and benzene but were insoluble in water. The solid melted at 70–72° C on a Vanderkamp block, and resolidified only very slowly. Nitrogen, sulphur, halogens, and phosphorus were not present in its

elementary composition. Even in concentrated hexane solution, no ultra violet absorption was observed, indicating the absence of unsaturation. Infra red spectra measured on a Perkin Elmer model 12A spectrophotometer equipped to handle micro samples, were found to be almost identical with those of long chain normal primary alcohols such as 1-docosanol.

Nilsson, Ryhage, and von Sydow² have isolated a neutral, crystalline substance melting at 70–74° from air-dried pollen of *Pinus montana*. Mass spectrometric investigation, using a special high temperature instrument revealed that their isolate was a mixture of 1 tetracosanol, 1 hexacosanol, and 1-octacosanol. Although our own mass spectrometric evidence is inconclusive it is quite likely that we, too, have isolated such a mixture.

The plant-growth regulating activity of the tobacco isolate as well as that of sixty long chain fatty alcohols and related compounds was measured by means of the *Avena* first-internode bio-assay³. Results of typical experiments are shown in Figs 1 and 2, in which shaded areas represent elongation which is statistically significant at the 1 per cent level. These values were reproduced on at least two subsequent occasions in each case. The details and results of further investigation will be discussed elsewhere in a future publication. However, in general only C_{18} to C_{22} alcohols and their acidic esters were found to exhibit growth regulating activity in this series.

The absence of 3-indoleacetic acid in tissues of Maryland Mammoth tobacco, coupled with the demonstration of growth regulating activity in a molecule very different from the indole type suggests that the present over-simplified concepts of the hormonal regulation of plant growth are in need of re-evaluation.

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Essential Pentosuria Renal or Enzymic Disorder

ESSENTIAL pentosuria is a rare, recessive genotypic metabolic disorder characterized by the excretion of gram quantities of L-xylulose. It was included among Garrod's "inborn errors of metabolism" and has usually been considered to be the result of an enzyme deficiency. Garrod's original concept of a hereditary metabolic anomaly has been broadened by some to include renal defects, and in regard to essential pentosuria, Knox² has recently stated "the paramount question of a renal or an enzymic mechanism is still to be decided".

Our experiments were based on the use of D-glucuronolactone to stimulate xylulose production in human subjects. Enklowitz and Lasker³ had in 1935 discovered this phenomenon in pentosurics by measuring the excretion of the pentose in urine and Touster and his co-workers⁴ more recently showed that

a small but definite effect is demonstrable in animals and in normal humans as well. Moreover, experiments using isotopes showed that D-glucuronolactone is a direct precursor of urinary L-xylulose in the pentosuria⁵, and that the metabolism of glucuronolactone in the pentosuria is blocked at L-xylulose⁶.

If a renal defect exists in pentosuria the administration of D-glucuronolactone should not cause a greater increase in blood xylulose levels of pentosurics than of normal individuals because the pentose would be so readily excreted by the pentosuria. If pentosuria is due to a metabolic (enzymic) defect on the other hand, glucuronolactone should result in higher blood xylulose concentrations in pentosuria individuals than in normal persons. Flynn⁷, using paper chromatography, found that glucuronolactone administration augments the trace of xylulose normally found in pentosuria plasma, but comparable experiments on normal individuals were not done.

Five gm of D-glucuronolactone, dissolved in about 200 ml of water, were taken orally in one dose by our subjects. This quantity is known to yield 1-2 gm of additional urinary xylulose in pentosuria subjects^{3,4}. At the times indicated in Table 1, blood samples were

Table 1 EFFECT OF 5 GM OF ORAL GLUCURONOLACTONE ON THE PLASMA XYLULOSE LEVELS OF NORMAL AND PENTOSURIC SUBJECTS

| Subject | Plasma xylulose (mgm/100 ml) | | |
|------------------|------------------------------|------|------|
| | Fasting | 1 hr | 2 hr |
| Normal (M K F) | <0.3 | <0.3 | <0.3 |
| Normal (R C B) | <0.3 | <0.3 | <0.3 |
| Pentosuria (I B) | <0.3* | 0 | 8 |
| Pentosuria (I B) | 2* | 7 | 11 |

* In two other samples of fasting pentosuria plasma, the xylulose level was less than 0.3 mgm/100 ml.

obtained by venipuncture from each subject. The heparinized blood was centrifuged to obtain the plasma, which was deproteinized with 20 per cent trichloroacetic acid (5 per cent final concentration). The filtrate was extracted several times with diethyl ether to remove the trichloroacetic acid and was then freed of ionic compounds by means of a mixed bed resin of 'Amberlite IR-120(H⁺)'-Amberlite IR-400 (acetate)' (3 gm of mixed resin per 5 ml of original plasma). The deionized solution was concentrated to dryness *in vacuo* at 45-55°, and the residue was dissolved in a small amount of absolute ethanol. After clarification by centrifugation, the solution was analysed by paper chromatography in 88 per cent phenol. Synthetic xylulose and pentosuria urine were used as standards. The values given in Table 1 are based on visual comparison of the plasma xylulose chromatographic spots with the standards, after spraying the paper strips with either naphthoresorcinol⁸ or phloroglucinol⁹ reagents. The use of several other sugars as standards showed clearly that the plasma pentose was xylulose. The lower limit of detection of the ketopentose was about 0.3 mgm per 100 ml of plasma.

All subjects were adult males in apparent good health. One (I B) exhibits typical findings of essential pentosuria. The two controls do not excrete readily detectable quantities of xylulose.

Table 1 clearly shows that the pentosuria plasma increases markedly in xylulose concentration after the administration of glucuronolactone, a result in full accordance with the concept of a metabolic defect. The magnitude of the increase is of the order expected from the known effect of glucuronolactone on urinary xylulose levels in persons with the anomaly. The unavailability of our subject for further experiments made it impossible to establish the time of attainment

of maximum blood xylulose concentration or to investigate the variation in the fasting xylulose level in the pentosuria. The plasma xylulose of the controls remained below the level of detection, undoubtedly a result of a considerable capacity to utilize xylulose as soon as it is formed from the administered glucuronolactone.

The missing or deficient enzyme in essential pentosuria is presumably triphosphopyridine nucleotide xylitol (D-xylulose) dehydrogenase, a very specific enzyme which has been found in the liver of several species¹⁰⁻¹². This enzyme catalyses the reduction of D-xylulose to xylitol in the glucuronate-xylulose, or C₆ oxidation, pathway of carbohydrate metabolism^{13,14}. The relationship of this pathway to the metabolism of xylulose in normal and pentosuria humans has been discussed in two recent reviews^{4,15}. There is no evidence to support the suggestion that L-xylulose excretion by pentosuria individuals may be due to the presence of an abnormal enzyme which stimulates the production of the pentose^{7,16}. The determination of the exact nature of the enzymatic abnormality in essential pentosuria will probably depend ultimately on a comparison of the concentration of the L-xylulose-xylitol enzyme in normal and pentosuria liver.

The glucuronolactone loading test described in this report not only appears to rule out the renal hypothesis for the pentosuria defect, but it may be of value in detecting heterozygotes carrying the pentosuria gene. This possibility is now being explored.

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RADIOBIOLOGY

Free Radicals in X-Rayed Seeds of High and Low Water Content, as Measured by Electron Spin Resonance

RECENTLY Caldecott^{1,2} and Ehrenberg^{3,4} have shown that contrary to earlier ideas dry stored seeds of barley are more sensitive to ionizing radiation than are normal stored seeds. These results have been confirmed by one of us⁵ in seeds of *Vicia faba*.

In order to find some possible explanation for this remarkable effect we have studied the free-radical content of X-rayed *Vicia faba* seeds by means of electron spin resonance absorption. The material used was an inbred line of *Vicia faba* var minor, Throws M.S. Winter Beans from Hasler and Co., Ltd., Dunmow, Essex. Measurements were carried out separately with embryos excluding the cotyledons

(that is, radicles and plumules), with pieces of cotyledons and with pieces of the testa using normally stored material (52 per cent relative air humidity) and dry stored material (25 per cent relative air humidity, storage 4 days over calcium eldorado at 20°C). The water content of the material under these conditions of air humidity was measured and is shown in Table 1.

Table 1 WATER CONTENT OF DIFFERENT PARTS OF LEGUM SEEDS AFTER STORAGE UNDER NORMAL OR UNDER DRY CONDITIONS

| Relative humidity of air (per cent) | 52 | 25 |
|-------------------------------------|------|-----|
| Plumules and Radicles (per cent) | 0.6 | 4.6 |
| Cotyledons (per cent) | 12.2 | 4.0 |
| Testas (per cent) | 12.0 | 4.3 |

Doses of 10,000 r X rays were given at 250 kV, 15 mAmp, using 0.5 mm copper + 1 mm aluminium filter intensity 500 r/min. The dry material was irradiated in micro desiccators. Within a few minutes after irradiation samples were transferred to quartz tubes and cooled down in liquid oxygen (00° K). The electron spin resonance spectrometer used for the radical detection operates at 10 kMc/s the cavity being cooled by liquid oxygen (ref. 6, pp. 52-53). The material was introduced into the cavity in weighed amounts so that the whole volume was always within $\frac{1}{16}$ cm of the centre of the cavity. The free radical concentration was determined by a comparison of the integrated absorption obtained from the sample and that obtained from a standard carbon sample of known radical content. It is estimated that the absolute accuracy of such measurements is about 50 per cent.

We found no free radicals in normally stored unirradiated material or in normally stored irradiated embryos and cotyledons (sensitivity about 10^{15} radicals per gm dry weight). However free radicals are present in normally stored testas after irradiation (about 8×10^{15} radicals per gm dry weight). We found no free radicals in dry stored unirradiated embryos and cotyledons, but obtained a distinct signal from dry stored unirradiated testas, indicating about 8×10^{15} free radicals per gm dry weight. These were not as might be suspected, induced by the freezing process (ref. 6, p. 241), as in dry testas an equal signal appears at room temperature. In dry stored irradiated material clear evidence of free radicals was found in all parts of the seed. The concentration in the testa had risen to about 2×10^{16} concentrations of about 7×10^{15} radicals per gm dry weight being calculated for embryos and cotyledons.

These results indicate that there is some correlation between the X ray sensitivity as measured by biological damage and the production or survival of radiation induced free radicals in seeds. In dry seeds higher concentrations of free radicals are built up during irradiation and the biological damage is greater. It may well be that these free radicals play an important part in the sequence of events from the primary effects of the radiation to the ultimate observed biological damage. This suggestion is supported by the recent results of Ehrenberg *et al.*^{7,8} from entire seeds of *Agrostis stolonifera*. Moreover certain after-effects in X rayed dry stored seeds⁹⁻¹² may be attributable to the action of such radicals whose survival depends upon conditions of storage. It should be borne in mind however, that relatively high concentrations of free radicals are induced by radiation in what might appear to be the less vital parts of the seed namely the testa and further that dry storage itself appears to induce free radicals. Dry storage also produces biological damage in the seeds.¹³

How closely these effects are connected is at present a matter for speculation but they are clearly of importance in the interpretation of further experiments.

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BIOLOGY

Interaction of Plant Growth Regulators in Regeneration Processes

In previous years much attention has been paid to the influence of growth regulators on regeneration processes, especially to the interactions of kinetin and auxin in morphogenesis of tissue cultures.¹ In experiments with *Begonia* leaves we have observed a decisive effect of auxin and kinetin on regeneration. In addition it could be shown that gibberellin profoundly affects the complex hormone system apparently controlling differentiation in higher plants.

In the experiments leaf disks (12 mm diam., cut so as to include a portion of a secondary vein) were used. After washing the leaves in 3 per cent hydrogen peroxide the disks were cut and kept for 60 hr. on an isotonic salts solution (pH 5.5) with or without addition of 2,4 dichlorophenoxyacetic acid, kinetin or gibberellin, or combinations of these. After this pre-treatment the disks were placed in Petri dishes on filter paper moistened with tap water.

Under the experimental conditions the control disks developed after 2-3 weeks a root at the base of the longest vein, and after a further 2-3 days a shoot appeared at the same position. This pattern of regeneration which so far has always been observed in these experiments (August 1958-July 1959) was shifted by treatment with 2,4 dichlorophenoxyacetic acid in favour of root formation. That is with concentrations of this acid between 10^{-6} and 10^{-8} gm/ml, often 3 or 4 roots were produced and these developed up to 8 days earlier than in the controls. At the lower concentrations (up to 10^{-7} gm/ml) production of the shoot was delayed for only 8 days relative to the controls but at the higher concentrations for at least 3-4 weeks or indefinitely.

Kinetin (6 furfurylamino purine) had a twofold effect. It not only suppressed the formation of roots

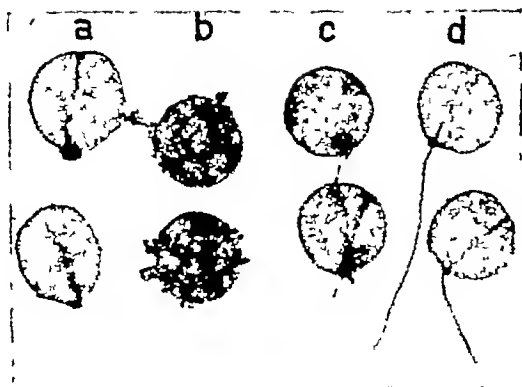


Fig 1 Effect of (a) gibberellic acid (10^{-6} gm/ml), (b) kinetin (5×10^{-6} gm/ml) (c) water (control), (d) 2,4-dichlorophenoxyacetic acid (10^{-5} gm/ml) on regeneration of leaf disks of *Begonia rex* six weeks after application. The disks (c) have the ventral surface uppermost.

or counteracted their promotion by 2,4-dichlorophenoxyacetic acid, but also abolished the polarity of shoot formation so that shoots were distributed over the whole area of both sides of the leaf. This latter effect was especially pronounced at a concentration of 5×10^{-6} gm/ml in the absence of added auxin (Fig 1). Kinetin had no effect on the time of appearance of shoots.

A third type of hormone which could be expected to influence the regeneration process is gibberellic acid. It is known that it can react synergistically with auxins² and it has been shown that it can replace kinetin³. Addition of gibberellic acid in these experiments led to surprising results. In concentrations between 10^{-6} and 10^{-5} gm/ml it inhibited both root and shoot formation. This inhibition could be relieved by addition of 2,4-dichlorophenoxyacetic acid at the same concentrations respectively, under these conditions the ability of the disks to form shoot and roots was roughly the same as in the controls. In contrast to 2,4-dichlorophenoxyacetic acid, kinetin was unable to counteract the inhibitory effect of gibberellin.

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Fertilization of Rabbit Ova *in vitro*

In reviews of the evidence for mammalian fertilization *in vitro*, Austin and Bishop¹ stated that "it seems best for the present to regard the case as *sub judice*". Chang² concluded that "up till now we still do not have a repeatable procedure to fertilize mammalian eggs *in vitro*". Since the recognition of 'capacitation' of spermatozoa in the female tract by Chang³ and Austin⁴, Thibault and his associates⁵⁻⁷ have reported cytological evidences of fertilization of rabbit ova *in vitro* by capacitated sperms. It was thought that unless living young are obtained by transplanting such fertilized ova into recipient rabbits, fertilization *in vitro*, as determined by cytological evidences, may not be sufficiently proved because such ova may be abnormally and/or incompletely fertilized, may die during the process, or may not be fertilized at all. This note reports a procedure to fertilize rabbit ova *in vitro* and the probability of normal development *in vivo* of such *in vitro* fertilized rabbit ova.

An oestrous rabbit was bred three times by fertile bucks at about 9 00 p.m. for the recovery of capacitated sperms, and two other rabbits were injected intravenously with sheep pituitary extract to induce ovulation for the recovery of unfertilized ova. Next day at about 9 00 a.m., before killing, an animal was bled by heart puncture or from the carotid artery in order to obtain fresh serum for the culture of ova. About 3-5 ml of freshly prepared Krebs-Ringer bicarbonate solution containing 0.25 per cent of glucose was injected into one uterine horn of the mated rabbit and the fluid withdrawn immediately and placed into 15 ml capacity small Carrel flasks. Progressive motile sperms from the uterine washings could be seen in most cases. The Fallopian tubes of the other two rabbits were flushed with Krebs-Ringer bicarbonate solution and the ova (still in mucous clot) were placed into a small Carrel flask that contained uterine sperms. These flasks were stopped with rubber and attached to a gentle rocking device placed inside an incubator at 38° C. After about 3-4 hr, the ova, free from the mucous clot but with corona cells still attached, were picked up with a capillary pipette and transferred into an 8 ml capacity Carrel flask containing 4 ml of 50 per cent heated rabbit serum (at 55° C for 20 min) in saline. After culture for another 18 hr the ova were picked out, separated, mounted *in toto* on a slide⁸ and examined under a compound microscope before fixation to determine the location of sperms. After fixation with acetic alcohol they were examined for the polar bodies, pronuclei, and the second maturation spindle, and then stained with Laemoid for checking details.

The ova thus examined were classified into four groups: (a) Unfertilized, the ova that had definite second maturation spindles irrespective of the presence of sperms. (b) Uncertain, those ova having no second maturation spindles but the nuclear configuration of which was at variance, some had one pronucleus, some had two groups of chromosomes, and some had several pronuclei. They may have been parthenogenetically activated, or fertilized, but died at an early stage. (c) Fertilized but dead, ova showing sperms on the zona or in the perivitelline space and with the nucleus at the anaphase of the second maturation division, some had a definite second polar body and had either cleaved into two cells or had two pronuclei, but most of them had fragmented. (d) Fertilized and cleaved normally, those cleaved into 4 cells and with either a second polar body or sperms in the perivitelline space.

Of 266 rabbit ova examined, 166 (62 per cent) were unfertilized, 23 (8.7 per cent) were uncertain, 22 (8.3 per cent) seemed to have been fertilized but died at an early stage, and 55 (21 per cent) cleaved normally and were considered definitely fertilized. Of these 51 ova, 36 were transplanted⁹ into the tubes of 6 recipient rabbits that had been injected with pituitary extract 18 hr previously. The recipient animals were allowed to deliver at term. Two recipients did not become pregnant, but 4 delivered 15 living healthy young. The probability of normal development of such *in vitro* fertilized ova is then about 42 per cent.

The procedure used in the present study is similar to that recommended by Thibault¹⁰, and the proportion of ova fertilized is similarly low. The concentration of sperms in the uterine washings ranged from 10,000 to 26,000 per ml and the proportion of fertilized ova was not correlated with the concentration of sperms. Furthermore, when uterine washings were centrifuged to concentrate sperms, or when a small amount of saline was used to wash the uterine horns

the proportion of ova fertilized was not increased. The proportion of fertilized ova was also not increased by using sperms recovered from the tubes of a mated animal (at 10,000 to 15,000 sperms per ml). In this case only 5 out of 41 ova (12.2 per cent) were fertilized. Autologous serum seems to be better than heterologous serum for culturing newly fertilized ova: when autologous serum was used 50 out of 102 ova (49 per cent) were fertilized and 43 of the 102 (42 per cent) cleaved normally but in heterologous serum 18 of 100 ova (17 per cent) were fertilized and 11 of the 100 (10 per cent) cleaved normally.

Due to the thick layer of corona cells on the zona pellucida, it was not possible to observe the penetration of sperm through the zona. Judging from their rate of cleavage, as compared with those ova recovered from the mated rabbit and cultured similarly, penetration of sperms probably occurred when the ova were in saliva rather than in serum. In some experiments the zona pellucida at the time of examination was very soft or partially dissolved. This may be due to a reaction between the zona and some factors in the uterine washing as it was shown that the zona of unfertilized ova dissolved in a few hours when transplanted into the uterus¹¹ or it may be that certain factors in the serum of a particular animal affect the zona in this way. At the time of examination the general appearance of a fertilized ovum is better than that of an unfertilized ovum. This shows that fertilization increases the resistance of the ovum to the artificial medium.

Although the proportion of fertilized ova is relatively low and sometimes no fertilization occurred due to infection or other unknown reasons under the present experimental conditions, it can be said that at least we have a repeatable procedure for fertilizing mammalian ova *in vitro* and that such ova are truly fertilized and able to develop into normal young. Further studies are planned to elucidate the mechanisms of mammalian fertilization *in vitro*.

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Mineral Uptake and Retention in Cotton grass (*Eriophorum vaginatum* L.)¹

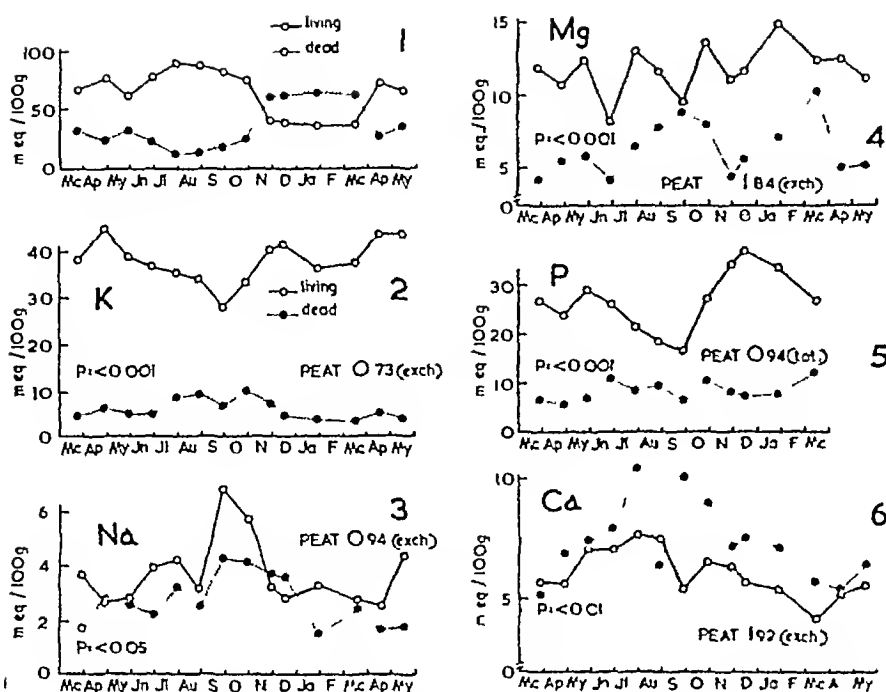
SEVERAL investigations²⁻⁴ have indicated the importance of mineral nutrients in determining the characteristic flora and vegetation structure of the various types of bog and fen. These and other exten-

sive examinations of the nutrient levels in the underlying peat and water have not yet been followed, however, by a parallel study of the actual amounts of macro elements taken up throughout the year by the principal mire species themselves nor has their rate of turnover of mineral ions been investigated.

In view of the extremely low nutrient status of raised and blanket bogs, where the only source of salts is apparently via dust and sea-spray blown inland⁵, nutrient supply, accumulation and turnover relationships may be at their most critical and accordingly, we have chosen for the present study a typical bog species, *Eriophorum vaginatum* L. obtained from a site near Meel Llynant, Merionethshire (altitude 1400 ft.). The needle-like leaves of this species grow from the base and die back from the tip, eventually falling over to become incorporated in the litter layer. Duplicate monthly samples were collected by hand pulling over a fourteen month period 1954-5, dead leaves and dead leaf portions were separated from living leaf material, each being dried and ground prior to analysis. Although both growth and die-back occurred on a small scale simultaneously throughout the year in the *Eriophorum* community, Fig. 1 indicates that there was an overall seasonal pattern of autumnal die back followed by a spring regrowth.

Sodium and potassium determinations were made by flame photometry on diluted ash solutions; calcium was also measured in this way by a method developed in this laboratory to minimize interference. Magnesium and phosphorus were determined photometrically using titan yellow and molybdate/stannous chloride methods, respectively. The glucose formed after one hour in boiling N sulphuric acid (R. E. Denar, Grass Res. Inst. Hurley, private communication) was determined photometrically using an anthrone procedure and a figure for carbohydrate⁶ calculated. The mineral levels are graphed as milliequivalents per 100 gm of carbohydrate free dry leaf material as shown the 'carbohydrate' correction being an attempt to eliminate errors due to seasonal variations in photosynthetic activity, etc. The results of our mineral analyses are in general agreement with those of Thomas and Trinder⁷ when allowance is made for the fact that they analysed unsorted leaf material collected throughout the growing season and expressed the results on a total dry matter basis.

Samples of peat taken at rooting level were analysed for total phosphorus and cations exchangeable with N ammonium acetate and the results which are similar to those of Goro and Allen⁸ included in the appropriate graphs as milliequivalents per 100 gm dry peat. Values for the ratio of average nutrient in living or dead material to the nutrient value for peat are as follows: potassium (living material) 52 (dead) 8; phosphorus (living) 28, (dead) 0; sodium (living) 4 (dead) 3; magnesium (living) 6 (dead) 3; calcium (living) 3 (dead) 4. These ratios, considered together with the graphed results indicate that *Eriophorum* concentrates potassium and phosphorus to a marked degree and further irrespective of any of their seasonal fluctuations in living leaves, these elements are translocated away prior to die back and thus not wholly incorporated into the litter. The ratios and graphed results for magnesium and sodium also suggest the possibility of a similar concentration and retention of these elements by living leaf tissue. The apparent increase in the calcium content of the dead material may be due to a fall in dry weight caused by breakdown of protein prior to die back. The results for



Figs 1-6 1 Annual fluctuation in living and dead fractions of leaf material per 100 gm dry matter. 2-6 Mineral nutrient content of living and dead leaf material throughout the year as milliequivalents per 100 gm. Carbohydrate free dry matter. 1 exchangeable (exch) or total (tot) nutrient content of peat included on appropriate graph as milliequivalents per 100 gm. dry peat (equivalent weight of phosphorus = 10.33). P level of significance of difference between mean mineral content of dead and living material.

potassium and calcium are in line with those obtained for *Fagus sylvatica* L. by Olsen⁶ who, however, observed no autumnal mobility of phosphorus or magnesium. Other experiments to be described elsewhere, suggest that the lower mineral values in the dead material were not caused by the 'washing out' effects of rainfall, a conclusion also reached for the beech⁸.

Thus the phenomenon of mineral retention may possibly be an important factor in extending the range of nutrient conditions under which *E. vaginatum* can successfully grow. Tussocks or 'islands' of this species may be regarded as nutrient reservoirs particularly of phosphorus and potassium, an item of practical significance as both leaves and peduncles of this species are extensively grazed by certain breeds of hill sheep, especially during the 'hungry-gap' period of early Spring. Mineral accumulation may also be a contributory factor to the successful way in which *Calluna* and other species colonize moribund *E. vaginatum* tussocks. In view of the strong potassium retention by living leaf tissue it would be interesting, in relation to radioactive fall-out, to investigate whether caesium behaves in a similar manner.

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Prevention of the Onset of Seed Dormancy by Gibberellic Acid

ONE of the striking properties of gibberellic acid is its ability to curtail the rest period of seeds and other dormant organs. For example, dormant seeds of lettuce¹, peach², *Arabidopsis*³ and barley⁴ germinate spontaneously when placed in solutions of gibberellic acid. However, no data are available concerning the effects of this substance on the onset of seed dormancy when plants bearing developing seeds are treated, although such effects might be predicted. Results obtained in this laboratory bear out this prediction.

For this study an inbred strain of *Avena fatua* was chosen. Seeds of this strain exhibit very deep dormancy such that neither the removal of the hull nor an incision into the seed (in air) has any beneficial effect in promoting germination. Further, even isolated embryos germinate only when supplied with gibberellic acid, or after prolonged leaching, or in an oxygen-enriched atmosphere. Thus, these seeds possess true embryo dormancy.

For these experiments plants were grown in a greenhouse during March-June, 1959. When the endosperm of the seeds had reached the 'milk stage' the stems were cut below the node of the youngest leaf and the cut end placed in an Erlenmeyer flask containing 200 ml. of an aqueous solution of gibberellic acid (potassium salt). In the preliminary experiment three plants were placed in each flask containing the concentrations 0, 10⁻³, 10⁻⁴, 10⁻⁵, 10⁻⁶, or 1000 p.p.m. gibberellic acid and kept in the greenhouse. When the solutions had been taken up, the flasks were replenished with distilled water. The seeds were collected at maturity (8-10 days after initiation of the experiment) and after a further 2 days they were tested for germination capacity. In this test seeds were placed in Petri dishes on filter paper moistened with a standard volume of a mixture of antibiotic solutions (Candidin 250 p.p.m., Neomycin 20 p.p.m.) which prevented fungal and bacterial growth, and kept in darkness at 20° C. and 100 per cent relative humidity. Twenty intact 'seeds' (caryopsis surrounded by hull) and 20 isolated caryopses were tested in each case. After 10 days the percentage germination of caryopses from plants treated with 10, 100 and 1,000 p.p.m. were 75, 100 and 100 per cent respectively. Similarly, intact 'seeds' germinated 30, 25 and 50 per cent respectively. The intact 'seeds' and isolated caryopses from those plants treated with distilled water did not germinate even after 20 days in the germination test.

This experiment was repeated using the same technique except that 6 plants were placed in each flask containing either 200 ml. distilled water, 10, 100, or 1000 p.p.m. gibberellic acid. After harvesting, the germination capacity of isolated caryopses was tested. For each experimental group, two replicates both consisting of 50 caryopses were employed.

The results shown in Fig 1 indicate the rate of germination. Clearly, treatment of plants with gibberellic acid resulted in the production of non dormant seeds. The effect here is particularly remarkable when it is remembered that even isolated embryos of seeds from normal, untreated plants are strongly dormant.

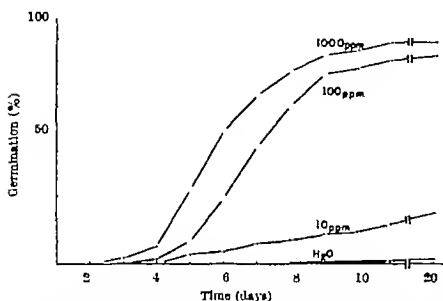


Fig 1 Germination of isolated caryopses from plants treated with water 10, 100 or 1000 p.p.m. gibberellic acid. Points on the curves represent the mean of 3 replicates each comprising 50 embryos. The standard deviation for all points was less than 2.

The most plausible and simplest explanation of these results is that gibberellic acid was transported into the seeds during development thus rendering them capable of spontaneous germination when placed subsequently under germination conditions.

In these experiments the gibberellin content of the seeds was augmented artificially. We have found that seeds of this species contain gibberellin like substances, and presumably, if in the development of the seeds the level of these naturally occurring gibberellins were increased there would likely be no rest period. Further it might be pointed out that results of experimental work in progress in this laboratory indicate that the beneficial effect of gibberellic acid depends on an antagonism between this substance and an endogenous inhibitor. It is an interesting speculation that differences in the level of naturally occurring gibberellins and inhibitors might be of general significance in the onset and maintenance of seed dormancy.

A similar effect has been reported by Lippert and his co-workers⁵ who produced non dormant potato tubers by treating the tuber bearing plants with gibberellic acid solution.

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MICROBIOLOGY

Microbiological Transformation of a Cardiac Aglycone

It has been shown recently by Brown and his co-workers¹ that when digitoxin was administered to rats or to adult humans some of it underwent hydroxylation at C₁₂ to give digoxin. This fact, suggestive of the possibility of such bioconversions to be effected by micro-organisms as well, prompted us to investigate microbiological transformation of the cardiac glycosides and their aglycones. In this communication we wish to report that the C₁₂ and C₁₃ hydroxylations of digitoxigenin.

Incubation of digitoxigenin was conducted with cultures of various species of micro-organisms. Extraction of the culture broths with ethyl acetate followed by concentration of the solution afforded crude extracts which were submitted to the examination of products by paper partition chromatography under the following conditions: Toyo Filter Paper No 51 developing solvents system 1, benzene ethyl acetate water (8.5:4)², system 2 benzene:methanol:water (5:3:2)³ ascending method at 20° C reagents trichloroacetic acid³ and 3,5-dinitrobenzoic acid⁴. Each case was accompanied by blank incubation (that is incubation with no substrate) for the purpose of comparison. The results of the experiments showed that at least three fungi among the strains of microorganisms examined, namely *Helicostylum puriforme* Bañier, *Cunninghamella blakesleeana* Lendner and *Gibberella fujikuroi* (Saw.) Wt., were able to convert digitoxigenin into other substances.

Helicostylum puriforme. On the paper chromatogram were observed two distinct spots, one of which had an R_F of 0.70 (system 1) or 0.12 (system 2) and the other an R_F of 0.49 (system 1) or 0.05 (system 2). These R_F values were indistinguishable from the respective R_F values obtained on concurrent chromatography of authentic digitoxigenin and digoxigenin. The rate of formation of digoxigenin seemed fairly higher than that of digitoxigenin. Under other fermentation conditions these products were not detected but another spot was found having an R_F of 0.35 (system 2) formation of which was more evident in the case of *Cunninghamella*.

Cunninghamella blakesleeana. Two intense spots of products appeared on the paper chromatogram. One of them exhibited an R_F of 0.80 (system 1) or 0.35 (system 2) which was not consistent with any of the R_F values of the so far known aglycones of digitoxigenin and the product awaits further scrutiny. The other of the two spots showed an R_F of 0.68 (system 1) or 0.12 (system 2) and coincided in R_F value with authentic digitoxigenin. The yield of the latter product was apparently somewhat lower than in the former case.

Gibberella fujikuroi. The product had an R_F of 0.46 (system 1) or 0.03 (system 2) and was identical with authentic digoxigenin.

Digitoxigenin and digoxigenin thus identified were further confirmed by comparison of their coloration and fluorescence on paper chromatogram and other properties with those of respective authentic samples.

Thus, we were able to find three strains of microorganisms which convert digitoxigenin into digitoxin, digoxigenin, or an unknown product and could open up future possibilities of microbiological transformation of cardiac glycosides for obtaining more useful compounds.

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cipate that a study of preservation under controlled conditions of water vapour pressure should enable a substantial improvement in recovery following storage.

We wish to express our appreciation for the assistance of Mr H F Harnor and Mr W L Campbell of the Maryland West Virginia Artificial Breeders Co-operative in supplying experimental material and in carrying out the insemination.

The opinions or assertion contained herein are our own, and are not to be construed as official or reflecting the views of the Navy Department or the Naval Service in general.

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Fractionation of the System Bringing About Oxidative Phosphorylation in *Azotobacter vinelandii*

RESPIRATORY CHAIN phosphorylation in a particle fraction of *Azotobacter vinelandii* is inactivated by incubation of the suspension in salt concentrations less than 0.01 M potassium chloride or sodium chloride, or 0.0008 M magnesium chloride, manganese chloride or calcium chloride. This inactivation is partially reversed by adding salts back to the inactivated suspension.¹ It has now been found that the inactivated suspension can be fractionated by centrifugation at 50,000 g for 30 min. The sediment contained 85-90 per cent of the reduced diphosphopyridine nucleotide oxidase activity, but restoration of oxidative phosphorylation was not possible unless the suspension was pre-incubated with the supernatant from this high-speed centrifugation, as well as with magnesium chloride (Table 1). Although after pre-

Table 1 REACTIVATION OF OXIDATIVE PHOSPHORYLATION BY A SOLUBLE COMPONENT

| Experiment | Pre-incubation mixture | | | | | Oxidative phosphorylation | |
|------------|------------------------|------|------|-------------------------|----------------|---|------------------------|
| | WSP | WSP* | WSP* | Serum albumin (0.005 M) | S ₂ | Time needed to complete oxidation (minutes) | P/O ratio (calculated) |
| 1 | + | - | - | + | - | 4.3 | 0.51 |
| | - | + | - | - | - | 4.5 | 0.42 |
| | - | - | + | - | - | 3.1 | 0.36 |
| | - | - | - | + | + | 5.3 | 0.03 |
| | - | - | - | - | + | 5.5 | 0.19 |
| 2 | + | - | - | + | - | 5.3 | 0.67 |
| | - | + | - | - | - | 5.3 | 0.16 |
| | - | - | + | - | - | 4.3 | 0.62 |
| | - | - | - | + | - | 2.5 | 0.09 |
| | - | - | - | + | + | 2.3 | 0.23 |
| | - | - | + | + | + | 1.5 | 0.11 |
| | - | - | + | + | + | 1.3 | 0.10 |
| | - | - | + | + | + | 1.3 | 0.19 |
| | - | - | + | + | + | 1.3 | 0.40 |
| | - | - | + | + | + | 1.3 | 0.40 |

WSP: washed small particles obtained by centrifugation for 2 hr at 140,000 g (bottom of tube) (ref. 9); suspended in 0.03 M Sorbeson phosphate buffer, pH 7.0. WSP*: washed small particles suspended in 0.005 M phosphate buffer, pH 7.0, for 30-60 min. at 0°. WSP†: sediment after centrifugation of WSP* for 30 min. at 50,000 g. S₂: supernatant obtained from this centrifugation.

The mixtures indicated were pre-incubated for 90-120 min. at 0° and were then added to a reaction medium used to measure oxidative phosphorylation with reduced diphosphopyridine nucleotide as substrate.

* S₂ was heated at 100° for 5 min. and filtered.
† S₂ was not present in the pre-incubation mixture but was added immediately before the measurement of oxidative phosphorylation.
‡ Three times as much S₂ as used in the measurements with WSP*

incubation this supernatant alone also catalysed oxidative phosphorylation, the oxidase activity was much too low to account for the increased P/O ratio obtained with particles preincubated with magnesium chloride and supernatant. It appears, therefore that the supernatant contains a factor which is necessary for the restoration of the activity of inactivated particles. This factor is destroyed by heating for 5 min. at 100°.

This fractionation resembles that carried out by Pinchot² with extracts of *Alcaligenes faecalis*. The conditions leading to the reversible inactivation of the phosphorylating system in *Azotobacter* are similar to those which bring about a reversible dissociation of a two stranded polynucleotide complex³, or, so far as decreasing the magnesium concentration is concerned to the dissociation of ribonucleoproteins in particles obtained from yeast⁴ and *Escherichia coli*.⁵ This provides some support for Pinchot's² suggestion that in his preparations a polynucleotide acts as a bridge holding together the necessary enzymes. It is possible that a factor necessary for oxidative phosphorylation in the particles obtained from *Azotobacter* is bound to the particles by means of such a polynucleotide complex which dissociates on lowering the cation concentration.

These experiments with *Azotobacter* recall also recent reports on the fractionation of the phosphorylating enzymes in particles derived from beef heart mitochondria.⁶ Phosphorylation was obtained by bringing together a particulate fraction (containing the oxidase), a soluble fraction and magnesium. Linnane⁶ found that no fractionation took place in the presence of magnesium.

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Transformation Reaction of Pneumococci in the Absence of Serum Factor

CONTRARY to the general proposition that transformation reactions of pneumococci cannot take place in the absence of serum factor¹⁻³ our experiments^{4,5} indicated that cells of R36NG, a pneumococcal rough strain derived from 11 D30S could be transformed to streptomycin resistant ones by means of purified deoxyribonucleate in diffusate media. But in these experiments deoxyribonucleate was kept present throughout the culture growth and the cultivation was continued overnight before plating on streptomycin plates, so that the population change after the occurrence of transformation reaction might have distorted the results. This possibility was completely excluded in the present experiment by the use of deoxyribonuclease which was added to the reaction mixture to stop the action of deoxyribonucleate at a definite time.

Streptomycin sensitive R36NG from a blood agar slant was inoculated into Adams and Ross medium⁶ and incubated overnight. The culture was added next morning to 4 volumes of fresh medium and

incubated for about 2 hours more until it showed good visible growth. One part of the preliminary culture and 17 parts of the medium were mixed and 1.8 ml of the mixture was distributed in test-tubes and incubated at 37°C. At a definite time 0.2 ml of deoxyribonucleate solution (100 µgm per ml) was added and 30 minutes later its action was stopped by adding one drop of deoxyribonuclease solution. The cultures were incubated further for 90 minutes in order to allow the streptomycin resistance to develop completely. One of the results is shown in Table 1. The

Table 1 TIME OF APPEARANCE OF COMPETENT CELLS

| Time of exposure to deoxyribonuclease (hr min)* | Number of resistant colonies (Quadruplicate experiments)† | | | |
|---|---|-----|---|-----|
| 0:00-0:30 | 0 | 0 | 0 | 0 |
| 0:30-1:00 | 0 | 0 | 0 | 0 |
| 1:00-1:30 | 0 | 0 | 0 | 0 |
| 1:30-2:00 | 0 | 0 | 0 | 0 |
| 2:00-2:30 | 18 | 0 | 0 | 0 |
| 2:30-3:00 | ‡ | ‡ | ‡ | 25 |
| 3:00-3:30 | ‡ | ‡ | ‡ | 201 |
| 3:30-4:00 | ‡ | 120 | 1 | 0 |
| 4:00-4:30 | 0 | 0 | 0 | 0 |
| 4:30-5:00 | 0 | 0 | 0 | 0 |

* Time from the start of the cultures

† Number of resistant colonies which appeared from 0.1 ml of the culture containing no serum

‡ Colonies covering large part of plate

§ Isolated but innumerable colonies

mean rate of transformation in 4 tubes between times 3:00 and 3:30, was about 0.05 per cent.

The effect of serum was next studied. The preliminary culture was grown in the absence of serum. In one series, one part of this culture, and 2 parts of normal horse serum (heated at 60°C for 30 minutes) and 15 parts of the medium were mixed, and 1.8 ml of this mixture was distributed in test tubes. In another series, no serum was added. As shown in Table 1, the test-tubes under the same conditions contained varying numbers of transformants, so in this case 3 tubes were subjected to the same conditions. Immediately after the addition of deoxyribonuclease a definite volume of culture was taken from each tube and mixed, and all the viable cells in it were counted. The number of transformants in the mixture from

3 tubes was counted after 90 minutes' incubation for phenotypic lag. Fig. 1 shows an example of these experiments. The number of whole viable cells in test-tubes containing serum was larger after 150 minutes' incubation than in those containing no serum. But more remarkable effects of serum were found in the number of transformants and their appearance. The competent cells, which are able to react with deoxyribonucleate appeared about one hour earlier, were present for a longer period of time and were more numerous in the presence of serum than in its absence.

These results throw doubt on the claim that serum factor is essential for pneumococcal transformation. In the system used here serum, as in the case of *H. influenzae*?, is not indispensable, but it may be an accessory factor, the effects of which appear to be related to the pattern of appearance of competent cells.

According to the generally accepted view, in order to study the mechanism of the transformation reaction in pneumococci, one has to consider 4 components, a competent strain, a transforming principle (deoxyribonucleate), a suitable medium for growth and serum factor. But the results of the present experiment have shown that the serum factor can be eliminated, and as a consequence the reaction system to be analysed has been made simpler.

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Incorporation of 5-Bromouracil into Transforming Principle of *Bacillus subtilis* and its Biological Effects

THE incorporation of 5-bromouracil into deoxyribonucleic acids of bacteria and bacteriophage¹ raised a problem concerning the biological effects of such incorporation. It has been shown that at least some of the cells of *Escherichia coli* containing 5-bromouracil in their deoxyribonucleic acid remain alive². Further evidence on this subject was obtained by the demonstration of the mutagenic effect of 5-bromouracil³; these results also indicated that 5-bromouracil was incorporated into molecules of deoxyribonucleic acid that functioned as heredity determinants. Similar results have been obtained with bacteriophage⁴.

It appeared of interest to make a further study of the above problems by the incorporation of 5-bromouracil into deoxyribonucleic acid that has transforming activity. The incorporation of 5-bromouracil into deoxyribonucleic acid of *Hemophilus influenzae* thus far could not be demonstrated⁵ presumably because this organism could not be grown under conditions in which it would require exogenous thymine. New possibilities have been opened by Dr. J. Spizizen's discovery of the transformation in *Bacillus subtilis*⁶, an organism easily cultivated on synthetic media. In preliminary experiments, the cultivation of the wild strain of *B. subtilis* in enriched broth⁷ containing 4 mgm of 5-bromouracil per ml did not result in a

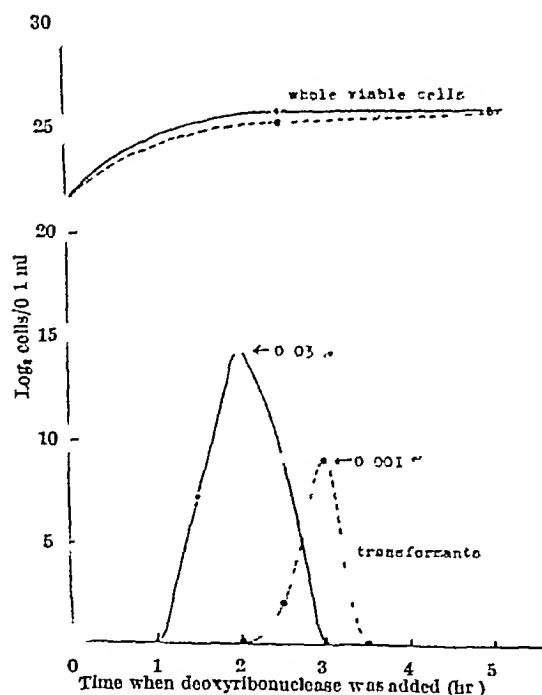


Fig. 1 Effect of serum —, 10 per cent serum, ----, no serum

demonstrable incorporation of this analogue into deoxyribonucleic acid. Use was therefore made of the fact that the uracil requiring strain may also partially require thymine and that aminopterin can be used to prevent endogenous methylation thus resulting in an uptake of exogenous thymine analogue.*

As donor of deoxyribonucleic acid (transforming principle) served a uracil requiring strain 265 of *B. subtilis*, kindly supplied by Dr Robert Guthrie, Children's Hospital, Buffalo. The strain was grown with aeration at 37° for 20 hr in enriched broth⁷ containing 200 µgm of 5 bromouracil and 200 µgm of aminopterin per ml. The cells were washed five times with 0.85 per cent sodium chloride solution and resuspended in a similar solution made 0.05 M with respect to sodium citrate and containing 1 mgm of crystalline egg lysozyme per ml. The cell suspension was shaken 15 min at 37°. It was observed that cells grown in the presence of 5 bromouracil and aminopterin were not lysed by lysozyme alone but did lyse upon the addition of a 15 per cent Duponol C solution to obtain final Duponol concentration of 5 per cent. This phenomenon is being investigated further.

Highly polymerized deoxyribonucleic acid was isolated and 5 bromouracil content therein determined as described in ref 7. The molar ratio 5 bromouracil 5 bromouracil + thymine was 12 per cent (average of 4 determinations).

For preparation of the transforming principle an aliquot of isolated deoxyribonucleic acid was deproteinized, precipitated and stored as described in ref 6.

The transforming principle prepared as above as well as the control one prepared in a similar way but with the omission of 5 bromouracil and aminopterin

from the broth were used in transformation experiments performed as described in ref 6 using as receptors the following strains: mutant 168 (indole-), kindly supplied by Dr T Spizizen; a methionine-mutant, *anarginine* mutant and a *pyridoxine* mutant isolated in this laboratory after ultra violet irradiation.

Table 1 TRANSFORMING ACTIVITY (*Bacillus subtilis*) OF DEOXYRIBONUCLEIC ACID CONTAINING 12 MOLE PER CENT OF 5-BROMOURACIL

| DNA µgm/ml | Transforming activity* | | | |
|---------------|------------------------|----------|------------|---------|
| | Pyridoxine | Arginine | Methionine | Indole |
| 1 | 42 (±10) | 23 (±10) | 94 (±4) | |
| 0.1 | 38 (±8) | 20 (±7) | 66 (±6) | 60 (±6) |
| 0.01 | 7 (±1) | 19 (±3) | 25 (±2) | 91 (±4) |

* In per cent of control without 5-bromouracil

The results are represented in Table 1 (average of 4 transformation experiments) and in Fig 1 (a typical experiment). First, it will be seen that in general the deoxyribonucleic acid containing 5 bromouracil has transforming activity. In the case of transformation from indole dependence to independence (indole marker) the transforming activity is not significantly affected in the cases of other markers, the activity is decreased to a degree different for each marker. These results could be interpreted to signify that either the activity of each marker is affected differently* by the same amount of analogue or else that the amount of the analogue in each marker is different, for example if normally the amount of thymine in each marker is different.

We wish to thank Dr J Spizizen for his advice on the transformation of *B. subtilis* and Mr Kenneth Rich for technical assistance.

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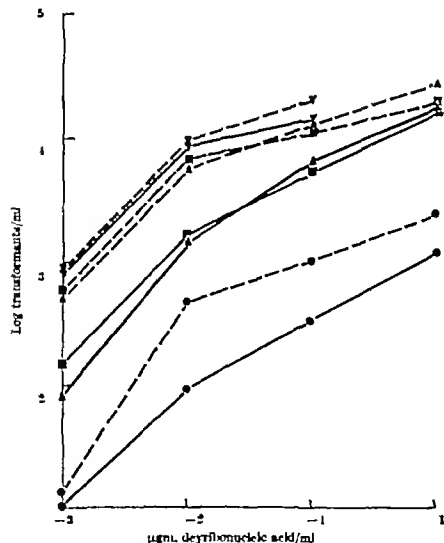


Fig 1 Comparison of transforming activities between deoxyribonucleic acid containing 5-bromouracil and normal acid of *B. subtilis*. Dotted line normal deoxyribonucleic acid, full line acid containing 5 bromouracil. Transformation from dependence (-) to independence (+) for the following markers: arginine (○) pyridoxine (△) methionine (■) and indole (●)

Psittacosis Elementary Bodies

In the course of an investigation of the developmental cycle of psittacosis virus certain morphological features of the mature elementary bodies have been observed.

Changes occurring in the appearance of the virus during a single stage infective process were studied by electron microscopy of ultra thin sections of chorio allantoic membrane of 8-10 day old chick embryos. The virus strain MOH 154, originally obtained from Sir Sam Bedson was adapted by repeated passage to grow on the chorioallantoic membrane which in 24-48 hr became oedematous and developed opaque white lesions. Membranes were harvested at timed intervals, fixed in a buffered osmium tetroxide solution and embedded in methyl and butyl methacrylate.

tivity value. Recently, Danielli⁴ has amended this relationship to the linear form

$$\log (M^{q+})_b = \frac{\varphi F}{RT} + \text{constant} \quad (1)$$

where $(M^{q+})_b$ is the concentration of metal cation of valency q in the bulk phase which gives the standard toxicity, φ is the electronegativity of the metal, F one faraday, R the gas constant, and T the absolute temperature. The arguments in favour of an equation of this type, which assumes that toxicity is dependent on the formation of an unionized complex between metal ions and cell surface components, have been given by Danielli⁵ in an earlier paper.

It was decided to investigate further the validity of equation (1) with reference to the fungitoxicity of metal salts many of which, particularly those of the heavy metals, are widely used as fungicides. The toxicities of aqueous solutions of nitrates of potassium, sodium, thallium, silver, barium, strontium, magnesium, zinc, manganese, beryllium, copper, nickel, mercury, lead, palladium, cerium and yttrium, of the sulphates of lithium and chromium, and of ruthenium chloride and osmium tetroxide were determined against conidia of *Alternaria tenuis*. The solutions were unbuffered and no spore stimulant was required. The standard test-tube dilution spore germination technique⁶ was used and the median effective dose (ED_{50}) determined visually from the probit regression lines. In Fig. 1 the logarithms of the ED_{50} values for the metal ions have been plotted against the electronegativities of the metals and fair agreement with the linear relationship proposed by Danielli is achieved, although all the metals do not share a common anion. The electronegativity values in Fig. 1 are from Pauling⁷, Gordy⁸, and Danielli and Davies³ (chromium, nickel, manganese, mercury, copper and lead) whilst the values for palladium, cerium, ruthenium and osmium are calculated from the first ionization potentials of the metals by the method suggested by Pauling⁷. Because of some uncertainties in Gordy's values for mercury, copper and lead it was decided to use the values of Danielli and Davies³ for these elements.

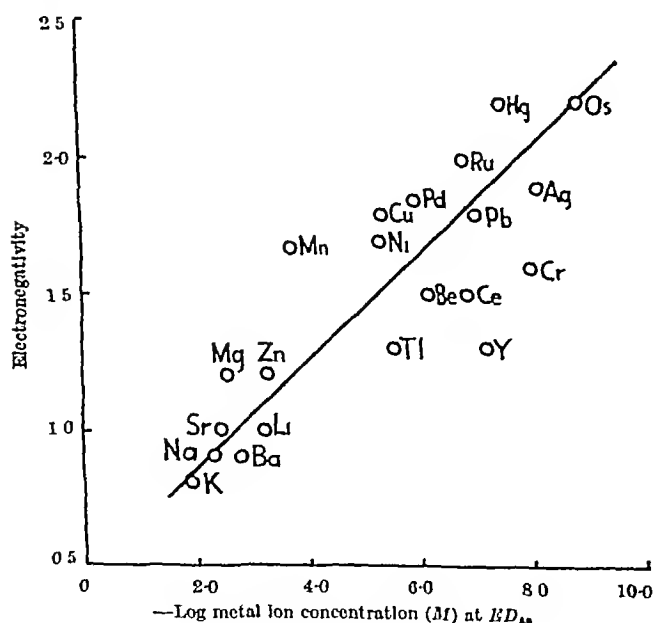


Fig. 1 A plot of the toxicity of metal cations to *A. tenuis* against the electronegativity of the metal

Horsfall⁹ has suggested that the fungicidal action of metal ions is primarily due to interaction at the fungal cell surface. The present work lends support to this hypothesis by showing that for the wide range of metallic salts examined, a general relationship of the type of equation (1) holds. Thus, it would appear that the primary toxic action of metal cations is the formation of an unionized complex with surface ionogenic groups, for example, phosphate, carboxyl and SH, and that the different toxicities of the metals can be correlated with the varying strength of surface binding.

A fuller account of this work will be published elsewhere.

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HISTOLOGY

Histochemical Localization of Oxidase Activity in the Mitochondria of the Human Heart

A REVIEW of the literature has failed to reveal any definitive histochemical localization of oxidase activity in cardiac as well as skeletal muscle. Recently, several new oxidase techniques have been reported which are capable of precise localizations at the cytochemical level.^{1,2}

In the present study, frozen sections (8 μ thick) of human heart muscle (obtained at autopsy and surgery) were prepared according to the Adamstone-Taylor cold-knife technique and mounted on chemically clean glass microscopic slides. They were incubated for 30 min at room temperature (about 24° C) in a substrate solution containing 10 mgm. N-phenyl-*p*-phenylenediamine (*p*-aminodiphenylamine) (British Drug Houses, Poole, England) and 10 mgm. *p*-methoxy-N-phenyl-*p*-phenylenediamine (varianine blue B base) (Carbic Color and Chemical Co., New York). The substrates were first placed in a 50.0 ml. Erlenmeyer flask and dissolved in 0.5 ml. reagent ethanol. Thirty-five ml. distilled water were added followed by 15.0 ml. 0.2 M tris buffer pH 7.4. The solution was shaken and filtered through folded filter paper into a Coplin jar. Incubating solutions containing 0.001 M potassium cyanide as well as 0.001 M sodium sulphide were also used. In addition the effect of adding cytochrome *c* (Sigma Chemical Co. St. Louis, Mo.) (20.0 mgm. per Coplin jar) to the substrate solution was observed. Some sections were pretreated with physiological saline for 30 min prior to incubation. These sections were afterwards incubated in substrate solutions with and without cytochrome *c*.

Following incubation, slides were transferred to a 10 per cent solution of cobaltous acetate in 10 per cent formalin containing 5.0 ml. 0.2 M pH 5.2 acetate buffer for 1 hr. They were then washed in running water for about 5 min and mounted in glycerol-gelatin or polyvinyl pyrrolidone.³



Fig. 1 Oxidase activity of mitochondria of human heart. Arrow points to intercalated disc ($\times 800$)

With routine incubations the distribution of dye corresponded to that observed with classical mitochondrial stains (for example, Regaud) (Fig. 1). An interruption of staining was observed in the intercalated disks. The localizations corresponded exactly to those described for heart sarcosomes (mitochondria) by Cleland and Slater¹ who employed the Altmann mitochondrial technique. The distribution of staining also appeared to correspond to the sarcosome pattern as seen with the electron microscope². In some areas intense perinuclear staining which corresponded to the localization of perinuclear sarcosomes, was observed.

Cyanide and sulphide completely inhibited the reaction as did pre incubation in physiological saline. However, the reaction in the saline treated sections was completely restored by addition of cytochrome c to the substrate solution. Addition of cytochrome c to routine incubation solutions augmented the staining intensity. Cytochrome oxidase is believed to be associated with mitochondria. Thus the localization of the staining reaction to mitochondria, as well as the results of the inhibitor and cytochrome c tests would indicate the presence of cytochrome oxidase.

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ANIMAL PATHOLOGY

Sex Chromatin in Cultured Human Tissues

The sex chromatin clump of Barr has been reported as occurring in human female tissues cultured *in vitro* for short periods, and as not occurring in long established cultures.^{1,2} The purpose of this communication is to provide a quantitative summary of the available knowledge in this respect and to indicate that sex chromatin apparently occurs routinely in suitably stained primary explants but not in long cultured cells.

Thus far sex chromatin has been reported in 7

benign outgrowths in 3 presumably cancerous growths from primary explants of human tissues and in an unspecified number of primary explants of thyroid tissue.³ In addition there have been reports of the absence of sex chromatin in 3 long term cultures known to be of female origin, that is, H.Ep No. 1, H.Ad No. 2 and HeLa.⁴ 10 cultures of male origin have been reported as essentially negative.

Herein are reported 38 new cases, 29 of female origin and 9 of male. With the exception of 1 amnion culture none of the male cells showed characteristic sex clumps. The one exception showed peripheral clumps with an incidence ranging to 12 per cent. Such positive cells were presumed to be contaminants of maternal origin. This case with other amnion cultures will be discussed in greater detail in a subsequent publication.

Of the 29 tissue cultures of female origin 6 were classified as cancer and 23 as benign. The malignant cultures were so called only if they were derived from cancer and showed the appropriate cytological characteristics *in vitro* growth. This precaution in classification is necessary since many primary explants of cancer tissue give rise only to cytologically benign fibroblast like cells presumably of stromal origin.

Of the benign cultures 11 were derived from lesions of the uterine cervix, 9 from amnions of female infants, 2 from thyroid lesions, and 1 from an endometrial carcinoma. Of the cultures exhibiting cancer characteristics *in vitro* 4 stemmed from epidermoid carcinomas of the cervix, and 2 from ovarian carcinomas.

20 of the 29 cultures displayed characteristic peripheral sex chromatin clumps in at least some of the cells. In a number of cases the incidence appeared low but this may probably be attributed in part to fading of the stain in the older preparations. The negative cases comprised the 2 arising from ovarian carcinomas and 1 arising from an amnion. These cultures were respectively approximately 24 months, 34 years and 24 years of age. The youngest was in the 8th transfer. The amnion was that designated A185 by Zitter and Dunnebaek.⁴ Samples of the 4 subline strains Nos. A1, A2, A3 and A4 were all negative. The sex chromatin positive cultures varied from 2 to 55 days in age. One was carried through 5 transfers, none of the rest through more than 3.

These cases with those previously reported justify the tentative inference that sex chromatin clumps appear invariably in the primary explants of human female tissues—benign or cancerous but that the sex chromatin feature is eventually lost in later transfers. Further evidence on this point is provided by recent primary explants of H.Ad No. 1. H.Ad No. 1 is a tumour of female origin which has been maintained in heterotransplant for almost 3 years and 70 generations.^{5,6} The recent explants in tissue culture do exhibit sex chromatin in contrast to the culture previously reported as negative.³ In this one case a change (loss of sex chromatin) which occurs in tissue culture does not occur in heterotransplant. As previously reported³, the culture of H.Ad No. 1 which did not show sex chromatin had been *in vitro* for 14 months. If our assumption is correct, this would represent the earliest reported loss of sex chromatin. The longest reported survival of sex chromatin appears to be in the case described by Orsi and Ritter⁷ as 10 weeks, 9 transfers. Sex chromatin might eventually prove to be a convenient indication that cells cultured *in vitro* have not undergone transformation. On the other hand while preliminary

cloning experiments do not favour such a possibility, it has not definitely been ruled out that 'transformation' of female cells into established strains is actually a process of selecting the sex chromatin negative cells in the original explant.

Whether or not the 2½-year-old negative female amnion culture reported here had become malignant, it did show a very high mitotic rate (74 mitoses per thousand cells in one count), and moderate variation in nuclear size. It may be true that the hypothetical development of cancer in tissue cultures of benign origin is invariably accompanied by a loss of sex chromatin. Since primary explants of female cancer developing *in vivo* have invariably shown sex chromatin *in vitro* when appropriately stained (but not always in tissue section²), it seems that at least in this one respect hypothetical malignant change *in vitro* is not identical with cancer development *in vivo*.

I wish to express my thanks to Dr J G Moore and Mr W W Brandkamp of this University who kindly permitted me to examine a series of their primary explants of cervical tissue, to Dr T H Dunnebaeke of the University of California at Berkeley who provided me with stained coverslip samples of a number of cultures, and to Dr H W Toolan of Sloan-Kettering Institute New York, and Miss M Tai who provided recent material from H Ad No 1.

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Detection of Thyroid Antibodies using Bentonite Particles

DEMONSTRATION of circulating thyroglobulin antibodies by the gel diffusion-precipitation technique is a simple procedure which can be used for routine laboratory diagnosis of Hashimoto's thyroiditis¹. Witelsky and Rose², Rolit and Doniach³ and Owen and Smart⁴ have also applied Boyden's tannic acid haemagglutination technique for detection of thyroid antibodies and have demonstrated its greater sensitivity over the precipitation technique. The tannic acid haemagglutination technique is however in our experience, less easy to adapt as a routine procedure because it is complex in its performance and requires minute attention to detail to produce consistent results. A recent report by Bozicevich *et al* on the successful use of bentonite particles, coated with human γ -globulin, in the detection of the rheumatoid serum factor prompted us to try this substance sensitized with thyroid antigen in the detection of thyroid antibodies.

Thyroid glands removed at autopsy were stripped of their connective tissue, weighed and then blended with twice their weight of physiological saline in a Kenmix blender for 10 min. The resulting homogenate was spun at 4,000 r.p.m. for 10 min to remove heavy cell debris and fibrous tissue. The supernatant from this centrifugation was then spun in a high-speed centrifuge at 27,000 r.p.m. for 45 min at 4°C. The supernatant was removed and stored at -20°C for use in both precipitation and bentonite sensitization tests.

Bentonite is a native colloidal hydrated aluminium

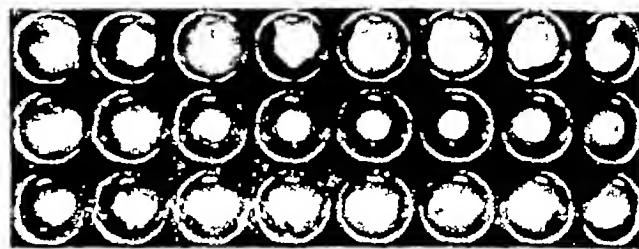


Fig. 1. A positive serum of titre 1 in 2,000 from a case of Hashimoto's disease compared with two normal sera in rows 1 and 3.

siliente, insoluble and free from gritty particles. 2.5 gm of bentonite (B D H) are added to 300 ml. of distilled water in a flask and thoroughly shaken to mix. 25 ml. of this mixture is transferred to a universal container which is then centrifuged at 3,000 r.p.m. for 10 min. The supernatant is discarded and replaced with 25 ml. of distilled water, the container shaken vigorously to mix and then recentrifuged. This process is repeated twice. At the end of the final wash the supernatant is removed and 2 ml. of thyroid antigen is added and mixed. After standing for 1 hr at room temperature the sensitized bentonite particles are washed twice in physiological saline and finally resuspended in 25 ml. of physiological saline.

Serial dilutions of the sera to be tested are made, as described by Rolit and Doniach³, in 'Perspex' agglutination trays. The dilutions range from 1/5-1/2,500,000 and are made with a single pipette using 0.25 ml. volumes and 2 per cent serum saline as a diluent. An antigen inhibition control is included. 0.1 ml. of sensitized bentonite is then added to each dilution and the trays placed in the refrigerator at 4°C overnight. The pattern of the deposited bentonite particles is read macroscopically and shows the opposite pattern to that encountered with red cell agglutination. Positive agglutination is shown by a small central round button of agglutinated particles and negatives by a thin carpet of bentonite over a wide area of the bottom of the cup (Fig. 1). Weak positives show a central button with a small carpeting around. The end-point is often sharp with no zone of weak positives, and weak positives are only included in the titre if the central button is well defined with little carpeting.

Care must be taken not to jog or disturb the trays after their removal from the refrigerator as this may result in false positives or alteration of titre.

Sensitized bentonite suspensions were used in titrating sera from a variety of cases of thyroid disease and from cases with no thyroid abnormality. In known cases of Hashimoto's disease, with positive precipitin tests, titres up to 1 in 25,000,000 were observed (cf. Owen and Smart⁴). Lower titres of the order 1/5-1/250 were found in a number of other types of thyroid disease. Occasional normal sera gave weak positives at a dilution 1/5. In comparing titres and for controlling the test we use a standard known positive serum and a normal serum together with an antigen inhibition control.

These results suggest that bentonite sensitized with thyroid antigen may be superior to tanned red cells for the detection of thyroid antibodies because of the ease of preparation and the simplicity of the technique.

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Relation of Invasive Capacity to Passage of Lymphocytic Cells through Cellulose Membrane Filters

In a previous paper¹ it was reported that when three lymphocytic tumours each with a different capacity to invade host tissues, were grown in Millipore Type AA filters (pore size $0.8 \pm 0.05\mu$) (Millipore Filter Corporation Bedford, Mass.) in double diffusion chambers the cells of the tumours were unable to penetrate the filter after growing for 60 days in an isologous host. More recent experiments with this filter have shown that while the cells of these tumours are able to pass through the AA filter there is nevertheless a striking difference in the capacity of the cells of an invasive and a non-invasive tumour to penetrate the pores of this membrane and establish a growing cell population on the other side.

The procedures for the construction of diffusion chambers and for introducing the cells into the chambers have been described in detail elsewhere.¹ The cells of the highly invasive lymphocytic leukaemia, L1210 and the relatively non-invasive lymphoma L1 were grown as ascites tumours in strain DBA/2 and strain A mice, respectively. Known numbers of tumour cells were placed on one side ('tumour side') of double diffusion chambers, the chambers sealed and inserted by laparotomy into mice of the host strain. Four sets of chambers were prepared as shown in Table 1.

One half of each set of chambers was removed from the animals after 30 days and the remainder after 120 days. The chambers were opened by cutting away the outer filters with a sharp knife to expose the AA filter in the centre and the contents of the two sides of the double chamber. The 'tumour' and 'non tumour' sides of the chambers were examined and an estimate was made of the amount of tumour tissue on the 'tumour side'. When no growth was visible on the 'non tumour'

side, the fluid was centrifuged and the sediment examined microscopically for the presence of cells. The cells on the centre filters were fixed in Orth's fluid and stained with haematoxylin.

Table 1

| Tumour | Set | Chambers (No.) | Tumour age (Days) | Number of cells (millions) | |
|-------------------------|-----|----------------|-------------------|----------------------------|--------|
| | | | | Tumour | Normal |
| L1 Generation 33 | A | 20 | 5 | 1.4 | 0.6 |
| | B | 20 | 13 | 1.3 | 0.06 |
| L1210 Generation 263 | C | 20 | 2 | 1.4 | 0.2 |
| | D | 20 | 5 | 1.4 | 0.05 |

The initial age of the tumour when placed in the chambers (Table 1) had no detectable effect on their behaviour. The cells of L1210 penetrated the AA filter during the first 30 days in the animal and established a visible amount of growth on the 'non tumour side' of the chambers. By 120 days the growth of the tumour, which appeared as a mass of white, pasty material, was equal in amount on both sides of the chamber. Examination of the 'non tumour' side of the AA filter in stained whole mount preparations showed L1210 cells sprinkled among flattened macrophages on the under surface of the filter (Fig. 1, top).

The behaviour of L1 differed markedly from L1210 in that growth of tumour was never macroscopically visible on the 'non tumour' side of the chambers. It was known from previous experiments that the L1 tumour did not have the growth potential of L1210 and indeed at 30 days L1 had not grown to the same mass as L1210 but by 120 days the volume of the growing cell mass of each tumour was roughly equal. At this time the 'tumour side' of the chambers were one half to completely full of packed cells. Thus, the mass of tumour tissue did not appear to be related to the penetration of the filter by the tumour cells.

When the sediment of the centrifuged fluid of the 'non tumour' side of the L1 chambers was examined with the phase microscope a few small lymphocyte-like cells with a thin rim of cytoplasm were seen at 30 days but by 120 days these free floating cells were no longer present. Although growth appeared to be healthy on the 'tumour side', (Fig. 1, bottom) living tumour cells were observed on the 'non tumour side' of only one L1 chamber after 120 days in the animal. With this exception, examination of stained filters failed to reveal viable tumour cells on the 'non tumour side' of the chambers; instead the only living cells were the macrophages that spread over the filter surface (Fig. 1 middle). In addition to the macrophages there were occasional clumps of rounded up cell ghosts with pyknotic and fragmented remains of nuclei. These appeared to be dead tumour cells and were identified thus because these dead cell clumps do not occur in chambers where only normal peritoneal cells are grown.

These results clearly demonstrate that two tumour cell populations, given an equal chance may or may not be able to penetrate an artificial barrier and establish growth at a distant site. It seems probable that some of the same mechanisms which operate in the artificial system of the diffusion chamber can also operate *in vivo*. One of the factors involved may be the number of cells needed for the establishment of a new focus of growth. The number of dead cells present on the 'non tumour' side of the L1 chambers

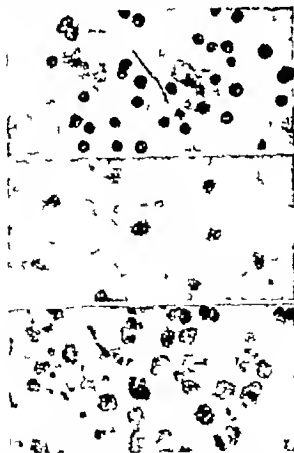


Fig. 1. Top: Spherical, deeply stained L1210 cells have penetrated the Millipore AA filter. Normal macrophages are spread out on the filter beneath the tumour cells. Middle and bottom: Photomicrographs of 'non tumour' and 'tumour' side of the same filter on which L1 cells were grown for 120 days. The middle photograph shows that only macrophages were present on the 'non-tumour' side of the filter even though L1 tumour cells were growing well on the 'tumour' side of the chamber (bottom).

suggests strongly that the tumour cells were capable of penetrating the filter but in small numbers which were with rare exception, insufficient to establish tumour growth. Similar results were obtained when small numbers of tumour cells were injected directly into mice. We found that inoculation of several thousand L1 cells was necessary for the establishment of the tumour in a new host, while Law² found that the injection of only ten L1210 cells was sufficient for transplantation of that tumour. This difference in the capacity of cell populations to survive may operate in aiding or hindering the establishment of new sites of growth by these tumours while they are growing in the host.

Variation in the capacity of tumour cells to survive has been interpreted as supporting the stem-line concept of tumour populations.³ If these results are to be interpreted in the light of the stem-line concept, it would be necessary to assume that the L1210 tumour is made up almost entirely of stem cells while the L1 tumour population is remarkably devoid of stem cells.

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GENETICS

Semi-Albino: a Third Sex-linked Allelomorph of Silver and Gold in the Fowl

In 1955, among 76,542 chicks hatched from the cross, Brown Leghorn sire by Light Sussex dam, there appeared two males which, instead of having the expected white (silver) coloured down of the Light Sussex, were brown. One was sold before its genetic importance was realized. The other cock when adult was light brown in colour, being of a similar hue to that of Brown Leghorn pullets, with a few black feathers on the wings and a black tail. The black and bright brown colours which are found on the bodies of Brown Leghorn cocks were absent. The bird was strong and vigorous, and lived until killed in 1958.

The absence of silver suggested that this allelomorph (*S*) had mutated either to the allelomorph for gold (*s*) or to some third form. The results of subsequent crosses confirmed that *S* was absent and that a new sex-linked mutant *sal* recessive to *s* had appeared and that this allelomorph gives semi-albino in the hemizygous females and homozygous males (Table 1). The mutation must have occurred

in the Light Sussex dam and not in her ancestors since silver was the gene that had mutated and she herself was not semi albino. Moreover, since two such cocks appeared in the same year but none was detected among a total of 303,334 chicks hatched between 1956 and 1958, it seems likely that a single mutant occurred during an early stage of oogenesis and that the resulting allelomorph was incorporated in at least two eggs. The mutant can be detected if it arises in the X-chromosome of a dam but only in half of those of a sire. Consequently we can say that the mutant has been observed in 2 out of the 379,876 X-chromosomes tested.

The semi-albino chicks (all descendants of the second mutant cock) were generally small at hatching, and did not grow as rapidly as the chicks of the other breeds and crosses with which they were reared. The cock chicks were slower in hatching and less active than the pullets. The first feathers were white in colour, but with increasing age many birds developed a buff tinge on the body feathers. This was particularly noticeable in the cocks. In dim light the semi-albino birds had considerable difficulty in seeing, and tended to collide with stationary objects. When adult some of these birds became practically blind due to the development of opacities in the eye lenses. In some cases the whole lens was opaque, while in others the lesions appeared as small spots. The incidence of egg peritonitis in the pullets at between twelve and fourteen months of age was high, and was the most common cause of death.

A similar semi albino controlled by a sex-linked mutant (*al*) has been reported from America by Hutt.¹ This is almost certainly the same as ours, but since it occurred in Barred Rocks and White Leghorns and not in a stock segregating for silver and gold, its allelomorphism with silver was not detected.

We wish to record the help received from Miss D. G. Kidd, who first observed the unusual appearance of the original bird and was responsible for rearing the experimental chicks, and from Dr. F. T. W. Jordan who carried out post-mortem examinations, and reported on the eye abnormalities.

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Table 1

| Year | Sire | Dam | Sex | Silver | Offspring gold | Semi albino |
|------|--|---|---------|---------------------------------|--------------------|----------------------|
| 1956 | Mutant (<i>sal</i>) | pure Light Sussex (<i>S</i> —) | ♂ | 27 (<i>Ss</i> or <i>Ssal</i>) | 0 | 0 |
| 1957 | Mutant (<i>sal</i>) | semi-albino (daughters) (<i>sal</i> —) | ♀ | 0 | 12 (<i>s</i> —) | 8 (<i>sal</i> —) |
| | | | ♀ | 0 | 18 (<i>ssal</i>) | 8 (<i>salssal</i>) |
| 1958 | Semi-albino (<i>salssal</i>) | semi-albino (<i>sal</i> —) | unsexed | 0 | 13 (<i>s</i> —) | 12 (<i>sal</i> —) |
| | | | ♂ | 0 | 5 | 2 |
| 1958 | Semi-albino (<i>salssal</i>) | pure Rhode Island Red (<i>s</i> —) | ♀ | 0 | 0 | 4 (<i>salssal</i>) |
| | | | unsexed | 0 | 0 | 8 (<i>sal</i> —) |
| 1959 | Semi-albino (<i>salssal</i>) × Semi-albino (<i>sal</i> —) | pure Rhode Island Red (<i>s</i> —) | ♀ | 0 | 0 | 2 |
| | | | unsexed | 0 | 18 (<i>ssal</i>) | 0 |
| 1959 | Silver (<i>Ss</i>) × Semi albino (<i>sal</i> —) | Semi albino (<i>sal</i> —) | ♀ | 0 | 0 | 23 (<i>sal</i> —) |
| | | | ♂ | 0 | 0 | 3 |
| 1959 | Silver (<i>Ss</i>) × Semi albino (<i>sal</i> —) | Semi albino (<i>sal</i> —) | ♀ | 0 | 0 | 1 |
| | | | unsexed | 0 | 0 | 0 |
| 1959 | Silver (<i>Ss</i>) × Semi albino (<i>sal</i> —) | Semi albino (<i>sal</i> —) | ♂ | 1 | 0 | 0 |
| 1959 | Silver (<i>Ss</i>) × Semi albino (<i>sal</i> —) | Semi albino (<i>sal</i> —) | unsexed | 0 | 1 | 0 |

Intraspecific Polyploidy and Evolution of Diverse Morphological Forms in *Convolvulus pluricaulis* Chols

Convolvulus pluricaulis Chols is a prostrate, spreading perennial wild herb commonly found on sandy or rocky ground under xerophytic conditions in northern India. The species is marked by great morphological variability, especially in size of the flower. Our cytological studies indicated the existence of intra-specific polyploidy in the species. The present investigation was, therefore, undertaken to study the possible relationship between cytological and morphological forms of the species.

The haploid chromosome number of *C. pluricaulis* with small flowers was determined as nine. Singh² reported $n = 10$ for the same species. Our observations along with those of Singh² thus indicate the presence of two cytological types in *C. pluricaulis*. Monitor studies in the large-flowered form revealed it to be a tetraploid with $n = 18$. The presence of eighteen bivalents in 50 per cent of pollen mother cells suggests it to be an allotetraploid. The fact that the remaining, 50 per cent of cells showed multivalent associations indicates an autotetraploid or a segmental polyploid origin.

As true allopolyploid forms usually do not show multivalent associations, the tetraploid in *C. pluricaulis* may be considered as an autopolyploid or a segmental polyploid. The general morphological gigantism shown by the tetraploid is an additional support for it to be regarded as an auto- or a segmental polyploid.

The existence of a natural polyploid series has not so far been recorded in any other species of *Convolvulus*.

Duthie¹ and Hooker³ have described *Convolvulus pluricaulis* var. *macra* as a large, densely hairy plant with large flowers. The morphological description of *macra*^{1, 3} is identical with the tetraploid studied in the present investigation. The fact that this variety has been seen to possess double the chromosome number of the small flowered type further supports the claim of the large flowered form to be given the rank of a variety. Intraspecific polyploidy has thus played an important part in the evolution of diverse morphological forms in *C. pluricaulis*. The variety *macra* is commonly found in Punjab and Delhi plains and up to an altitude of 3 000 ft. in Kashmir. The small flowered form which represents the diploid condition is very rare at high altitudes. The distribution of the large flowered variety is quite in conformity with the general concept that polyploids are found to be more tolerant to extreme ecological conditions than are their diploid relatives.

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SOCIAL SCIENCES

Main Stages of Social Evolution in Man

PROF GRAHAM CLARK has given tentative estimates of the population of England and Wales, or Britain, in early times. These figures together with the somewhat firmer estimates for the historical period¹ form the basis of Figs 1 and 2. L. S. Palmer gives tentative estimates of the number of general kinds of materials used for making things². These form the basis of Figs 2 and 4.

The difficulties of attempting to quantify stages of cultural development are well known. But of the graphs below, we may say in the words of Stuart Piggott in another connexion (ref. 3 and personal communication, 1959), "While obviously open to criticism in detail at almost every point, it is felt that the broad pattern is sound and that some sort of graphic statement, however tentative, must be attempted. Whereas the slopes of these curves are liable to revision in the light of future knowledge, it is probable that the main 'kinks' are real which for the present purpose is what matters. It is hoped that a small group of specialists may soon give this topic the attention which it seems to deserve."

The 600 000 or so years of the existence of tool-making man are occupied, at the zoological level, by a number of different species. But at the sociological level there are, perhaps, two or three main stages of social evolution which may be generally recognized.

Figs 1 and 2 suggest a division into a long and relatively static stage followed by a short stage of rapid change. By reploting on a larger scale how over, the beginning of the recent upsurge can be traced back to the introduction to Britain of agri-

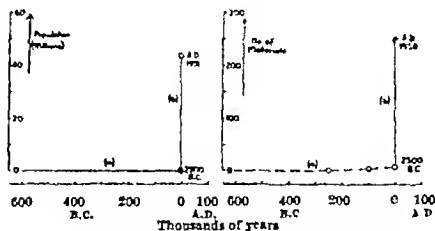


Fig. 1

Fig. 2: Plot of estimated number of general kinds of materials used for making things, against time, after Palmer (ref. 2). The graph shows the number of materials on the y-axis (0 to 250) and thousands of years on the x-axis (6000 B.C. to 0 A.D.). The curve shows a long static period at a low level until around 4000 B.C., followed by a sharp rise to a peak of about 250 around 2000 B.C., and then a decline to about 50 by 0 A.D.

Fig. 2

During earliest times and ice ages the level for populated areas replaces that for Britain.

culture and the neolithic way of life. This probably occurred about 2,500 B.C.⁴ Just before that, the total population of Great Britain may have been of the order of 4,500, with rather more than 3,000 people in England and Wales.¹ The 'number of materials', *sensu* Palmer, may have been about 11.

This primary division is in fact into (a) the food gathering stage and (b) the food producing stage⁴.

The best tripartite classification seems to be obtained by splitting up stage (b), in which such great change occurred, rather than by subdividing the longer stage (a)

At least one further and distinct step in social evolution has undoubtedly taken place since 2,500 B.C. In recent years, many writers have compared the inception of agriculture with the events of the past few centuries, with the 'industrial revolution', or that plus the scientific and technological developments since. These include G. P. Thomson and J. H. Plumb⁵, besides J. Hawkes, C. Hawkes and V. G. Childo. They rank the beginning of agriculture as possibly even as important as our recent changes. Figs 1 and 2 depict the beginning of agriculture as the more important. There is at least the clear implication that no such rapid and fundamental social changes have occurred in between.

Figs 3 and 4, in which the ordinates are logarithmic⁶, are of interest in this connexion. On the right-hand side of each plot, a new step is seen to arise, corresponding to the changes of recent centuries. But

in political structure, communication and education—among other aspects. Recently, we have more power

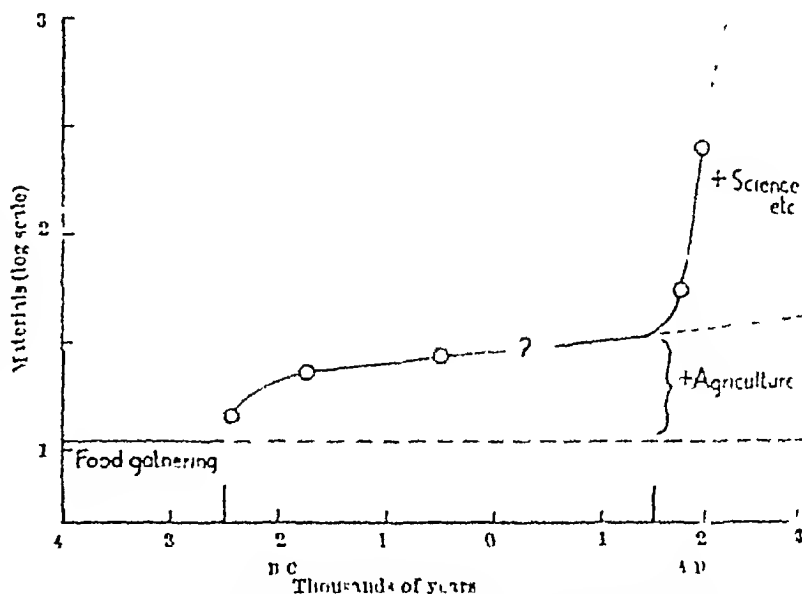


Fig 4 Logarithm of the estimated number of materials, against time (schematic), adapted from Palmer (ref. 2)

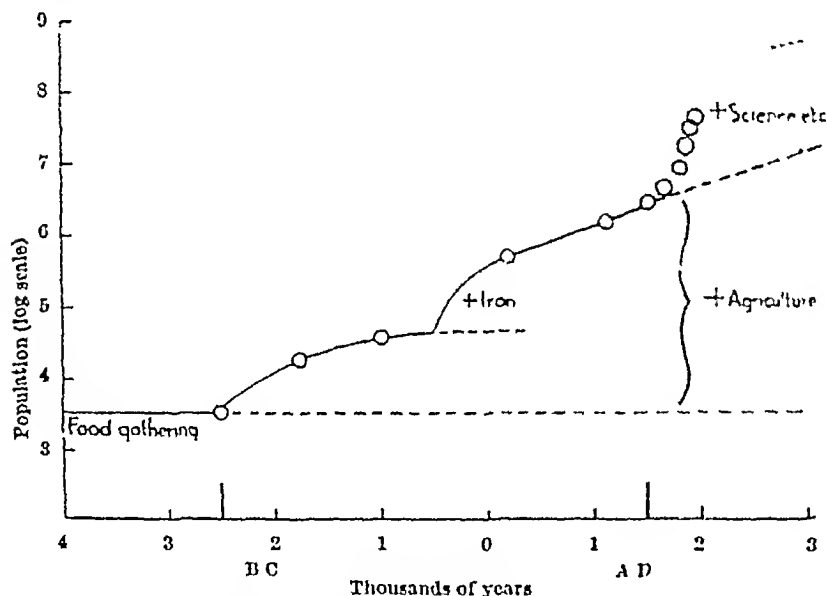


Fig 3 Logarithm of the estimated population of England and Wales, plotted against time (schematic), earlier data adapted from Clark (ref. 1). (With iron tools, agriculture became possible over a much larger area)

an important general inference of these plots, and of collateral historical data, is that the recent and rapid social changes—of which contemporaries themselves have been conscious since the 1760's—must be regarded as having commenced at least by about A.D. 1500.

A further general inference is this: that we seem to be not yet past the middle of a long sigmoid curve of social evolution. (In Britain the population curve is turning over, but not yet the curve for scientific knowledge⁷.) Barring accidents, we may expect as much further social development in the next 500 years as in the past 500. After some such period, consolidation, rather than advance, may again set in.

Since A.D. 1500, there have been conspicuous changes in trade, transport and finance, in industrial techniques, experimentation and scientific theory,

driven machinery and modern science. It is not easy to pick the right word to describe the long-term social transformation in the midst of which we are at present living. But perhaps we may say that we are now entering the 'scientific' stage of human society.

Thus, in conclusion, and aided by tentative quantitative data, it is proposed to recognize as the three main stages, to date, of the social evolution of man: (1) *The food gathering stage*, commencing more than half a million years ago; (2) *The proto-agricultural stage*, commencing locally, near the junction of Asia and Africa, some ten thousand years ago, and reaching Britain about four and a half thousand years ago; (3) *The scientific stage*, commencing in Britain and elsewhere about A.D. 1500; but this third main stage is a stage of social evolution of which even the more advanced countries are still only upon the threshold.

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June 3

- ¹ Clark, J. G. D. "Archaeology and Society" (London, 1957).
- ² Russell, J. O. "British Medieval Population" (Albuquerque, 1946).
- ³ Palmer, L. S. "Man's Journey through Time" (London, 1957).
- ⁴ Pigott, S. "The Neolithic Cultures of the British Isles" (Cambridge, 1954).
- ⁵ Childo, V. G. "What Happened in History" (Harmondsworth, 1942).
- ⁶ Plumb, J. H. "England in the Eighteenth Century" (Harmondsworth, 1956).
- ⁷ Thomson, G. P. "The foreseeable Future" (Cambridge, 1955).
- ⁸ Pettersson, M. L. R. "A Survey of Science" (London, 1953).
- ⁹ Price, D. J. "Discovery", 17, 240 (1950).

MANAGEMENT PROBLEMS IN UNDER-DEVELOPED COUNTRIES

IN a recent broadsheet which reviewed the prospects for nuclear power, Political and Economic Planning referred to the potential market in under developed territories for a small reactor similar to that for modestly powered gas turbine and diesel driven generating sets. Such a reactor, if cheap with the advantages that it can be sited where the power is needed and its fuel requirements are small with the consequent elimination of transmission lines and high fuel transport cost, could transform areas at present undeveloped or unexploited. Whether such reactors will actually help to raise the standard of living of millions of people who are now forced to do with little or no power and to rely on inefficient fuel burning or human labour or on animals does not depend entirely, however, perhaps even primarily, on the ability of the scientists and technologists of the United States, Britain or the U.S.S.R.—the only three countries at present able to provide nuclear reactors for export the knowledge of how to work them and the necessary instrumentation and servicing—to design and manufacture such a reactor at a low enough price. It depends at least as much on the provision of efficient management in the countries where the reactors are to be used.

This aspect of technical assistance has not been entirely overlooked in earlier discussions of that broad problem, but Political and Economic Planning has now examined its implications more fully in a further broadsheet, "Management and Under developed Territories" (No 434, June 1, 1959)*. The broadsheet is indeed primarily concerned with the problems which confront expatriate firms already operating in such countries, one after another of which are insisting that such firms must bring local nationals into their managerial and technical staff. Technically qualified nationals, however, have been very hard to find both for lack of local technical education and for lack of the basic education necessary to acquire technical qualifications. In principle management positions were open to anyone capable of filling them but in practice Europe and North America have been the only sources of supply.

The broadsheet emphasizes the close connexion between political and economic factors in the under developed territories, but to the scientist and technologist it is of special interest for its analysis of the way in which Western firms established in such countries have sought to meet this demand and of the phases of their consequent staffing policy. Factors are emphasized which should be noted by those who proceed to such countries under schemes of technical aid no less than by those who enter the service of expatriate firms. Particularly is this true of the concluding section of the broadsheet, which discusses

the influence of the political climate in such countries and the attitude that is adopted towards Western institutions and ways of doing things. The main assumption on which Western aid to the poorer countries has so far been based—that if enough technical knowledge and capital are injected into a country which is very deficient in both, it is on the way to becoming rich and developed—is frankly challenged.

The shortage of educational and training facilities in under developed countries, especially in Africa, has led many firms to set up their own but this has meant both finding young men capable and willing to attend courses of higher education, and persuading young men already receiving higher education in local or European universities that the opportunities genuinely exist. Competition for the talent available locally is keen and sometimes the supply of young men of good calibre is limited by the practice of requiring scholarship holders to enter government service for a period. Moreover a man not fully trained to the standards of a Western concern may be by local standards fully equipped for a senior post.

The broadsheet naturally does not enter into the problems of promotion policy which can easily arise but these possibilities of friction have to be considered in framing a staffing policy and they are not diminished where race and class form the basis of politics as they do now to a large extent in under developed countries. Political pressure towards nationalization in the sense of increasing the proportion of nationals employed, may not allow the time required to determine a wise staffing policy and to build up a tradition of fundamental values of honesty, truthfulness and loyalty which like the readiness to assume responsibility may require to be nurtured and strengthened in different countries in different ways. While a necessary minimum of academic knowledge may be demanded of scientific or technical staff it would be wrong to expect the same response from the graduates of such countries as from their European counterparts. Some allowance must be made for the local environment.

Nor is it simply a matter of adapting an organization to its environment. Changes in management technique may be required and care should be taken that expatriate staff who are selecting, training and working with national colleagues develop their own powers of understanding at least to the extent of being able to comprehend the mental processes of such colleagues—to assess justly their character and ability and to assist them in their difficulties of adjustment to their job and to their European colleagues. Moreover as Planning points out the emergence of common problems of development and the disparities in supplies of trained men between countries and the need for the parent company to keep in close touch

*Planning Vol 21, No 434 (1 June, 1959) Management and Underdeveloped Territories, Pp. 113-150 (London: Political and Economic Planning 10/6) 2s. 6d.

with the problems of local companies, encourage the development of a managerial staff with wide experience outside their own countries, and this widening of opportunities for men of all races to reach positions of responsibility will probably place a practical limit upon the employment of nationals as such in any one local company.

Summarizing the stages through which the staffing policies of parent firms have passed, the broadsheet notes that up to the Second World War, overseas firms were staffed largely by expatriates, who generally made careers abroad; and there was a general prejudice against business careers on the part of Western-educated nationals, even if educational facilities had been adequate for them to enter the executive ranks. This was succeeded by a phase in which national talent was created where necessary, either by internal training or by the formation or support of educational opportunities outside the firm. Now a third phase is emerging. The arrival of the locally recruited executive has coincided with—and is partly responsible for—the rapid disappearance of the expatriate career, as distinct from the job, abroad. Now, at least among the international concerns, staffing policy is developing along the lines of equipping management with international, rather than national, experience.

The aim of this policy is to obtain a greater cross-fertilization of ideas through an extensive system of overseas postings during the development of the career of an executive. The concept of an expatriate career is being eliminated by offering jobs abroad as an integral part of management training and promotion. This new type of policy should not only improve the quality of management but also contribute to greater adaptability. It clearly has implications in respect of education for management in Britain, and although it should ensure that on the Western side the weakness of rigidity is avoided, it should also be remembered that rigidity is equally dangerous where nationalism is encouraged.

It is here that the broadsheet, referring to Turkey and Iraq as examples, challenges the assumption that technical aid, applied in Western manner through institutions of Western style, can alone provide all that is needed, and quotes in support Mr M. Ionides's recent address, "Technical Aid: the Role of the West", to the Royal Institute of International Affairs. Western institutions, Mr Ionides argued, adapted to societies where the initiative comes from below, cannot fully satisfy the needs of a society where the flow of initiative is from the top downwards. In particular, Western institutions are not organized to tap the immense capital resources in such countries already existing in the form of unused man-power; they can only touch the fringes where a cash-economy exists.

More and more capital and technical assistance are being supplied to the centres of sophisticated Western style economy in the under-developed countries, sharpening the contrast with the surrounding rural economy, and whetting appetites for higher standards of life. Capital investment from

outside, from the top downwards, cannot fill the gap and the balance of influence of the West has so far diverted the attention of these countries from their need to help to work out their own ways of filling this gap by mobilizing the reserves of labour. Western-inspired ideas of industrialization naturally put the emphasis where the system works best, this attracts enterprise and initiative away from the much-needed widespread small-scale development. Nor does the large scale project which the West can provide and which most governments in these under-developed territories request, because they want to develop in the Western manner, teach the simpler methods and provide the training in them that are needed or supply where it is needed the organizing ability essential for a start. It does not even provide the experience or outlook required to initiate or operate schemes which are not primarily aimed at securing profits.

This is a formidable argument, and it emphasizes the close connexion between economic and political factors in the under-developed countries. If it is correct, the assistance programmes sponsored by governments and international agencies may require extensive modification. Deficiencies there cannot be made up by goodwill or flexibility on the part of the branches of Western industry and commerce already established in those countries. Be that as it may, the prospects for the export of the small nuclear reactor should be the brighter in such a context, but the opportunities for Britain here and elsewhere will also depend on the attention given to training for management, and the quality and width of outlook and wisdom of the trained man-power which she is able to send overseas—as administrators, technologists or scientists—and whether in government or other public service or in ordinary industrial or commercial life.

CLASSICS OF NUTRITION

A History of Nutrition

The Sequence of Ideas in Nutrition Investigations
By Prof. Elmer Verner McCollum. Edited by H. Bentley Glass. Pp. x+451. (Boston, Mass. Houghton Mifflin Company, 1957.) 6 dollars.

The Englishman's Food

A History of Five Centuries of English Diet. By the late Prof. Sir Jack Drummond and Anne Wilbraham. Revised, and with a new chapter by Dorothy Hollingsworth. Pp. 482+8 plates. (London: Jonathan Cape, Ltd., 1958.) 36s. net.

HERE are two volumes of outstanding interest and importance. It is not an exaggeration to say that each of them is indispensable to all serious research workers, and other students of nutrition.

E. V. McCollum, now professor emeritus of biochemistry of the Johns Hopkins University, is the doyen of nutrition authorities, pre-eminent as a pioneer investigator himself, and at the same time the leading historian in this field. The respect and regard in which McCollum is held throughout the world are indicated by the fact that he was among the

first to be accorded the honour of election as an honorary president of the International Union of Nutritional Sciences, and that he is also to be the honorary president of the Fifth International Congress of Nutrition to be held in Washington, D C in 1960.

In the judgment of the present writer, an essential part of the greatness of such men as McCollum and Drummond is that they have the ability to regard science as a matter of historical development and growth, rather than as a mere catalogue of facts or a repository for items of knowledge. It is a pity that this historical outlook is not more widely encouraged to day in our colleges and universities. All too common is the student superficially self-satisfied, who supposes that when the lecturer turns to discuss the historical evolution of his science rather than to present him with ready-made summaries of current information then is the time when he can relax or quietly fall asleep. Yet the fact is that no student can hope to acquire a proper understanding of the existing teaching in his chosen sphere except by learning how the current views have come to be accepted and what is the actual foundation for them. Indeed to the young student aspiring to become a research worker one might go further and say that unless he is genuinely interested in studying the bases of knowledge—that is to say, following the reasons why certain beliefs, theories or scientific explanations are held, the stages through which accepted notions have gradually travelled, in other words their historical background—he is not likely to have the mental approach that makes a successful investigator. We may extend the argument to the teacher himself. He is a less good teacher, and a less efficient teacher who is content to leave his student with no more than the statement that such-and-such is now the established view, and that is all there is to it. He is the better teacher, and the more stimulating teacher, who gives his pupils an explanation of the following kind: formerly certain ideas were considered well founded; but later they had to be modified in some respects because of newer knowledge and fuller understanding, and that is the reason why the presently accepted belief is so-and-so, but that nevertheless various rival opinions are often justified on any topic, and that there are always bound to remain gaps in our knowledge and room for further developments and the possibility of wider interpretations.

No doubt it is this mental approach which has served to make Prof McCollum not only a leader in nutritional thought but also a famous experimenter, and the instigator of so much fine work by his 'school' of colleagues and pupils. One of his own most celebrated contributions dates back to 1913-15 when he gave the first demonstration of the probable multiplicity of "fat-growth factors" and by the designations "Fat-Soluble A" and "Water Soluble B" set the stage for the system of classifying the vitamins now familiar to all. No less influential in provoking thought and moulding opinion was his celebrated book "The Newer Knowledge of Nutrition", the first edition of which appeared in 1918, and which may be regarded as the earliest of the modern treatises on nutrition. In a sense, "A History of Nutrition" can be considered as an up-to-date revision of "The Newer Knowledge of Nutrition". In this new work, the reader will find an impressive survey of the whole field and one that is at the same time scholarly, well balanced, illuminated by a sound, critical judgment and a wise discrimination.

The treatment is sufficiently comprehensive, in the course of its 450 pages, to cover the ground adequately and without anywhere becoming laborious, wearying or unwieldy. Much of the text is the result of careful and loving original bibliographical research by the author himself. It is certain that any future writers on nutritional history will have to turn to McCollum's new book as their starting point.

As to the new edition of "The Englishman's Food" one need say no more than that on its first publication in 1939 it immediately became the standard work on the dietary conditions of, and the food habits of ourselves and of our ancestors during the past five centuries. Nothing covering the same ground had been available previously, or has been published since, and this second edition was sadly overdue. Miss Dorothy Hollingsworth has done her work conscientiously and well in revising the book and bringing it up to date, and has added a useful new chapter on "The Application of the Newer Knowledge of Nutrition". Unhappily because of the increasing costs of printing the publishers found it necessary to reduce the overall size of the book, with the result that some of the earlier chapters have had to be shortened, chiefly by the omission of quotations from historical texts, some of them of fascinating interest. Many of us will regret this, but such is the sad lot of authors to day.

LESLIE J. HARRIS

FLOW OF COMPRESSIBLE FLUIDS

Mathematical Theory of Compressible Fluid Flow
By Richard von Mises. Completed by Hilda Geringer and G S S Ludford. (Applied Mathematics and Mechanics. A Series of Monographs prepared under the auspices of the Applied Physics Laboratory, Johns Hopkins University.) Pp xiii+514. (New York: Academic Press, Inc. London: Academic Books Ltd., 1958.) 15 dollars.

THIS book was originally planned by von Mises, but owing to his untimely death he was unable to complete his task. With the aid of some notes he left, Hilda Geringer (Mrs R von Mises) and G S S Ludford were however able to complete the work. The first three chapters were written by von Mises himself and the remaining two are due to the above-named authors, to whom everyone should be grateful for preserving so much of the last important work of von Mises.

The material contained in the book is intended for the research worker and the graduate student but it should be of value to anyone making a serious study of aerodynamics. The basic theory is developed in a clear and simple way that is easy to understand. Great pains are taken to explain fully fundamental concepts and the significance of the various assumptions made in the development of the mathematical methods for the solution of certain aerodynamic problems. The concept of a specifying equation is introduced which, with the usual four equations of Euler connecting the velocity components of the flow, the pressure p and the density ρ , enables these five unknowns to be determined. The most common forms of the specifying equation are $\rho = \text{const}$ for incompressible flow, and $f(p, \rho) = 0$ for compressible flow, where p and ρ are at all times connected by a one-to-one relation.

In scope the book is somewhat limited. Only one- and two-dimensional flows are fully discussed and

in the main only problems of inviscid flow for which exact solutions have been found are considered. No attempts are made to assess the practical value of these theoretical results by comparison with experiment.

Chapter 1 gives the basic equations for different types of flow under various conditions and Chapter 2 is concerned with general theorems of use in the study of rotational flows, the hodograph method and the theory of characteristics. Chapter 3 is devoted to one-dimensional flow and contains sections on the effects of viscosity, heat conduction, simple wave propagation, shock reflexion and shock collision. A thorough presentation of the hodograph method, with a full discussion of recent advances in the theory, is included in Chapters 4 and 5. Special attention is given to the treatment of shock waves and the book ends with an article on transonic flow. The main text is followed by an appendix of some forty pages of relevant and most interesting biographical and historical notes.

W P JONES

THE METALLURGY OF MAGNESIUM

The Physical Metallurgy of Magnesium and Its Alloys
By Prof G V Raynor (International Series of Monographs on Metal Physics and Physical Metallurgy, Vol 5) Pp ix+531 (London and New York: Pergamon Press, 1959) 75s net

PROF G V RAYNOR'S latest book provides the first predominantly theoretical survey of the subject of magnesium and its alloys, and it will most certainly form a valuable companion volume to those books published in recent years concerned mainly with the technological aspects of magnesium metallurgy. Both students and those concerned with development in industry will welcome this authoritative work, which is presented so as to give the theory first, followed by a review with examples of the alloy systems formed by magnesium.

The first part of the book (Chapters 1-7) deals with the fundamental nature of magnesium, its electronic constitution, and the effects of alloying. This section contains a masterly ten page summary of the electron theory in general, before presenting a critical account of the qualitative and quantitative studies that have been made of the electronic constitution of magnesium. Magnesium is in a most interesting electronic state, and the author discusses, in a chapter on the lattice spacings of magnesium alloys, electronic interpretations of departures from Vegard's law, and lattice spacing changes due to temperature changes and to the application of tensile stress.

After a description of the general alloying behaviour of magnesium, in terms of the Hume-Rothery factors of atomic size, and relative- and electro-negative valency effects, an extensive account is given of the occurrence of intermediate phases in magnesium alloys. In particular, the structures of 'normal valency' compounds and Laves phases are considered in some detail, and the chapter is concluded by some pertinent observations as to why precipitation of these intermediate phases seldom leads to a high response to age-hardening in magnesium alloys.

This section of the book is concluded by an account of the deformational characteristics of single crystals

and polycrystalline aggregates. After a fairly elementary description of edge and screw dislocations, the crystallography of slip and twinning in magnesium at room and elevated temperatures is outlined. Rupture, and the development of preferred orientations, are also considered, and an account of creep characteristics concludes the chapter.

The second part of the book (Chapters 8-17) describes and discusses the alloys of magnesium, considering the solute metals from the various groups of the Periodic Table in turn, stress being laid on those of present or potential importance. A selected list of references is provided at the end of each chapter—the literature being reviewed up to and including 1957. Rapid reference to this part of the book would be made easier by the more generous provision of sub-headings, as the alloys in each group are discussed.

A review of this nature emphasizes our ignorance of the fundamental mechanism of many technological processes, and many fields for further research are indicated. The suggestion of "submicroscopic precipitates" in, for example, the creep-resistant magnesium-cerium alloys will certainly whet the appetite of electron microscopists. There is, in fact, rather a dearth of photomicrographs in the book (there being only two sets), doubtless due to the high cost of their production. The value of the second set of micrographs is also reduced by the absence of any supplementary information—magnification preparation, etc.

An account of the systems formed with gaseous elements or compounds concludes the review, an interesting discussion of the oxidation characteristics of the metal being included here. The final chapter summarizes the influence of alloying on the mechanical properties of magnesium. The book contains more than 200 diagrams—the phase diagrams being particularly well produced. This robust, well bound volume will surely grace the shelves of students and research workers alike for many years to come.

J W MARTIN

BIOLOGICAL PROPERTIES OF PHENOLS OF PLANT ORIGIN

The Pharmacology of Plant Phenolics
Proceedings of a Symposium held at Oxford, April 1958. Edited by J W Fairbairn. Pp ix+161 (New York: Academic Press, Inc., London: Academic Books, Ltd., 1959) 6 dollars, 30s.

IT is not often that an attempt is made to present within the space of 150 pages a review of the biological properties of such a wide variety of chemical substances as the plant phenolics. It can indeed be argued that such a review can be of little value because the plant phenolics comprise a miscellaneous assortment of substances having nothing in common beyond the presence of an aromatic hydroxyl group, and some may feel that the choice of subject-matter has been made even more arbitrary by the inclusion of the chapter on adrenaline, noradrenaline and 5 hydroxytryptamine, since these substances are not of plant origin and owe their characteristic pharmacological properties to the presence of an amino group rather than to the presence of a phenolic group.

Even if the fundamental pattern of this book—the proceedings of a symposium held in Oxford last year—is regarded as slightly illogical, it represents,

nevertheless, an important contribution to the field of structure-activity relationships

The book begins with a concise authoritative chapter by J H Burn on adrenaline and other nitrogen containing phenols mainly of animal origin, and is followed by another chapter, by R T Williams, summarizing what is known concerning the fate of phenolic compounds in the body. In the third chapter W B Whalley discusses the toxicity of plant phenolics as a group providing a useful introduction to the next five chapters which describe in more detail the action of specific groups of compounds. J W Fairbairn who is also the general editor, discusses the anthraquinones, and J D Biggers goniostein and related compounds which exhibit oestrogenic activity and in a separate chapter hypericin and similar compounds that cause photo-sensitization. Three chapters are devoted to the flavonoids and their effect on capillary blood flow. In the first M F Lockett considers the evidence in support of the view that they act directly on capillary permeability and tensile strength while in the other two F Doods and J Lavollay and J Neumann present the case for indirect activity mediated through adrenaline and ascorbic acid. The last two chapters of the book deal with plant phenolics in food and wine, J Masquelier directing attention to the high bactericidal activity of some wines and E C Bate-Smith concluding the book on the reassuring note that most of the phenolic constituents of foods are fortunately pharmacologically inert.

The book is well printed and free from errors. Its value is greatly enhanced by the list of references given at the end of each chapter and by summaries of the discussions that took place at the symposium. Most pharmacologists, organic chemists, biochemists and pharmacologists will find much of interest and value in this volume.

F A ROBINSON

ORCHARD SCIENCE

Tree Fruit Production

By James S. Shoemaker and Benjamin J. E. Teskey.
Pp vii+466 (New York: John Wiley and Sons Inc. London: Chapman and Hall Ltd. 1959).
56s. net

ADVANCES in plant physiology, in plant breeding, in plant protection and in the knowledge of plant toxicants, are to-day being paralleled by advances in crop husbandry and soil management and in tree shaping and growth control. The impact of these advances on commercial fruit growing is being influenced by economic considerations. While the facts are the major concern of the appropriate specialist who may be quite ignorant of the over-all subject of pomology, the teacher of pomology as the term is now generally understood must be keenly aware of the progress being made in all the branches of fundamental science that affect his subject and be willing and able to incorporate the new knowledge in turn into his teaching and demonstrations.

With specialist fruit crop research stations in many parts of the world now more or less well staffed and equipped, new knowledge supposedly new knowledge or old knowledge recapitulated is being published so plentifully as to embarrass alike both teacher and taught. From time to time experienced teachers give us the benefit of their selection from among this wealth of material and if they are

competent teachers and are critical in their selection, the result is a good book.

Dr Shoemaker is such a teacher, and this book written in collaboration with Dr Teskey bears evidence of a wide ranging but careful selection of subjects (there are more than 800 references, the majority of them within the past 20 years) and a commendable compression of the essential material, an 11 page double-columned index makes for easy reference. Text books on husbandry are difficult to illustrate, and this one is no exception, line drawings and diagrams like those on grafting are clear and good. Photographs of plantations and many field operations, like picking and pruning, do not reproduce well.

The authors have covered apples, pears, cherries and plums all of which interest us in the British Isles. Peaches, apricots, nectarines and quinces should interest our Western and Southern European neighbours, and citrus fruits are also the concern of the countries bordering the Mediterranean sea. The authors were not catering for this wide public but aimed at producing an up-to-date guide to current orchard and fruit plantation practice for use in Canada and America. Nursery practice, site selection and modification, planting considerations and varieties for particular purposes are all discussed together with tree nutrition, pest and disease control, soil and plantation management and harvesting as well as handling and storage. There is a special chapter on the cultivation of dwarf apples and pears, evidently in response to demands from students for information on this subject. For a long time European growers have been particularly expert in controlling tree size and yield and American growers may face many difficulties in adapting European methods to their needs.

Though essentially written for students this book contains much that will interest fruit growers and their advisors in many parts of the world.

H W MILLS

SCHIZOPHRENIA

Schizophrenia: Somatic Aspects

Edited by Derek Richter. Pp viii+181 (London and New York: Pergamon Press 1957). 40s. net

Chronic Schizophrenia

By Thomas Freeman, John L. Cameron and Andrew McGhie. Pp xi+168 (London: Tavistock Publications Ltd. 1958). 21s. net

A New Approach to Schizophrenia

By Julius I. Steinfield. Pp 150 (London: Hutterton Medical Publications Ltd. 1958). 21s. net

SCHIZOPHRENIA is a major cause of disability in most parts of the world. In countries for which statistics are available it constitutes approximately half the chronic population of mental hospitals. Almost one in every hundred persons is fated to suffer from the disease, and the majority, particularly the men, break down in the second and third decades of life. The wastage of human life and the amount of suffering and social dislocation it causes are probably greater than that due to any other single disease. The International Congress of Psychiatry held two years ago was devoted wholly to this subject. Its deliberations served largely to bring home the failure to

achieve any substantial advance in knowledge of its causation since the condition was first described by Kraepelin and later further defined by Bleuler.

These three books reflect three of the commoner types of theoretical approach adopted in the vast literature on the subject—the organic or somatic approach, the psychoanalytic and the sociometric.

The monograph edited by Derk Richter contains a number of essays dealing with the present state of knowledge in relation to the anthropometric aspects and the electroencephalographic, neuropathological and endocrinological observations. There is a study of metabolic changes in recurrent schizophrenia, one on the effects of drugs introduced into the cerebral ventricles, a paper on the therapeutic effects of diet and on the symptoms induced by medication which are at times scarcely distinguishable from those observed in schizophrenics. One paper attempts to reconcile the observations suggesting that a mutant gene is the primary cause with those that imply that environmental causes are of some importance. The picture of present knowledge that emerges is encouraging. Schizophrenics differ as a group from normal controls in respect of body build and in relation to a whole range of biochemical tests. There is some evidence that histologically demonstrable changes occur in some parts of the brain. The schizophrenic also responds abnormally to a wide range of drugs. But all these changes are without specificity and the degree of overlap with normal control groups is so great for all anomalies that they are rendered useless for purposes of diagnosis. In many instances uncertainty remains as to whether we deal with manifestations of causal agents, with effects of the disease or the results of long periods of institutional care. Moreover, with the possible exception of Gjessing's celebrated work on disturbances of nitrogen metabolism in the very small group of cases of periodic catatonia, none of the differences found has been so far successfully exploited to advance knowledge in relation to etiology, prognosis or classification. The one hard fact which shines clear and constant through this nebulous matrix of data is that the hazard for developing schizophrenia in the sib of a schizophrenic is sometimes that for a member of the general population, for his child sixteen times, for a dizygotic twin some thirteen times and for a monozygotic twin between seventy and eighty times as great. Although its significance remains unclear, the recently demonstrated difference in the chance of being admitted to mental hospital with schizophrenia in the different social classes has been already confirmed in a number of countries and promises to be an equally clear and consistent observation.

The dismally slow rate of progress along organic lines has led some workers to throw up the sponge and to devote their energies to the uncovering of meaningful associations in the mental life of the schizophrenic. The theoretical framework for this kind of endeavour is usually provided by one of the schools of psychoanalysis. The stringent controls considered essential for scientific inquiry to ensure that findings are not interpreted in accordance with preconceived theory are often regarded as inapplicable or irrelevant. The psychoanalytic exploration and treatment of schizophrenia has in recent years attracted enthusiastic adherents, it had previously been considered therapeutically useless.

The book by Dr Freeman and his colleagues deals with observations and treatment inspired by psycho-

analytic thinking and carried out in two schizophrenic schizophrenic patients. They corroborate the view expressed by Bleuler that the essential pathological disturbance produced by this disorder is a weakening of the functions of the ego leading to breakdown of its boundaries and failure to distinguish between self and non-self or inner and outer. Variations in the form of the disease are ascribed to the degree of ego function. The disturbances of thought, affect and volition and the disturbance of perception characteristic of the schizophrenic are considered to stem from the change in the ego function. Although this is regarded as the essential psychological disturbance, the problem of etiology is left open. The therapeutic programme based on this finding is directed towards ego building, and includes fostering closer and more durable relationships between patients and nurses, efforts to communicate at the patient's own mental level, and the assumption that stimulation of the body affects awareness of the self, such things as stroking the hand and making a record of bath-time. The effect of the measures on ward atmosphere and on individual patients are said to have been gratifying. No clear analysis of the results is given.

Exploration of the inner life of the schizophrenic is a form of inquiry, and a premature reliance on quantitative data in a field such as this is probably unfruitful to new ideas. Some German psychiatrists who do not subscribe to psychoanalytic teaching have testified to the beneficial effect exerted by this kind of endeavour when initiated in a mental hospital where formerly a predominant influence was the so-called 'objective' psychiatry, the adherents of which at times unwittingly treated the patient almost as if he had been an inanimate object.

However, the scientific merit of theories cannot be decided by pragmatic considerations. The breakdown of ego boundaries here described as the source of psychological disturbances in schizophrenia is easily applicable as a metaphorical description for the disturbances in delirium, dementia, dreaming and depersonalization, which are quite different phenomena. Moreover, a very large number of other explanations have now been proposed, all clearly to be illuminating for the understanding and effective treatment of schizophrenia. Thus, Steinfield's book states that oral frustration in infancy is the root cause. Excessive hunger in early life overstimulates the vegetative mechanisms, which may then remain in a state of high cathectic threshold. He has more than a suspicion, for reasons not made explicit, that in encephalopathic similar mechanisms may be at work.

As in other fields of scientific inquiry, insights and 'intuitive leaps' in psychiatry have to be treated with respect—those of others no less than one's own—which is precisely why none deserves serious consideration until its relevance and heuristic value have been objectively demonstrated so far as possible.

Many observations cited in the first book suggest that the slow progress of scientific inquiry in this field may be partly due to the heterogeneity of schizophrenia. Recent genetic, clinical and epidemiological data show promise for discovery of the natural lines of division between the different variants in the syndrome. When this has been achieved, progress in the definition of causal agents in schizophrenia, whether psychogenic or physiogenic, is likely to be accelerated.

MARTIN ROTH

The World of Learning 1958-59

Ninth edition Pp xii+1139 (London Europa Publications, Ltd., 1958) 130s net

THE ninth edition of the "World of Learning", which is now well established as a valuable guide to scientific, cultural and educational institutions throughout the world follows the pattern of its predecessors, but is considerably enlarged due to the world wide expansion of scientific and technological research, and to the recent foundation of many universities and technical colleges in the relatively undeveloped countries.

The first section devoted to Unesco, describing its aims, programmes, organization and finance, is followed by a short account of the work and structure of the International Council of Scientific Unions and other international organizations, together with brief statements of their objects and the names of their principal officers.

The remainder of the book is divided alphabetically into the various countries of the world (by their names in English). The arrangement of entries for Great Britain—which occupy 88 pages—affords an indication of the scope of the work: learned societies and professional associations, research institutes, libraries, museums and art galleries, universities and university colleges, centres of adult and technical education, schools of art, music and dramatic art, agricultural colleges, and education trusts. In general the entry for each institution includes its address, the names of its leading officials, and for each university a complete list of professors is given. Where applicable, the titles of any publications issued by the body concerned are also listed. The entry for the U.S.S.R. which occupies 38 pages, lists the members of the Soviet Academy of Sciences and the heads of its various departments and research organizations. Forty-one Russian universities are listed with their faculties, but the names of their professorial staffs are not given. A long list of the very numerous institutions of higher education and research of the Soviet Union are however, included. The largest single entry, comprising 190 pages, relates to the United States of America.

There is an alphabetical index of institutions, but none of persons, mentioned in the book.

Handbook of the Rubi of Great Britain and Ireland
By the late W. C. R. Watson Pp xi+274 (50 figures) (Cambridge At the University Press 1958) 63s net

PROFESSIONAL systematists tend to be superior about brambles and batologists, partly because in Britain at least, batology has been primarily an amateur study, but perhaps more particularly because the *Rubi* refuse to comply with orthodox ideas, and, like slum children in a respectable neighbourhood, are a perpetual affront to the dignity of those who value orderliness and correct behaviour. It was perhaps vain to hope that Mr. Watson's long awaited monograph would finally set the seal of respectability upon this sprawling and troublesome group, but the opinions of one who studied the brambles assiduously for more than forty years must be given careful consideration. Every line of this admirably produced monograph bespeaks seriousness of purpose, integrity and industry, and the wealth of Watson's knowledge is testified time and time again throughout the book though perhaps most strikingly in the introductory pages. What a pity

the author did not live to publish a separate and more elaborate essay on brambles and bramble classification, for it must be confessed that his generalizations and *obiter dicta* though perhaps controversial are vastly more intriguing than his detailed and somewhat desiccating descriptions of the three hundred and ninety-one species said to occur in Britain. Admittedly everything possible has been done in keys, descriptions and illustrations, to convey the author's mature conclusions to the reader, but language and art have their limitations, and the fond hope that the book will furnish the means of identifying every native species met with is perhaps a shade too optimistic. The unenlightened sees only one black berry, the observant possibly half a dozen but only the specialist, with twenty or more years' experience behind him, can hope to recognize the majority of the species included in this book, and then—who knows—the specialist may wish to add a further hundred species of his own to the British list for one suspects that *Rubus* species, like parallel lines, can be extended to infinity. R. D. MEIKLE

Annual Review of Entomology

Vol. 4 Edited by Edward A. Steinhilber in association with Ray F. Smith Pp viii+467 (Palo Alto Calif. Annual Reviews, Inc. 1959) Published in co-operation with the Entomological Society of America 7 dollars

A REVIEWER always likes to imagine editors and authors feverishly scanning his Olympian judgements and then departing to brood on the error of their ways. While experience must inevitably destroy this pleasant picture it is gratifying to notice the present coincidence. Volume 4 of the Annual Review of Entomology fulfils almost entirely the critical requirements suggested in reviews of the previous volumes in these columns. Thus we have a volume broadly based not only in subject matter but also in the geographical distribution of its contributors: a review which includes several papers on subjects at the growing points of entomology—insect physiology, ecology and control—and finds space for one or two on the borderline of other sciences such as the role of insects as disease vectors. In fact, it would be a dull entomologist indeed who could not find something of interest or profit in the present volume.

If this standard is maintained then critical interest can be transferred to a higher level, although in the present volume the general concept is good, a few of the individual treatments fall short of this standard and degenerate into the "card index" type of review. Review articles of the highest quality must not only present a selection—for in these days that is all it can be—of the literature but must also strive to produce some stimulating and if possible enlightening synthesis from it.

In matters of detail the present volume is as well produced as its predecessors and at last each article has a bibliography in alphabetical order, the index is good although several misprints and incorrect page numbers appear here.

But these are small matters compared with the solid value and interest of this volume, the Entomological Society of America, which this year terminates its financial obligations to the "Review" must be congratulated on bringing into being a work which, on present standards, will be of great value to every entomologist.

P. T. HARRIS

RADIOCARBON DATING OF PREHISTORIC WOODEN TRACKWAYS

By DR H GODWIN, F.R.S., and DR E H. WILLIS

University Sub-department of Quaternary Research, Botany School, Cambridge

THE purpose of building corduroy tracks is to avoid detours, and prehistoric examples of these wooden structures have been preserved by continuous water-logging. It is not surprising, therefore, that increased wetness of climate should have caused many former routes to be flooded, and have induced first the construction and then the preservation of wooden trackways. Thus there is an expectation that, were it possible to determine the age of a number of trackways, their ages would be grouped at distinct periods of climatic deterioration.

Corduroy tracks, however, have not been studied typologically, and apart from axe marks on the timber and the chance of associated archaeological finds, they have been very difficult to date, until the advent of pollen-analysis, and, more recently, of radiocarbon dating.

Both techniques have been applied to the problem of dating several of the wooden trackways revealed in recent years by peat-cutting in the derelict raised bogs of the Somerset Levels. Some of these have been described already¹, and descriptions of others are being prepared for publication (*Phil Trans Roy Soc Edinburgh*). They run between the Mendip and the Polden Hills and the low islands that project through the intervening flat lowlands of the Glastonbury Levels.

The six Somerset trackways so far dated, and also certain associated wooden platforms, all occur at a comparable stratigraphic horizon in the bogs. This is at the surface of a very dark, highly humified *Sphagnum-Calluna-Eriophorum* peat, and its junction with a *Cladium-Hypnum* peat. The lower peat is indicative of the growth of heather-clad bogs receiving water only as rain or snow, in a condition of arrest or slow growth: their gentle convex surfaces could easily have been traversed on foot and offered little obstacle to passage across the levels. The overlying *Cladium-Hypnum* peat by contrast points unmistakably to flooding by calcareous water from the big catchment area of the Mendips and Polden Hills. Such flooding imposed very circuitous routes between one hill ridge and another and the evidence suggests that the wooden trackways were built in consequence of the flooding and that their preservation was ensured by its continuance.

Several of the trackways were also shown to be close to the same pollen-analytic zone-boundary, and upon this evidence it was suggested that the tracks were probably built about the transition between the Bronze Age and the Iron Age. This supposition was strengthened by the occasional discovery upon the timber of the markings of the small thick axes of Late Bronze Age type, and by the recovery of two bronze spearheads at comparable stratigraphic levels, one of the Late Bronze Age and the other of late Middle Bronze Age.

Radiocarbon dates have now been obtained for the wood of the trackways and also of the peat in which they are embedded. The assays were made with

carbon dioxide at 2 atmospheres pressure in a copper proportional counter of about 2-litres volume².

Table 1 DATING OF WOOD FROM TRACKWAYS*

| | Years B.P. |
|--------------------------------------|------------|
| Q 52 Meare Heath track (Bulfield's) | 2830 ± 110 |
| Q 39 Shapwick Heath track (Foster's) | 2850 ± 110 |
| Q 303 Westhay track (Sandford's) | 2470 ± 110 |
| Q 306 Blakeway farm track | 2800 ± 110 |
| Q 7 Vipers track (Dewar & A) | 2600 ± 110 |
| Q 312 Vipers track (Dewar & A) | 2520 ± 110 |
| Q 313 Nidons track (Dewar & B) | 2639 ± 110 |
| Q 311 Vipers platform | 2585 ± 120 |
| | 2410 ± 100 |
| | 2640 ± 110 |

* 1 or fuller information on the provenance of the samples see ref. 3

It will be seen that these all lie between 450 and 900 B.C., which is certainly Late Bronze Age in this part of Britain. The datings are supported by those of the associated peat.

Table 2 DATING OF PEAT ASSOCIATED WITH TRACKWAYS*

| | Years B.P. |
|--|------------|
| Q 53 Meare Heath track—subjacent peat | 2730 ± 110 |
| Q 44 Shapwick Heath track—subjacent peat | 3310 ± 110 |
| Q 309 Blakeway farm track—subjacent peat | 2790 ± 110 |
| Q 316 Nidons track—peat at track level | 2790 ± 120 |
| Q 318 Nidons track—subjacent peat | 2642 ± 120 |
| Q 319 Nidons track—subjacent peat | 2482 ± 120 |
| Q 317 Nidons track—superjacent peat | 2628 ± 120 |

Whereas the results from Nidons track suggest close contemporaneity between the track itself and adjacent peat, at the other sites the greater age of the underlying peat supports the field evidence that some erosion or wastage of the peat surface had occurred before the trackways were constructed.

As long ago as 1908 a monoxylous boat had been recovered from the bog deposits near Shapwick Station, but under conditions that did not allow any dating or reference to a stratigraphic horizon. It was apparent that it could not have been embedded while the bogs were covered by heather and cotton grass and it seemed likely that it related to a substantial flooding period. The curator of Taunton Castle Museum, where the boat is now preserved, kindly provided enough wood for the following radiocarbon assay.

Q 357 Shapwick boat 2305 ± 120 years B.P.

It will be seen that this assay places the boat within the Early Iron Age, so that it is younger than the wooden trackways and indeed corresponds in age with the *Cladium-Hypnum* peat of the major flooding episode of this time.

There is a good deal of evidence in various parts of north-western Europe that about 600 B.C. there was in progress a change of climate towards increased rainfall and lower temperatures. It has been made the boundary between the Sub-boreal and Sub-atlantic climatic periods, it is an important pollen zone boundary and is often marked by 'recurrence surfaces' in peat bogs. In view of the likelihood that this climatic change was also widespread in Britain it is interesting to append the radiocarbon dates

from three further wooden trackways that we determined

Table 3 TRACKWAYS OUTSIDE SOMERSET

| | | Years B.P. |
|-------|------------------------------|------------|
| Q 310 | Fordy—Little Thetford, Cambs | 2500 ± 110 |
| Q 310 | Brigg Lincs. | 2562 ± 120 |
| Q 43 | Kate's Pad, Pilling, Lancs. | 2'60 ± 120 |

It was already known from associated prehistoric finds that the Brigg trackway clearly belonged to the Late Bronze Age to Early Iron Age transition. Pollen analytic evidence and a single sherd from the Fordy trackway had already suggested a similar age for that structure. It is now strikingly evident that indeed all the trackways belong to the one archaeological period.

A NEW FOSSIL SKULL FROM OLDUVAI

By DR. L. S. B. LEAKEY
Coryndon Museum Nairobi

ON July 17, at Olduvai Gorge in Tanganyika Territory, at Site FLK my wife found a fossil hominid skull, at a depth of approximately 22 ft below the upper limit of Bed I. The skull was in the process of being eroded out on the slopes and it was only because this erosion had already exposed part of the specimen that the discovery was possible. Excavations were begun on the site the following day and continued until August 6. As a result, an almost complete skull of a hominid was discovered. This skull was found to be associated with a well defined living floor of the Oldowan pre-Chelles Acheul culture.

Upon the living floor, in addition to Oldowan tools and waste flakes, there were the fossilized broken and splintered bones of the animals that formed part of the diet of the makers of this most primitive stone age culture. It has not yet been possible to study the fauna found on this living floor, but it can be said that it includes birds, amphibians, reptiles such as snakes and lizards, many rodents and also immature examples of two genera of extinct pigs, as well as antelope bones, jaws and teeth.

It is of special importance to note that whereas the bones of the larger animals have all been broken and scattered, the hominid skull was found as a single unit within the space of approximately one square foot by about six inches deep. Even fragile bones like the nasals are preserved. The expansion and contraction of the bentonitic clay, upon which the skull rested and in which it was partly embedded, had resulted over the years, in its breaking up into small fragments which have had to be pieced together. The bones, however, are not in any way warped or distorted. A large number of fragments still remain to be pieced together.

This very great difference between the condition of the hominid skull and that of the animal bones on the same living floor (all of which had been deliberately broken up) seems to indicate clearly that this skull represents one of the hominids who occupied the living site, who made and used the tools and who ate the animals. There is no reason whatever, in this case, to believe that the skull represents the victim of a cannibalistic feast by some hypothetical more advanced type of man. Had we found only fragments of skull or fragments of jaw, we should not have taken such a positive view of this.

Of course prehistoric trackways were built at other periods than this, and the Groningen laboratory has dated an Irish example as follows:

GRO 272 Corlona Co Leitrim 3385 ± 170 years B.P.

None the less the consistency of the English results is striking and strongly underlines the importance of carefully recording and dating those unregarded prehistoric monuments.

¹ Clapham, A. R. and Godwin H. *Phil Trans Roy Soc. B* 233 233 (1948).

² Godwin H. Walker D. and Willis E. H. *Proc Roy Soc. B* 147 352 (1957).

³ Godwin H. and Willis E. H. *Amer J. Sci. Radiocarbon Supp.* 1 63 (1959).

⁴ Mitchell G. F. *J. Roy Soc. Antiq. Ireland* 88 49 (1958).

⁵ Smith A. G. *Proc. Prehist. Soc.* 24 78 (1953).

It therefore seems that we have in this skull, an actual representative of the type of man' who made the Oldowan pre-Chelles Acheul culture.

This skull has a great many resemblances to the known members of the sub-family of Australopithecinae. Some scientists recognize only one genus namely *Australopithecus*, and treat Broom's *Paranthropus* as a synonym, others consider that the demonstrable differences are of such a nature that both genera are valid. Personally, having recently re-examined all the material of the two genera, in Johannesburg and Pretoria I accept both as valid.

The Olduvai skull is patently a member of the sub-family Australopithecinae and in certain respects it recalls the genus *Paranthropus*. In particular this is the case in respect of the presence of the sagittal crest, the great reduction in the size of the canines and the incisors, the relatively straight line of these teeth at the front of the palate, the position of the nasal spines and the flatness of the forehead. In certain other characters, the new skull resembles more closely the genus *Australopithecus* for example in respect of the high cranial vault, the deeper palate and the reduction of the upper third molars to a size smaller than the second, all of which are features to be found in *Australopithecus* but not in *Paranthropus*.

The very close examination and direct comparisons which I have personally made in South Africa have convinced me that, on the basis of our present state of knowledge, the new skull from Olduvai, while clearly a member of the Australopithecinae differs from both *Australopithecus* and *Paranthropus* much more than these two genera differ from each other.

I am not in favour of creating too many new generic names among the Hominidae, but I believe that it is desirable to place the new find in a separate and distinct genus. I therefore propose to name the new skull *Zinjanthropus bosei*. This generic name derives from the word 'Zinj', which is the ancient name for East Africa as a whole, while the specific name is in honour of Mr Charles Boise, whose constant encouragement and financial help over since 1948 have made this and other important discoveries possible. I would also like to acknowledge the generous help received from time to time from the Wenner Gren Foundation and the Wilkie Trust.

The following is the preliminary diagnosis of the new genus and the new species

Zinjanthropus gen. nov.

Genotype a young male with third molars not yet in wear and sutures relatively open, from FLK I, Olduvai

A new genus of the Hominidae, sub-family Australopithecinae, which exhibits the following major differences from the genera *Australopithecus* and *Paranthropus*

(a) in males a nuchal crest is developed as a continuous ridge across the occipital bone,

(b) the inion, despite the great evidence of muscularity, is set lower (when the skull is in the Frankfurt plane) than in the other two genera,

(c) the posterior wall of the occipital bone rises more steeply to form, with the parietals, a very high-vaulted posterior region of the skull,

(d) the foramen magnum is less elongate and has a more horizontal position than in *Australopithecus* (in the crushed skulls of *Paranthropus* it is not possible to be quite sure of the plane of the foramen magnum),

(e) the presence of a very massive horizontal ridge or torus above the mastoids. This is much more marked than the normal type of supra-mastoid crest,

(f) the mastoids are more similar to those seen in present-day man, both in size and shape,

(g) the presence of a strong wide shelf above the external auditory meatus, posterior to the jugal element of the temporal bone,

(h) the shape and form of the tympanic plate, whether seen in *norma lateralis* or in *norma basalis*. In this character the new skull has similarities with the Far Eastern genus *Pithecanthropus*,

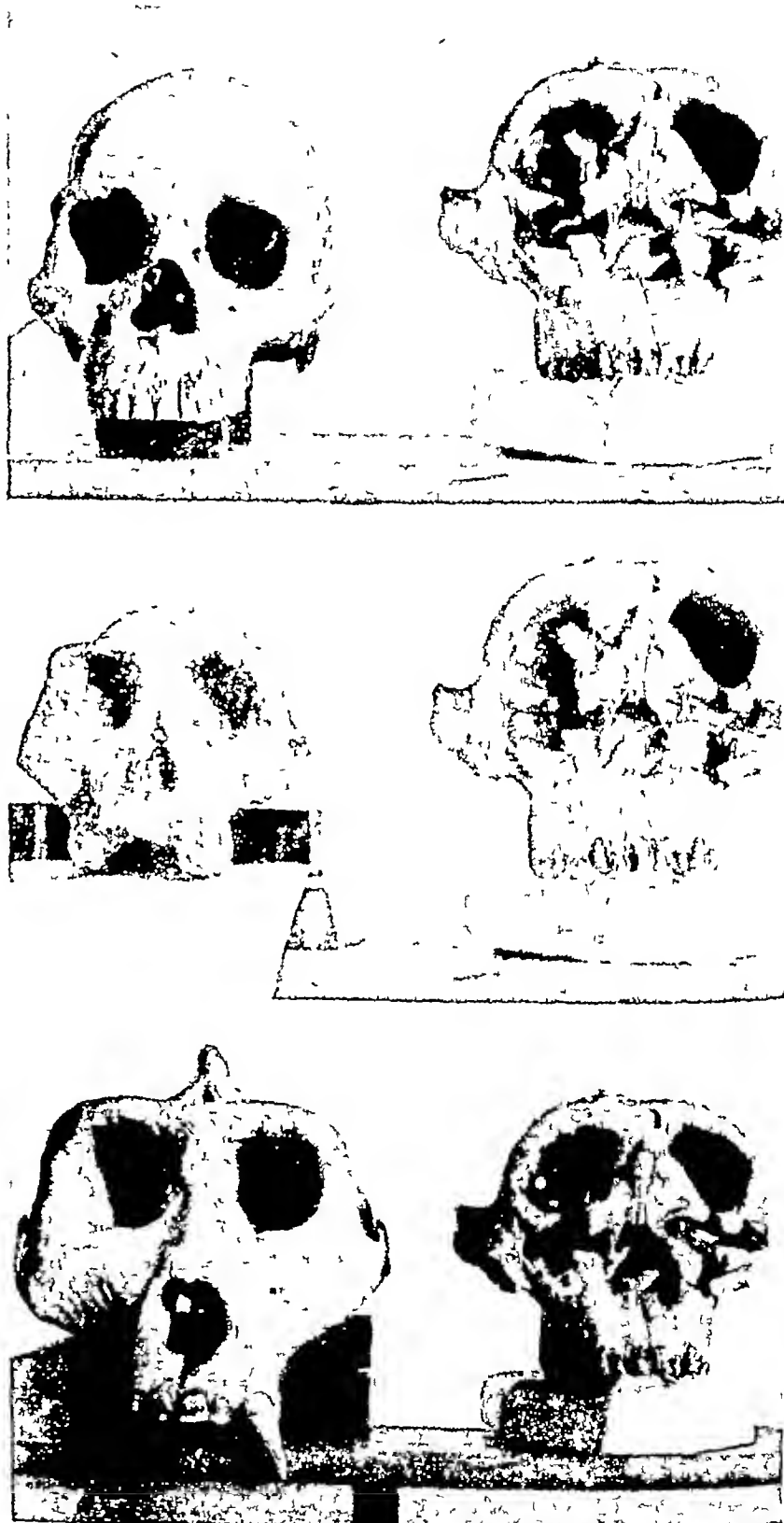
(i) the very great pneumatosis of the whole of the mastoid region of the temporal bones, which even invades the squamosal elements,

(j) the massiveness of the jugal element of the temporal bone relative to the total size of the temporal bone,

(k) the way in which the parietals rise almost vertically behind the squamous elements of the temporal before bending over to become a dome,

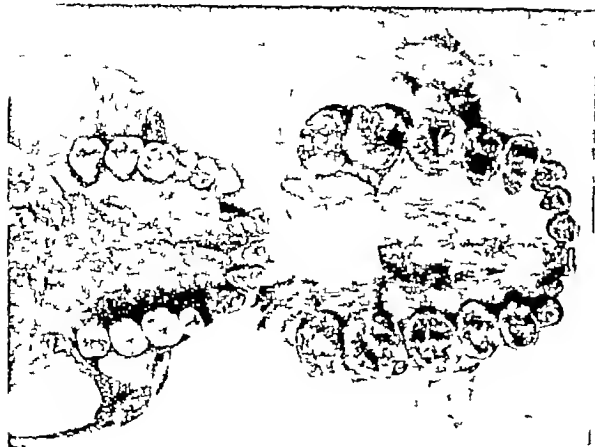
(l) the relative thinness of the parietals in comparison with the occipitals and the temporals,

(m) the very prominent and keeled anterior margin of the crests on the frontal bone for the anterior segment of the temporal muscles in the region of the post-orbital constriction (even the most



Des Bartlett-Armand Denis Production

Fig 1 Above The new skull compared with the skull of an Australian aboriginal. Note the very long face, the architecture of the malar region, the unusual nasal bones, the torus above the mastoid, the sagittal and nuchal crests. Middle The new skull compared with a cast of the most complete adult of *Australopithecus*. Note the difference in the size and shape of the face, the shape of the tympanic plate, the low position of the inion, the huge mastoid, as well as the difference in the shape of the malar region and the supra-orbital area. Below The new skull seen next to that of a gorilla.



Des Dartlett-Armand Denis Productions

Fig. 2. The palate of the new skull compared with that of an East African native

muscular male *Paranthropus* exhibits nothing comparable)

(n) the very unusual position of the nasion, which is on the most anterior part of the skull, instead of being behind and below the glabella region

(p) the very great absolute and also relative width of the inter-orbital area with which may be associated the shape of the nasal bones which are much wider at the top than at their inferior margin

(q) the whole shape and position of the external orbital angle elements of the frontal bone

(r) the very deep palate which is even more markedly like that of *Homo* than in *Australopithecus*, and is quite unlike the form seen in *Paranthropus*, except in respect of the more or less straight canine incisor line which has already been commented on, as a character recalling *Paranthropus*

(s) the conformation of the malar maxillary area of the cheek. In all known members of the genera *Australopithecus* and *Paranthropus* there is a buttress of bone which runs down from the malar towards the alveolar margin of the maxilla in about the region of the fourth premolar. In *Zinjanthropus* this buttress is wholly absent and the form of arclutecture of this region is that which is found in *Homo*

(t) the very great area of muscle attachment on the inferior margin of the molars,

(u) the relatively greater reduction of the canines in comparison with the molar-premolar series than is seen even in *Paranthropus* where it is a marked character

Zinjanthropus boisei sp. nov.

A species of *Zinjanthropus* in which the males are far more massive than the most massive male *Paranthropus*. The face is also excessively long. Males have a sagittal crest at least posteriorly. Upper third molars smaller than the second.

The above is only a preliminary diagnosis of the genus *Zinjanthropus* species *boisei*. It is recognized that, if and when further material is found the

diagnosis will need both enlarging and possibly modifying

The whole question of generic value is one which is relative. There are some who maintain that *Australopithecus* and *Paranthropus* are not generically distinct and who will wish to treat *Zinjanthropus* as a third but less specialized species of a single genus, but the differences seem to be too great for this.

I must now turn to the absolute and relative geological age of the new skull. As stated earlier, *Zinjanthropus* comes from Olduvai Gorge, about 22 ft. below the upper limit of Bed I. It was found in association with tools of the Oldowan culture on a living floor and with associated fauna.

In the past it has been customary to regard Olduvai Bed I as a part of the Middle Pleistocene, not differentiating it from Bed II. During the last few years however detailed excavations at sites BK II SHK II and HWK II have shown that there is a constant and well marked break between the top of Bed I and the base of Bed II. It is incidentally on this clearly defined land surface that Chellean Stage I living sites are found.

There has also been found a great deal of new faunal evidence and it is now clear that the fauna of Olduvai Bed I is the same as that of Ormo, and that both are generally of the same age as that of Taung.

In other words, it is now necessary to regard Olduvai Bed I as representing the upper half of the Villafranchian and not the lower part of the Middle Pleistocene. So far as relative dating is concerned it now seems clear that in the Far East the Djetia beds belong to the Middle rather than to the Lower, Pleistocene, so that the new Olduvai skull would be older than the oldest *Pithecanthropus*.

In South Africa the deposits at Taung and Sterkfontein are now regarded as belonging to the upper part of the Lower Pleistocene. They must therefore be regarded as generally contemporary with Olduvai Bed I. The Makapan beds are a little younger, in all probability, while Swartkrans is of Middle Pleistocene age as are the upper beds at Sterkfontein which are now yielding stone tools.

With the Taung child, therefore, and the *Australopithecus* fossils from the lower beds at Sterkfontein, the new find represents one of the earliest Hominidae with the Olduvai skull as the oldest yet discovered maker of stone tools.

The following approximate measurements will indicate the size of the new specimen

| | |
|--|-------------------------------------|
| Length frominion to glabella | about 174 mm |
| Greatest breadth at supra mastoid torus | 138 mm |
| Greatest breadth of brain case on squamosal element of the temporal bones | 118 mm |
| Height (in Frankfurt plane) from nasion to a point vertically above it in the sagittal plane | 99 mm |
| External orbital angle width | 122 mm |
| Inter-orbital width | 52 mm |
| Post orbital width | 85 mm |
| Palate-length from front of incisors to a line joining back of third molars | 84 mm |
| Palate width at second molars | 62 mm |
| Palate width at third premolars | 6 mm |
| Length of molar-premolar series | 72 mm |
| Teeth measurements | |
| M3 | 21 x 16 mm |
| M2 | 21 x 17 mm |
| M1 | 18 x 15.5 mm |
| P1/4 | 18 x 12 mm |
| P1/3 | 17 x 11.5 mm |
| P2 | 7 x 7 mm |
| C1 | (both damaged but about 16 x 5 mm.) |

ASPIRIN AND ALGESIMETRY

By DR C V WINDER

Parke, Davis and Co., Detroit 32, Michigan

ASPIRIN relieves mild natural pain of various causes and locations. It is reasonable to expect, therefore, that it should raise the minimal noxious stimulus required for an experimental nociceptive response in animals or for experimental pain perception in man. This has been realized in several laboratories with satisfactory validity, but experiments have failed. Success and failure by respective procedures exist side-by-side in the same laboratory without explanation. We, like others, have repeatedly failed to demonstrate an effect of intraperitoneally administered aspirin on the threshold amount of mechanical pressure on a rat's tail required to induce squeaking¹. We have succeeded, on the other hand, in showing an effect by the same route on the threshold intensity of radiant heat, applied to the back of guinea pigs, that is required to elicit a twitch of the skin muscles². The success is often repeated³, and the dose of aspirin required is in appropriate relationship to doses of morphine or meperidine required in the same procedure—all high, relative to human doses.

Magnitude of Experimental Anti-nociceptive Effect

The greatest rise in nociceptive threshold caused by increasing intraperitoneal doses of aspirin in the guinea pigs is about 30 per cent^{2,3}. Similarity of this magnitude to that originally reported by Wolff *et al.*⁴ for the rise in radiant thermal threshold for pain perception in man is only coincidental. When the guinea pigs were given aspirin by stomach tube instead of intraperitoneally, even large, toxic doses caused no more than 10–15 per cent rise in threshold⁵. When Wolff's group adopted a less biasing experimental design with placebo control, a change bearing no relationship to the change in route of administration in guinea pigs, the ceiling of effect in man also became 10–15 per cent⁶. The factors responsible for the larger intraperitoneal effect in guinea pigs remain unknown.

A similar small effect of aspirin was observed in dogs by Andrews and Workman⁷, using the same stimulus-response system afterwards used in the guinea pigs, and later by Richards⁸. Eagle and Carlson⁹ tabulated a very small effect of aspirin on the rat's threshold to mechanical stimulation of the tail. Hart¹⁰ and Bonnycastle *et al.*¹¹ obtained definite effects in rats with respective modifications of the D'Amour-Smith¹² procedure (tail flick in response to radiant heat). Gibson *et al.*¹³ reported significant effects of the sodium salt of aspirin on the threshold strength of electrical stimulation of the rat's rectal mucosa required to induce squeaking. Deneau *et al.*¹⁴, working with experimental deep pain of calf muscles in man, exhibited a clear-cut 10–15 per cent rise in the threshold stimulus associated with aspirin administration. Benjamin¹⁵ showed that aspirin significantly delays the time when pain terminates work being done by the human forearm deprived of circulation, and presented results suggesting that more intensive work with less precise procedures would also show aspirin effects of statistical significance.

Thus, it seems inescapable that a small and subtle anti-nociceptive effect of aspirin can be demonstrated in the laboratory with brief noxious stimulation not obviously associated with inflammation, though the conditions required are poorly understood.

Site of Experimental Antinociceptive Effect

Cook and Bonnycastle¹⁶ could find no effect of aspirin on spinal reflexes. They¹¹ found that relatively large amounts were required in the chronic spinal rat, as contrasted with the intact rat, to influence the tail-flick response to radiant thermal stimulation. It is inferred that at least a portion of the acute experimental anti-nociceptive action of aspirin, perhaps varying among successful experiments, occurs at neural mechanisms above the spinal level.

In this connexion, it is classical knowledge that nociceptive responses are potentially complete at the spinal level, especially in lower species, but that in the intact animal they are under constant control of a balance of active inhibitory and excitatory influences from high levels (for example, ref. 17). Unfortunately, since Irwin *et al.*¹⁸ pointed out that the tail flick and the skin twitch are like other nociceptive responses in this respect, many writers have spoken of these two responses as "merely spinal reflexes"¹⁹ even in the intact animal. Winter and Flataker²⁰ and Bonnycastle and Cook^{11,16} have commented on this error.

Possible Role of Neurological Summation

During early work on twitch in the skin of the guinea pig, we found² that sensitivity of the threshold stimulus intensity to morphine varied significantly with the area and duration of the radiant heat stimulus. We selected as near optimal a large area (730 mm²) and an intermediate duration (4 sec), determining threshold intensity as the dependent parameter. With this in mind, I suggested six years ago²⁰ that use of a pattern of stimulus characteristics emphasizing spatial or temporal neurological summation might in some way be a factor of success in demonstration of an anti-nociceptive effect by aspirin. The area of stimulation employed by Wolff's group⁶ ordinarily was about 80–310 mm², and presumably that of Andrews and Workman⁷ was similar. Hart¹⁰ prewarmed the rat's tail subliminally, thus providing a likelihood of temporal summation. Bonnycastle¹¹ pointed out the probable importance of his less intense and more prolonged stimulus. Deneau's¹⁴ pressure cuff affected a large muscle mass. Gibson's¹³ rectal electrode was relatively large. Benjamin's¹⁵ uncirculated forearm was a considerable mass of tissue.

This will recall the well-known opinion of Wolff's group⁶, based on work with liminal 'pricking pain', that pain sensation is neurologically unique in lacking the property of spatial summation. Rather, these workers' results would seem to indicate a very pronounced central occlusion of a smaller liminal field by a larger one², reflecting at once the poor

local sign of pain and a very efficient central convergence of excitation. Even so, spatial facilitation manifests itself near the lumen either for the subiective sensation¹¹ or for the nociceptive response¹²

Insufficiency of Central Anti-nociceptive Action Alone

However real a central neural action so small and subtle as that of aspirin seems inadequate by itself to account for the efficiency with which the drug relieves natural pain. Goetzi¹³ came to this conclusion on viewing his own negative experimental results with aspirin together with older work. Now there are more positive kinds of evidence.

During the past two decades many compounds of miscellaneous structure have been reported in the pharmacological literature to possess experimental anti-nociceptive potencies in animals more or less superior to that of aspirin but inferior to that of codeine. Many of these have been tested clinically but none has been generally accepted. Two such compounds with which we have worked were more powerful anti-nociceptives in guinea pigs than aspirin and, by contrast with aspirin were significantly though not strongly anti-nociceptive in rat tail pinching experiments (α piperidyl 3,4-dichlorophenylacetic acid, monohydrochloride and 1 (1 piperidyl) 1-cyclohexanecarboxamide, monohydrochloride synthesized by E. M. Jones and P. J. Ehrlich (1950-51), evaluated for anti-nociceptive action by J. Wax, J. Lyon, S. Kaprielian, V. Burr, M. Been and C. V. Winder (1950-54)). Yet, in natural human pain, both were significantly ($P = 0.05$) inferior to aspirin if, indeed effective at all¹⁴.

The history of salicylamide is instructive. The anti-nociceptive action of this old compound is sufficiently greater than that of aspirin to be demonstrable in many laboratories. Yet the drug's analgesic efficacy, long in doubt before the recent attention it has enjoyed, is now again in serious doubt¹⁵. Derivatives of salicylamide even more potent as anti-nociceptives in animals also have failed as yet of clinical acceptance, at least one being significantly¹⁶ and another fairly probably¹⁷ less effective than aspirin in natural pain.

It is therefore now reasonably clear that a degree of experimental central anti-nociceptive action somewhat greater than that of aspirin is not, by itself, predictive of clinical analgesia. It is conceivable though unsupported that the quality of central action by aspirin differs from that of many other kinds of agents in such manner that, even though small it could account for relief of natural pain.

One consequence of this working attitude is that many of us need no longer be so concerned with boxes of experimental compounds having no more anti-nociceptive action than say, salicylamide excepting those for which evidence can be found of some adjunctive action that could potentiate a small anti-nociceptive effect in the relief of pain.

Adjunctive Anti-preinflammatory Action

Returning to aspirin in search of some adjunctive property, one sees most prominently the drug's well established anti-rheumatic effect, a fairly specific anti-inflammatory action in the acute phases of rheumatic diseases. It could be a suppression of some rather early process—a proinflammatory process—in the course of reaction by tissue to injury. The same process could lead both to stimulation of

pain endings and, eventually to frank inflammation. It could be a process more or less common to early tissue injury associated with various kinds of natural pain. It would probably take longer to develop than the duration of most experimental noxious stimuli.

The hypothesis that a peripheral anti-preinflammatory property is essential in the relief of natural pain by aspirin gains stature on again considering salicylamide. Doubt concerning the analgesic efficacy of this agent, in spite of supra-aspirin anti-nociceptive potency, parallels doubt concerning its anti-rheumatic efficacy¹⁸. A complementary test of the hypothesis is provided by aminopyrine. With a similar order of anti-nociceptive potency the unquestioned analgesic efficacy of this drug parallels its unquestioned anti-rheumatic efficacy.

Harris proposed several years ago¹⁹ that the pain relieving effect of aspirin could be explained entirely in terms of a peripheral anti-inflammatory action. The present hypothesis differs in considering rather, an anti-preinflammatory action as an adjunct which as may become apparent later on, is probably not entirely sufficient by itself.

Adjunctive Actions of Other Kinds

It is likely that other properties of aspirin sometimes contribute to its ability to relieve mild pain. In pre-equilibrium phases of certain febrile states the antipyretic effect may relieve muscle soreness in part via reduction of muscle tonus.

The hypothetical necessity of an anti-preinflammatory action in aspirin or aminopyrine for significant relief of natural pain would correlative require that another kind(s) of adjunctive action be identified in the acetanilid group. Neither acetanilid nor acetophenotidin is clearly antirheumatic in ordinary clinical doses²⁰ nor is N-acetyl-p-aminophenol known to be, yet all are considered able to relieve mild pain^{21,22}. However, all have the underlying anti-nociceptive action. Acetanilid and acetophenotidin are perhaps, more potent than aspirin in this respect²³. N-acetyl-p-aminophenol the main metabolic intermediary of both²⁴ and perhaps substantially responsible for their anti-nociceptive action²⁵, is about equally potent²⁶. Moreover, all are antipyretic^{27,28} and, in addition, seem to possess a pattern of sedative and relaxing properties²⁹ that could be importantly adjunctive to the anti-nociceptive action³⁰.

Insufficiency of Adjunctive Properties Alone

Analgesic efficacy in the acetanilid group thus suggests an underlying importance in a mild analgesic agent of anti-nociceptive action, small and subtle though it may be. Mere absence of pyrexia, malaise and muscle tension, or of anxiety, or presence of mild sedation, is not *per se* generally analgesic.

The case of phenylbutazone indicates that anti-rheumatic potency alone is insufficient for prediction of general analgesic efficacy. This drug is now well known to be the most potent anti-rheumatic agent outside the cortisone group, yet there seems to be no firm evidence for utility in relieving pain except in grossly inflammatory diseases. Correspondingly though large intravenous doses were anti-nociceptive³¹, we have been unable to detect such action at sublethal intraperitoneal doses in guinea pigs or at a fourth the LD_{50} of the drug intraperitoneally in rats³². Fewer rheumatologists are now referring to phenylbutazone as 'analgesic' action and more to its anti-inflammatory action.

Lack of known usefulness of cortisone like agents as general-purpose analgetics may not be pertinent. These glucocorticoids possess a different kind of peripheral anti-inflammatory action³⁴, perhaps not impinging so specifically on particularly early reactions to tissue injury that lead directly to stimulation of pain receptors.

Thus, it has been our working hypothesis for the past few years that the small, central, anti-nociceptive action of aspirin or aminopyrine, though necessary, is not sufficient by itself for mild analgesia, but is effectively potentiated (?) by a peripheral anti-preinflammatory action related to non-steroidal anti-rheumatic action which, however, is also insufficient alone.

One interesting implication is an explanation of the old and growing clinical popularity of mixtures of codeine with aspirin, or of aspirin and acetophenetidin. The anti-nociceptive effects of the two or three agents would be additive. The more general sedative effects of codeine and acetophenetidin would, perhaps, add. The combined anti-nociceptive effect would amplify the peripheral anti-preinflammatory effect of the aspirin and the sedative effect of the codeine and acetophenetidin. The end clinical action of the combination of drugs might be somewhere between addition and multiplication of the individual drug effects.

A Laboratory Model of Pre-inflammation

For several years we have been studying the influence of drugs and chemicals on development of erythema on albino guinea pigs following exposure to ultra-violet energy³⁴, a procedure first employed by Wilhelmi^{32, 35}. This experience has strongly influenced development of the foregoing hypothesis.

In a standardized procedure wherein the erythema is developed 2 hr. after exposure, divided-dose pre-treatment with a typical non-steroidal anti-rheumatic agent delays the appearance of the erythema in a proportion of animals depending on dosage. Significantly effective divided doses of various agents in the experiment closely approach daily anti-rheumatic doses in the clinic, on a body-weight basis.

Aspirin and aminopyrine are effective in this test, they are anti-rheumatic, anti-nociceptive and analgetic. Salicylamide is not effective, it is doubtful as an anti-rheumatic, and, in spite of easily shown anti-nociceptive action, is doubtful as an analgetic. The two supra-aspirin experimental anti-nociceptives mentioned earlier that were found ineffective as clinical analgetics²³ were not effective in this test³⁶. Phenylbutazone is most potently effective, it is most potently anti-rheumatic, yet not clearly anti-nociceptive and not, apparently, generally analgetic. The acetanilid group presents the same problem discussed earlier. These agents are not effective in the ultra-violet erythema test at dose-levels that would be tolerated, they are not usefully anti-rheumatic, but, nevertheless, their anti-nociceptive action apparently provides an underlying basis for mild analgesia, perhaps essentially aided by a more general action on the central nervous system.

The ultra-violet tissue injury sets off a pre-inflammatory phenomenon amenable to influence by non-steroidal anti-rheumatic agents. Presumably it is related to a pre-inflammatory phenomenon in various painful tissue states which these same agents influence when, provided they also have some central anti-nociceptive effect, they relieve pain.

Cortisone-like agents do not influence the erythema³⁴, have different kinds of effects on inflammatory processes, and are neither anti-nociceptive³⁷ nor known to be generally useful as analgetics. The more potent analgetic agents from codeine upward do not delay the erythema and have no specific anti-rheumatic effect. Their pain-relieving actions are central and are associated with sufficiently robust experimental anti-nociceptive effects so that there is no great difficulty in comparing them in the laboratory in terms of acute, non-inflammatory pain.

One can only speculate on the nature of pre-inflammatory processes induced by noxious tissue states, leading to stimulation of pain endings and eventually to frank inflammation, and susceptible to agents like aspirin. It is conceivable that some clarification might come from work now being done in several laboratories on activation of proteases and/or globulins, formation of kinins, release of potassium, etc.³⁷

More Complete Laboratory Models of Natural Pain

If the ordinary experimental noxious stimulus is, perhaps, too brief to allow development of the pre-inflammatory state upon which aspirin seems to have an essential component of its action, then it is natural to consider having this state pre-established as a part of the eventual total stimulus. We were therefore gratified to note a description by Randall and Selitto³⁸ of a laboratory model of inflammatory pain—measured pressure applied to the inflamed and oedematous foot of the rat. One is reminded of Selumachier's³⁹ earlier work on the effect of aspirin on experimental pain thresholds of inflamed human skin.

Using the inflamed foot, Randall and Selitto found sodium salicylate, acetophenetidin, N-acetyl *p*-amino phenol, and phenylbutazone effective in raising the threshold pressure required for a nociceptive response. It is somewhat discouraging that aminopyrine was not significantly more effective than sodium salicylate—a deviation from clinical experience. It is interesting and more understandable that acetophenetidin and N-acetyl *p*-aminophenol were only a half to a quarter as potent as sodium salicylate, even though they were more potent central anti-nociceptives as measured with the normal, uninfamed foot. This agrees with the absence either of anti-rheumatic and anti-erythemic (ultra-violet) effects of these two agents at tolerated dosage, or of any obvious means for reflexion of their adjunctive sedative properties in the results. Also, it is gratifying that phenylbutazone was only slightly more potent than sodium salicylate, and would thus be predicted to have general analgetic utility, if any, only at doses much larger than can safely be employed clinically for the anti-rheumatic effect. This agrees with the present lack of clinical evidence of general utility as an analgetic, and with absence of clear anti-nociceptive action at subtoxic doses (*supra*).

Randall and Selitto³⁸ suggest a liability in their model that we believe may be inherent in any involving oedema³⁴—a liability to induce effects from vascular disturbances caused by the agent on test. It will be interesting to study the properties of a model in guinea pigs combining the relatively non-oedematous³⁴ ultra-violet inflammation and the acute, wide-area radiant heat stimulus^{2, 3}.

Recently, mice injected intraperitoneally with appropriate amounts of phenylquinone⁴⁰ or acetic acid⁴¹ have been observed to 'writhe'⁴⁰ or 'stretch'⁴¹.

repeatedly and for long periods. The phenomenon is suppressed by suitable doses of aspirin or amino pyrine, as well as by the more potent central analgetics. The stimulus, presumably noxious, differs in two important respects from those considered heretofore. First, it is applied to a larger tissue surface, potentially bringing into play a much broader pattern of neurological convergence. Secondly, it is present for a longer time at once providing possibilities of temporal neurological summation and of maturation of preinflammatory processes. In terms of the present thesis, any or all of these factors would improve sensitivity to agents like aspirin or aminopyrine.

High doses of acetophenetidin required to suppress writhing in one laboratory¹⁰, and of salicylanilide in another¹¹, recall again the poor activity of these agents as anti-rheumatics or anti-erythromes (ultra-violet) and suggest that the writhing stimulus leans to some extent on a pre-inflammatory component. Discrepancy between the two laboratories in effective doses of sodium salicylate is puzzling. Suppression of the writhing by a variety of chemicals and drugs¹² renders the phenomenon rather enigmatic at present.

It may be that, with increasing attention to matters like extensivity, duration and quality of stimulus as well as to higher level neurological conditioning¹³, research workers will gradually resolve the differences between experimental and natural pain so long and vigorously emphasized by Beecher¹⁴.

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CHANCE AND PROBABILITY

IF the fundamental concepts of mathematical probability and their role in statistical theory are still subject to sharp controversy after three centuries of discussion by the acutest minds we can scarcely expect that the concepts of psychological probability, born within the past decade, should already have found general acceptance. It is not indeed clear to every one where mathematical probability ends and where psychological probability begins if it is justifiable to separate them at all. The papers presented at a session of Section J (Psychology) during the York meeting of the British Association at least shared the view that the study of psychological probability unquestionably offers im-

portant opportunities for research into hitherto unexplored realms of mind and behaviour. The three papers presented were "Wishful Seeing in a Gambling Situation" jointly by Dr John Boloff and Mr Kenneth Warwick (Queen's University of Belfast) and read by the former 'Chance and Uncertainty' by Dr W. Mays (University of Manchester) read in his absence by Dr D. McMahon and 'The Psychology of Luck', by Prof John Cohen (University of Manchester).

The paper by Dr Boloff and Mr Warwick was devoted to an experimental study of perceptual autism, an expression coined by Prof C. D. Murphy in 1947 to refer to those subjectively distorted

changes in perception which have the effect of gratifying the observer's needs—in other words, wishful seeing. The context of the experiments was a type of gambling situation. As a point of departure they took various investigations by Murphy and his colleagues designed to establish the autistic phenomenon and they discussed the criticism that the observations could be explained in terms of the familiar notions of 'expectancy' or, alternatively, in terms of 'response availability' without postulating a special autistic mechanism. Thus if a hungry man, on being shown an inedible object, says that it is something edible, it does not follow that he says so because he sees it as such but merely because he would naturally be thinking of things to eat. Dr Beloff's experiments were designed to rule out these alternative explanations.

Three distinct experiments were conducted. In the first the subject had to guess which of four possible visual stimuli would appear in a brief tachistoscopic exposure. Before each exposure the subject was told that a square (with a cross inside) would be shown with one of the sides missing, and he had to guess which one it would be. He was given money with which to bet on his guess. On the autistic hypothesis the guesses should tally with the bets on a statistically significant number of occasions.

In this first experiment there were two series of presentations, one random and one biased. In the random series, the subject presumably had no 'reason' to believe that a particular card was more likely to appear at a given trial, whereas in the biased series it was experimentally possible to distinguish between what the subject 'expected' and what he 'wanted' to appear. There was a significant autistic effect, in spite of marked individual differences in patterns of response. This led Dr Beloff to suggest that autism is a feature of personality and, in this sense, akin to optimism.

In order to meet the possible objection that this outcome was due to 'response availability', the second experiment introduced a new series which required the subject to bet on the card which he expected *not* to appear, and to forfeit his bet if it did. The reward series again revealed an autistic effect but not the penalty series, the bet-guess correspondence being at chance-level.

In the third experiment a further attempt was made to ensure that the hypothesis of 'expectancy' could be eliminated by depriving the subject of the power of deciding which of the four cards was to be rewarded. The subject now won his bet if the stimulus corresponded to a particular counter drawn at random in advance of the exposure. This experiment seemed to show clearly that "once desire is divorced from expectancy by introducing an *arbitrary* system of rewards and penalties, the autistic effect no longer operates". Without denying that emotions may influence perception autistically, Dr Beloff concluded that there is no need to assume a special central determinant, as proposed by Prof Murphy.

Dr Mays's paper discussed certain logical and psychological issues arising in the study of probability in general. He began by referring to Venn's views expressed in his "Logic of Chance" (1876) and passed on to a more detailed criticism of Prof S. E. Toulmin's contribution to an Aristotelian Society symposium on probability in 1950. As to Prof Toulmin's question of the meaning of 'probability', Dr Mays stated "the answer is probably very little, since it refers to a generalized situation, not always

specifiable by concrete operations". In his view Prof Toulmin under-estimated the extent to which adult thinking is permeated by technical ideas deriving from games of chance.

Dr Mays stated that psychologists had studied the pragmatic understanding of probability from two points of view: that of methodology and that of concept formation. He thought that the initial impulse to study subjective probability had come from experiments on extra-sensory perception, and suggested that descriptions of the way people behave in experimental probability situations ought not to be taken as a guide to rational behaviour, that is, as ethical norms, which subjective probability, in the sense used by Ramsey and Savage, is evidently meant to be.

Much of Dr Mays's paper took the form of a critical résumé of the views of certain psychologists, notably Goodfellow and Piaget. The main feature of Piaget's work, he declared, is to take "the abstract calculus of probabilities as an objective standard of mature behaviour, and deviations from it (the so-called illusions) as a mark of immaturity". The concept of 'chance', according to Piaget, is not an intellectual intuition, but has to be learnt, since the child endeavours to find a causal factor in everything he observes, he cannot apply the notion of equiprobability of probability situations. The child's notion of probability, in Piaget's view, only appears when he has built up a system of logical operations enabling him to contemplate possibilities (in terms of combinations and permutations) beyond what actually happens.

Dr Mays believes that there is little to be said in favour of the belief in a special type of subjective probability postulated to cover what he described as "really an amalgam of emotional attitudes, intellectual systems, etc.", an approach which reminded him "of the instinct psychologists and the Aristotelians who postulated a new type of instinct for every form of behaviour".

Prof Cohen placed the study of luck in the context of psychological probability. The belief in luck, he suggested, originated in the attempt to master life's uncertainties. As societies become more civilized their uncertainties do not diminish. Hence the idea of luck survives with full vitality. The examination of luck formed part of a systematic series of studies initiated at Manchester in 1952, into those forms of thought and behaviour which characterize states of uncertainty: choice, estimation, prediction, inference, risk-taking, and decision-making generally, and the method of investigation was at once experimental and developmental. He ventured to make two inferences from his earlier inquiries which had a bearing on the present one. First, the idea of 'randomness' is alien to the human mind, which is essentially pattern-seeking or, in more general terms engaged in an implicit or explicit search for meaning. Secondly, there is evidence that our minds act as unwitting 'computers' and, under certain conditions, an analogy can be drawn between quasi-additive and quasi-multiplicative operations in psychological probability and the fundamental properties of mathematical probability.

Prof Cohen then considered the meaning of 'luck' in terms of observed usage, principally in the twofold sense of 'unearned advantage' and 'fortuitous intervention'. He illustrated the survival of beliefs in luck by reference to the fact (as he had found) that young and old alike still have their lucky colours.

days and numbers. Moreover, people are believed to have stores of luck which can be depleted and replenished, and there is evidence that women felt themselves to be luckier than men.

Prof Cohen was mainly concerned to describe experimental demonstrations of the effect of a belief in luck on expected performance and achievement. Thus, a subject could estimate realistically his likely performance at any given task. This estimate could then be compared with other estimates of his likely performance if he thought he would be (a) lucky, (b) very lucky, (c) unlucky, (d) very unlucky. From a variety of experiments of this kind it seemed that, within a given range of tasks, to be lucky signified an expected improvement in performance of some 10 per cent and to be very lucky, of 20 per cent. Unluck meant an expected deterioration of 30 per cent and very bad luck anything up to 80 per cent.

An allied effect of the belief in luck could be measured in terms of the proportion of attempts in which the subject expected to succeed at particular tasks varying in level of difficulty. Here too, the pattern of realistic estimates could be compared with the pattern of estimates of success with varying degrees of expected luck and unluck. Psychological probabilities derived in this fashion revealed that when tasks are of comparable subjective difficulty the patterns of estimates of expected performance bear a striking mutual resemblance. Furthermore, a pessimistic under-estimation of one's capacity appeared when the task seemed subjectively easy and an optimistic over-estimation when it seemed hard. A generalization of particular interest could be embodied in the formula

$$\psi_i^p + \psi_i^{1-p} = 1$$

where ψ represents the psychological probability, p the *a priori* probability of success and 1 (and \bar{p}) the degree of luck (or unluck) to which the original estimate relates. What is conveyed by this formula

is the empirical observation, based on many experiments, of the quasi-additive character of psychological probabilities. Suppose for example, that the *a priori* probability of a subject's success at a task is 0.1, and that his corresponding psychological probability if he thinks he will be very 'lucky' is 0.6, then when the *a priori* value of success at a similar task is 0.0, his psychological probability of success if he thinks he will be very 'unlucky' turns out to be approximately 0.4. The additive property appears when the values of ψ are derived from estimates made after as well as in advance of performance.

A different analysis was employed by Prof Cohen to measure the frequency with which we think good or ill fortune will befall us. In his experiments, the estimate of performance which is regarded as most realistic is expected by the subject to occur on some 52 per cent of the occasions, the lucky (or unlucky) outcome on some 17 per cent and the very lucky (or very unlucky) outcome on some 7 per cent. These experiments Prof Cohen believes shed light on the basis of our aspirations. For in everyday life we are often governed by unrealistic considerations, and what we are in fact prepared to undertake may depend basically on what we imagine we should achieve if we were lucky or unlucky. The range and pattern of psychological probabilities might justify the assumption of a sort of inner standard deviation* of judgment.

Prof Cohen also spoke at some length of social repercussions of a belief in luck, particularly as a stabilizer in allaying socio-economic envy, and in discouraging mutiny, and he referred to the 'magical significance of the practice of disparagement, both of self and of others'. In conclusion he drew a parallel between individual and cultural psychological probability in that the phenomenon of pseudo subjective dependence (or the Monte Carlo fallacy) has its analogue in the cyclic, as contrasted with the linear, conception of time and history which characterizes traditional and archaic cultures.

COAST EROSION AND ACCRETION

IT is almost true to say that, despite the full and interesting reports of the Royal Commission on Coast Erosion (1907-11) little effective action on the coasts of Britain was taken until the severe flooding of 1953 occurred. A Departmental Committee was then appointed under the chairmanship of the late Lord Waverley, and in 1954 made two relatively short reports containing a number of recommendations. Three of them are particularly relevant to this article. No. 10 reads 'that steps should be taken to ensure proper co-ordination of researches. Recourse might well be had for this purpose to the constitution of two consultative and advisory standing committees. There should be close co-operation on research matters between British and Dutch scientists, engineers and Governments'. Recommendations 2 and 3 emphasized the necessity of research into 'the behaviour and suitability of vegetation for use on sand, shingle and other material adjacent to the sea', and 'the urgency of research into the movements of beach material off-shore banks and related coastal problems'. Thus the discussion organized by Sections E (Geography) and K (Botany) at the recent British

Association meeting at York was particularly relevant.

The two standing committees referred to have been formed, and the one devoted to sea defences is that most concerned with this article. The other is primarily concerned with tidal and oceanographical matters. The sea defence committee under the chairmanship of Mr E. A. G. Johnson, of the Ministry of Agriculture, Fisheries and Food, has already made three reports to the Ministers concerned (Agriculture, Fisheries and Food, Housing and Local Government, and the Secretary of State for Scotland). The committee is very alive to the physical and ecological problems affecting our coast, and Mr G. Cole who acts as secretary, was one of the speakers at York. It is the first time in Britain that such complete co-ordination on coastal problems has been attained. Mainly through the personnel of the committee very close contact is maintained with the Hydraulics Research Board, the Nature Conservancy, the Building Research Station (in connexion with sea wall and sea-bank construction), and the universities. Since too radioactive and other tracers are becoming more and more significant

in coastal work, there is also a close link with Harwell

In practice the erection of sea defences of one kind or another is the work of engineers, either consultants or those connected with river boards, or local or national authorities. But all who are interested in the coast are concerned among other matters with the source, supply and maintenance of beach material, and with the holding of dunes and the formation of marsh. Experience has shown all too often that indiscriminate building of groynes and walls may have very serious effects in other places. Since the natural protection of much of our coast is a good beach, it is all important to study how it is to be maintained. Careful surveys made by members of the Department of Geography at Nottingham showed that it took 5 or 6 years before the Lincolnshire beaches were restored fully to the level they reached before the 1953 flood scoured them almost completely. In many cases it is possible to assume with a fair degree of certainty that a beach is fed by lateral transport. If this is interfered with at some locality, sites to leeward are bound to suffer. But there are places, for example Scott Head Island, where it is not unreasonable to assume that new material comes more from offshore than alongshore. This matter of offshore supply is one that is frequently debated, and one that perhaps can be finally settled only by tracer or aqualung methods. Already some useful results based on observations by divers have been obtained at Scripps Institute of Oceanography and a beginning has been made in Britain by the physiographic unit of the Nature Conservancy. Careful observations by trained men in water down to a depth of perhaps 100 feet may help very greatly in many shore problems. These more recent methods of approaching the question of supplies of beach material do not in any way mean that the type of studies already in use should be discontinued. Far from it, they should be pursued vigorously, and to 'know' a beach implies a long study. It may sometimes be necessary in building defences to act hurriedly, and it may happen that the result is successful. In general, however, the study of a beach over a period including all types of weather likely to act upon it is desirable. Moreover, it is also valuable to be able to make comparative studies. Conditions are never exactly the same in any two places, but a great deal can be learned by studying comparable localities on different parts of the coast.

The four papers that followed the introductory remarks dealt mainly with specific problems and places. Dr M. C. Pearson, of the University of Nottingham, discussed the biology of the sea buckthorn (*Hippophae rhamnoides*). This shrub enters the succession of sand-binding plants after the marram grass stage. It is found in Britain only on coastal sand dunes, and is common on certain parts of the east coast. Dr Pearson's studies have been made at Gibraltar Point, a nature reserve at the north-eastern corner of the Wash. It has been found that most of the plants originate from underground stems and but very few from seed. This is partly explained as a result of the predation of seeds by birds and small mammals. The shrub carries big spines, and so may form a deterrent to grazing animals and even to picnickers. In that sense it may have value in keeping certain parts of the dunes free from erosion caused by trampling. In any event it is of value in fixing the dunes, and it is used partly in that way in Holland. Further research work on this interesting species is planned.

Mr Cole's paper was concerned with the gathering and stabilizing of sands, silts and clays by vegetation. He pointed out that only along a relatively short distance (60-70 miles) of the total length of the coast of England and Wales do dunes form the sole or partial defence, and salt marshes cover even less distance. He discussed several interesting examples of the artificial accumulation of sand dunes around brushwood or other type of fencing or obstacle, and also the effect of various grasses in their relation to dune and marsh growth. The remarkable growing power of marram was pointed out, but he stressed the view that its ramifying and long roots may have little effect in binding the sand. The building of a new dune by British Railways at Dawlish Warren, and the planting on it of tree lupin (*Lupinus arboreus*) following the marram, was taken as a good example of the artificial production and maintenance of sand dunes.

In the development of marshes the planting of *Spartina* was mentioned. This grass has spread rapidly on the south coast and is now invading, sometimes all too successfully, the east coast. Dr D. Ranwell, of the Nature Conservancy, has recently been engaged upon methods for its eradication. It will be noted that *Spartina* in this paragraph is not followed by any specific name. Dr C. E. Hubbard, of Kew, has shown that the grass which has grown so extensively in Southampton Water and is regularly used for planting and reclamation elsewhere is not *S. townsendii* but rather a chance offspring of that plant, and that so far it has not been given a specific name.

Mr Cole very rightly made the point that it is wrong to rely too much on one or two species. If for some reason disease developed in marram or *Spartina* grave difficulties might arise. There should be experimentation with vegetation and, in certain carefully controlled circumstances, we should introduce foreign species. The idea of a 'coastal garden' in which such experiments could be made has already been adumbrated.

Mr C. Kidson was also concerned with this same point. He has studied certain parts of the coast in great detail, and as physiographer of the Nature Conservancy he has been able to make comparisons with many other parts. His studies on the Somerset coast have shown the value of *Spartina* in accumulating sand and silt, and it is estimated that in part of Bridgewater Bay the level of the foreshore has been raised 5-7 feet since 1928. But here again all is not as it should be. *Spartina* may act locally almost like a groyne, and it is able to hold up the longshore transport of shingle. In one place 60 feet of spartinetum was overridden by shingle in one year. The shingle beach behind, cut off from its supply, was combed down in big storms and became lower and so less of a protection to the land behind. Mr Kidson also directed attention to the interesting work that is now being carried out along the west coast of Denmark. There the foreshore has been built up by *Salicornia* spp. and *Puccinellia maritima*. Their spread has been much aided by the building of low brushwood dams and shallow drainage channels. He also directed attention to the possibility of *Suaeda fruticosa* holding mobile shingle. It is a habit of this shrub to grow at the head of marshes and at the foot of shingle ridges. Prof. Oliver, in his studies of Blakeney Point, directed attention to it many years ago. It is doubtful if the plant can be a real deterrent to shingle movement.

The remaining paper, although given earlier in the sequence, dealt with the coast of part of Lancashire

Mr Gresswell, of the University of Liverpool, has made several extensive studies of this. It is put last here because it was rather less concerned with vegetation than were the others. Nevertheless South Lancashire is faced with a dune coast, and one made up of perhaps more than any other dune area in these islands. The speaker discussed the erosion at Formby and the accretion at Southport. This coast illustrates extremely well how difficult it is to estimate what will happen in the future. Formby and district have been suffering loss for some 50 years, before then the same area was gaining at about the rate it is now losing. Inland of Southport and Formby is a belt of rich agricultural land below the level of high tides and only protected by the dune belt. The dunes have long been controlled, and extensive pine forests cover part of them. But these will not stop erosion. Extensive sea walls may do so and in a limited way so also may bulk accumulation—the artificial gathering of sand by brushwood groynes and careful planting. This will increase the amount to be eroded by the waves—it cannot stop the erosion. It may also be possible to raise the height of the beach by building groynes and stopping the sand which moves both to north and to south away from Formby. But then how will this

affect Southport? The lesson has been learnt a little farther north: the protection of Blackpool has starved the beaches at Fleetwood and caused severe damage there.

Change is constant along the coast, it is most noticeable in those parts faced by soft cliffs or by low-lying ground fringed by dunes and marshes. It is much slower, and perhaps not measurable in a life time, on a coast faced by cliffs of resistant rock. Coastal studies are not only of significance to all dwellers along the sea and owners of land adjacent to it, but they are also of particular interest to workers in many branches of science, archaeology and history. Coastal defence, in the long run, must benefit by the more leisurely rate at which certain experimental work has to be undertaken. Botanists, physiographers and others of several of our universities are now much concerned with coastal research and their findings are appearing with some regularity. The more we know of any particular stretch, the more certain will be the effect of any future defence work that may be necessary. The four papers presented at the meeting of the British Association at York may be regarded as samples of the interest which coastal research is now provoking. J. A. STEENS

OBSERVATIONS OF THE RUSSIAN MOON ROCKET LUNIK II

THE 250 ft radio telescope at Jodrell Bank was used to receive the transmissions from the second Moon rocket launched by the U.S.S.R. Observations were made on the evenings of 1959 September 12 and 13 on frequencies of approximately 183.0 Mc/s and 19.992 Mc/s. The only other part of the radio spectrum searched was in the region 19.99–20.01 Mc/s but no signals from the probe were found.

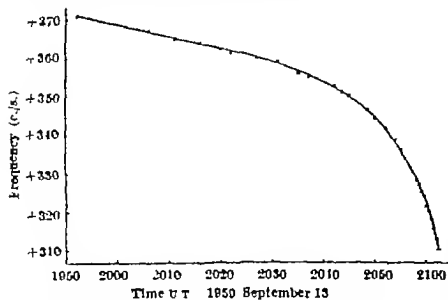


Fig. 1. The variation of received frequency in cycles per second deviation from 19.992 Mc/s plotted for the last hour of the flight of *Lunik II*.

The primary feeds consisted of a folded wire dipole without reflector for the 20 Mc/s band and a folded dipole with reflector for 183.0 Mc/s. The 183.0 Mc/s signal was received on a communication receiver with a band width of 5 kc/s, and the 19.992 Mc/s on a receiver with variable band width 750 c/s being employed for most of the time. Both frequencies

carried the familiar bleep bleep modulation pattern and although clearly audible the signals were not strong enough to permit reliable estimates of signal strength. The signals on both frequencies ended abruptly and simultaneously at 21h 02m 23s UT on September 13.

Within the limits of the 2° beam of the radio telescope at 183 Mc/s, and the rather heavy fading of the weak signals, there was no significant deviation of the position of the rocket from the predictions received from Moscow.

The precise frequency of the 19.992 Mc/s signal was measured by comparison with a frequency standard to an accuracy of $\pm \frac{1}{2}$ c/s. On the evening of September 12 the measured frequency varied uniformly at 4 c/s per hour between 20h 30m and 22h 30m UT. The rate expected from the effect of the Earth's rotation alone is about 6 c/s per hour, thus the rocket was at that time being slightly retarded by the Earth's gravitational attraction. The variation in frequency over the final hour of the rocket's journey on September 13 is plotted in Fig. 1. The smooth nature of this curve indicates that no guiding rockets were used during this period. The slope of this curve is a direct measure of the line of sight acceleration and hence, using the Moon's mass, gives a maximum distance from the Moon for each point on the curve. The acceleration at the end of the curve is that expected for an object moving directly towards the centre of the Moon at a height of 70 km \pm 150 km from the Moon's surface and can therefore be taken as positive confirmation that the rocket did indeed hit the Moon somewhere within 7 minutes of arc from the centre of the lunar disk. The velocity of impact derived from these data is approximately 3 km/sec \pm 0.5 km/sec.

We are indebted to our Russian colleagues for computing the tracking data for the radio telescope

J G DAVIES
A C B LOVELL

Jodrell Bank Experimental Station,
University of Manchester

On September 13, attempts were made to observe the impact of the Russian vehicle upon the Moon. The telescope used was the 12.5-in reflector with which extensive lunar observation has been carried out since 1949.

The impact area had been indicated as that of the Maria Serenitatis, Tranquillitatis and Vaporum. Such an area would be impossible to cover adequately. Since it seemed reasonable to assume that the Russians intended to land the vehicle as close as possible to the apparent centre of the lunar disk, it was considered best to use a reasonably high power ($\times 300$ to 400) and concentrate solely upon the Mare Vaporum region.

Predicted impact time was 21h 01m UT. Nothing was recorded at this time, but at 21h 02m 23s UT (± 2 sec) a minute pinpoint of light was recorded, it appeared suddenly, and faded out within half a second. The lunar co-ordinates are estimated as $+085^\circ +195^\circ$. This places the position as in the Hyginus area, close to Schneckenberg.

Though seeing conditions were good, the phenomenon was so uncertain and so close to the limit of visibility that it seemed unwise to trust it. A report was at once sent to the Director of the Lunar Section of the British Astronomical Association, at Man-

chester, to await confirmation. Since it now seems that both time and position are in good agreement with other observations, there is a possibility that the phenomenon did in fact represent the impact.

PATRICK MOORE

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On September 13, observations were made with the hope of observing the landing of the Russian *Lunik* on the Moon, using a reflecting telescope of 15½-in aperture with a power of 300. The sky was very clear and surface details on the Moon clearly defined. The Russians had said it was aimed at the Mare Tranquillitatis, Serenitatis and Vaporum, that is, the region to the north-west of the geometrical centre. Last Sunday the Moon had sufficient libration to bring this region nearer to the centre as seen from the Earth than usual.

This area of hundreds of square miles was 'swept' regularly. The stated time for impact arrived and nothing was seen. I decided to continue for a short while and 1½ min after the stated time, at 21h 02m 23s UT, I was looking at the Mare Vaporum, the nearest part to the centre. At this point, north of the Hyginus Cleft and close to Schneckenberg, I observed a pinpoint of light and a kind of dark ring just as though dust had been disturbed and heated. This lasted a few seconds.

I understand that this observation is in accordance with the work of other observers.

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NEWS and VIEWS

Engineering in the University of Birmingham

Prof G F. Mucklow

PROF G F MUCKLOW retired this summer from the Chance chair of mechanical engineering, University of Birmingham. He is succeeded by Dr S A Tobias, assistant director of research in the Department of Engineering, University of Cambridge. Prof Mucklow has held the chair since 1940. He was educated at Rugby, McGill University and the University of Manchester. He was for a short time a research associate of British Motor and Allied Manufacturers before taking up the post in 1923 as lecturer in engineering at the University of Manchester. He is well known for his work on compression-ignition engines, super-charging, exhaust pipe effects, wave-action in gases and related topics. During his tenure of the Chance chair, the Department of Mechanical Engineering has been greatly expanded. Prof Mucklow has played a prominent part in the development of postgraduate courses of instruction for men returning from industry. The first course to be established was that in production engineering, and this was followed in 1950 by a most successful course in thermodynamics. He has seen the Department rehoused in excellent buildings which were officially opened in 1954.

Prof S A Tobias

DR S A TOBIAS, who succeeds Prof Mucklow, was born in Vienna in 1930. He received his education at the University for Technological and Economic

Sciences, Budapest, Hungary, and graduated in 1943. For four years after that he worked in industry as a design engineer of machine tools. Tobias came to Britain in 1947 as a British Council Scholar, becoming a research student in the Department of Engineering, University of Edinburgh, where he received his Ph.D. in 1950. During 1951-54 he was an Imperial Chemical Industries research fellow at Edinburgh, working on problems of linear and non-linear vibrations, and received his D.Sc. Edinburgh in 1955. In that year he was appointed assistant director of research in the Department of Engineering, University of Cambridge, where he has built up a flourishing research school in the field of non-linear vibrations and in problems arising in metal-cutting processes.

Agricultural Botany at Bangor

Prof Alun Roberts

PROF R ALUN ROBERTS is retiring from the chair of agricultural botany at the University College of North Wales, Bangor. At Bangor the Departments of Agriculture, Agricultural Botany and Agricultural Chemistry are separate and independent, and, unlike most of the other universities where agriculture is taught, there are no subordinate professorships in those subjects. Prof Alun Roberts was appointed professor at Bangor in 1945, where he had been independent lecturer in agricultural botany during 1921-40, when he was seconded as executive

officer to the Caernarvonshire War Agricultural Executive Committee. His secondment was later transferred to the Welsh Department of the Ministry of Education, in order to study its problems in rural Wales. Plant ecology, especially of the grasslands of Snowdonia, has been the favourite subject of research of Prof Alun Roberts and his colleagues. His knowledge of early settlements and of Welsh history, enriched by long and close study of old estate manuscripts, enabled him to link up ecological changes with past land use. Particulars of early settlements and later stocking of lowland and upland with summer migration of the inhabitants from Hendre to Hafod, have added interest to his ecological studies. In addition to his scientific, historical and literary activities, he has found the time to serve on such bodies as the Royal Commission on Common Lands, the Welsh Land Sub Commission and Nature Conservancy. His knowledge of land use past and present, makes him a specially valuable member.

Prof J L Harper

DR J L HARPER has been appointed to succeed Prof Alun Roberts. He gained honours in the final honours school of botany in 1946 at Magdalen College Oxford, and was awarded the senior Mackinnon scholarship and a Department of Scientific and Industrial Research postgraduate scholarship. In 1949 he carried out research at the Imperial College of Tropical Agriculture and Colonial Microbiological Research Institute Trinidad. He gained his D Phil in 1950 for his work in the interactions of soil micro organisms. Dr Harper is a lecturer in agriculture at University College Oxford, and has been a member of the Board of the Faculty of Agriculture and Forestry since 1957. While he has published much in the realms of plant pathology and of genetics he is perhaps best known for his researches in experimental ecology. By inoculation and practice he is an ecologist in the widest sense, and from an agricultural point of view, in matters of woods prefers to start with the biology of control rather than with chemical applications. Dr Harper, who gained a Rockefeller Foundation award, is at present working in the Department of Dr G Ledyard Stebbins, Davis University, California. He will not take up his appointment at Bangor until next year.

Ministry of Agriculture, Fisheries and Food

Dr H R Barnell

THE Ministry of Agriculture, Fisheries and Food has announced the appointment of Dr H. R. Barnell as chief scientific adviser (food) in succession to Dr N C Wright (see *Nature*, 182 631, 1958), who has been appointed to the office of deputy director general of the Food and Agriculture Organization of the United Nations.

Dr Barnell was educated at Luton Grammar School and at Downing College, Cambridge. In 1929 he obtained first-class honours in the Natural Sciences Tripos Pt II (Botany) and was awarded the Frank Smart Prize. He was afterwards Frank Smart Student in botany. He was a research student in the Cambridge Department of Botany from 1929 to 1932. After a period as research assistant and lecturer in the Cambridge School of Agriculture he was appointed to the staff of the Low Temperature Research Station of the Imperial College of Tropical Agriculture, Trinidad. His work in Cambridge was on the biochemistry of cereals, and in Trinidad primarily on the biochemistry of the banana in

relation to the refrigerated and gas storage of tropical fruits. In 1943 he returned to the United Kingdom as a member of the Dehydration Division of the Ministry of Food and was eventually transferred to the Scientific Adviser's Division where he was primarily concerned with developments within fields of food science and technology. In this connexion he not only played a major part in developing the food aspects of Commonwealth defence science but also was largely responsible for initiating and planning the programme of work of the Ministry's Experimental Factory and Research Establishment at Aberdeen. In 1950 he was appointed deputy chief scientific adviser.

In the course of his official work Dr Barnell has made wide and warm personal contacts throughout the food industry not only in Britain but also overseas, where he has travelled extensively in North America, Central and South Africa, Australia and India. He has served on the governing bodies of a number of food industry's research associations and was one of the Ministry's assessors on the Food Investigation Board of the Department of Scientific and Industrial Research. He is a member of council of the Institute of Biology. Dr Barnell's outstanding contributions in the building up of the Scientific Adviser's Division make his choice as chief scientific adviser a particularly appropriate one.

Difficulties in the Present Systems of Superannuation

A QUESTION was raised in the House of Commons on July 2 regarding difficulties in the exchange of teachers between universities and colleges of technology arising out of their differing schemes of superannuation. In reply Sir Edward Boyle, Parliamentary Secretary to the Ministry of Education, said that the possibility of transfer between the two superannuation systems had been exhaustively considered and found to be impracticable. There were, however, arrangements for integrating service under the two schemes and he believed these were not as widely understood as they might be. Sir Edward Boyle said he was investigating the matter. Transfer had proved impracticable because the pensions under the university scheme were based on an insurance policy and differed in content and kind from those under public service superannuation schemes. Mr Allen pointed out that to fill vacancies in the colleges of advanced technology and the regional technical colleges it will be necessary to go to the universities for the senior posts. However, at present the difference between the two schemes was causing many suitable university candidates to decline posts as principals and heads of departments in colleges of technology.

The Zero Gradient Synchrotron

IN A press report dated June 27 1959 the US Atomic Energy Commission gives details of a large orbital accelerator for protons, to be constructed at the Argonne National Laboratory, Lemont, Illinois. Economic factors always entail a compromise between high energy and high intensity in proton synchrotrons but improvements in design may materially enhance the output obtainable at a given cost. The technical advances known as alternating gradient focusing led to the design of the 26 GeV proton accelerators at Cern, Geneva, and at Brookhaven but these machines may prove to be limited in beam intensity to about 10^{11} particles per acceleration pulse. In the Argonne Laboratory machine

gradient focusing is not used and the uniform guiding magnetic field is forced beyond the saturation value over a vacuum system of relatively large aperture. Beam stability is obtained by wedge-focusing effects at the boundaries of the sectors into which the 200-ft diameter magnet ring is divided. As a result of the fairly large aperture and high injection energy (50 MeV), pulses of about 10^{12} protons of an energy of 12.5 GeV are expected. Much of this beam should be available outside the machine.

The Argonne Zero Gradient Synchrotron and its associated equipment will cost 20 million dollars. It will provide a strong source of all known particles and anti-particles and, since it will be especially suited to the study of rare events, it may lead to the discovery of new phenomena. The cost of such research now far exceeds the resources of individual institutions, and the development of great national or international laboratories, in which many university teams conduct research with one accelerator, is a natural consequence. The new undertaking at Argonne, which it is hoped to complete during 1962-63, has many similarities to that at Harwell, where a 7 GeV proton synchrotron is under construction for the National Institute for Research in Nuclear Science.

Higher Education in the U S S R

A BIBLIOGRAPHICAL survey of technical and vocational education in the U S S R by M I Movšovič, issued as No. 30 of educational studies and documents by the United Nations Educational Scientific and Cultural Organization (Technical and Vocational Education in the U S S R: a Bibliographical Survey. By M I Movšovič. Pp. 53. Paris: Unesco, London: H M Stationery Office, 1959. 5s net), covers vocational education at the elementary, secondary and higher levels. Besides books and articles, bibliographies and periodicals are dealt with in a separate section. Generally, publications are presented chronologically within each section and the articles are fairly fully annotated or summarized.

Planning in Pakistan

A BROADSHEET, "Planning in Pakistan" (*Planning*, Vol. 25, No. 433, April 20, 1959. Pp. 85-112. London: Political and Economic Planning, 1959. 2s 6d), which emphasizes the stimulus to central economic planning derived in the new countries of Asia from independence and the prospect of foreign aid, gives a clear but concise account of the progress of planning in Pakistan. After reviewing the effects of partition and planning in the early years, the broadsheet outlines the Five Year Plan, published in May 1956 by the Pakistan Planning Board established in July 1953, and then describes the performance and prospects of the plan. Political and Economic Planning concludes that although Pakistan is passing through a difficult phase in its economic, as in its political, development, it is tackling its difficulties with vigour. Performance, however, in some spheres remarkably good, has been uneven, and, regarded as a whole, inadequate. Big mistakes have been made, particularly because of over-ambitious schemes, and too optimistic assumptions about foreign exchange and sterling earnings, and import savings. Brilliant results in industrial development do not balance the failure to develop agriculture. Nevertheless, Pakistan's economy is basically sound. It is learning from past errors and preserving its zeal to plan and work for prosperity.

International Council of Museums

THE fifth General Conference of the International Council of Museums was held in Stockholm during July 1-8 under the presidency of Dr. Georges Salles (France). The Conference was preceded by meetings of certain committees and commissions held at Oslo and Copenhagen. Dr. Torsten Althin was chairman of the Swedish National Committee which carried out all the complicated organization for the meeting. About 350 delegates attended. The theme of the Conference and the lectures was "Museums as Mirrors—their Potentialities and Limitations". An important session dealt with the inauguration of the International Centre for the study of the preservation and restoration of cultural property. This Centre, established in Rome by the General Conference of Unesco, is designed to strengthen relations between all who are interested in the preservation of their cultural traditions. Dr. H. J. Plenderleith, recently of the British Museum, has been appointed the first director, and at Stockholm he outlined the policy of this new Centre. It aims to collect documentation on the efforts already made in this field, co-ordinate research in order to avoid overlapping, and give advice to all those requesting it. The Centre will also assist and facilitate the training of experts and is destined to become the institution best informed about the results already achieved and the research in progress. The foremost requirement at present is that the great countries should support this venture and ensure its existence after the period guaranteed by Unesco. It was agreed that the next triennial conference should take place in Holland in 1962 under the presidency of Sir Philip Hendy (National Gallery, London).

Geophysical Journal

THE appearance of the first number of the second volume of the *Geophysical Journal*, published by the Royal Astronomical Society, is a suitable opportunity to stress the contribution which this journal is making to the growth of pure geophysical research, especially in Great Britain. The fundamental importance of the papers, the careful refereeing and the speedy publication are heartening. Half this particular number contains original material. The other half consists mainly of a review of palaeomagnetism and two shorter reports, one on a geophysical meeting and one on current geophysical research in Canada.

The Australian Journal of Statistics

THE Statistical Society of New South Wales is publishing a new journal, namely, *The Australian Journal of Statistics*. It is to be issued three times a year, and will contain material relating to statistical theory and methods and their application to all branches of learning. The *Journal* will give Australian statisticians an opportunity to present their work to the public without undue delay. The editor is H. O. Lancaster. The first number runs to thirty-four pages, and besides introductory material and a "News and Notes" page, contains three papers. The price of this number is 10s, which is perhaps a little high for such a slim volume, but even so the Society has had to have outside financial support from some dozen organizations. The *Journal* will no doubt satisfy a need among Australian statisticians, who are making valuable contributions to the development of statistics, and every success is to be wished to the Society in its new venture.

Soviet Rubber Technology

THE appearance of a regular translation of the monthly Soviet journal *Kauchuk i Rezina* under the title *Soviet Rubber Technology* (No 1, June 1959) English translation of *Kauchuk i Rezina*, Vol 18, January 1959 Pp 64 Annual subscription rates Ordinary, UK £10 10s Abroad 50 US dollars or equivalent R.A.B.R.M. Members and U.K. non profit-making institutions £5 5s Obtainable from MacLaron and Sons Ltd, 131 Great Suffolk Street, London, S.E.1 is a welcome addition to the scientific literature of the U.S.S.R. available in the English language. The translation, which is being carried out by the Research Association of British Rubber Manufacturers under the auspices of the Department of Scientific and Industrial Research Translations Unit, combines technical competence and accuracy with a pleasant and readable style. It is stated that the journal 'deals with the efficient use of raw material, the automation of manufacturing processes in the rubber industry and improvements to the design of tyres and industrial rubber goods. Articles describing the most important chemical research of interest to the rubber industry are also included. The first issue includes, in addition to original research contributions, more general articles reviewing industrial organization in the U.S.S.R. and news items. The scientific papers are about equally divided between chemistry (polymerization processes, compounding vulcanization etc.) and physics (properties of rubber compounds fatigue and adhesion of tyre cord, etc.). The journal gives a good general insight into the technical and industrial problems of the Soviet rubber industry.

The Wellcome Trust

THE second report of the Wellcome Trust covers the period September 1, 1956–August 31 1958 (Pp 72+3 plates London The Wellcome Trust 1959), in which £1,059,919 was allocated by the Trustees, compared with £1,170,164 in the twenty years 1937–56 covered by the first report. The fourth and final report on the findings of the Wellcome Marston Archaeological Research Expedition to the Near East, published in June 1958 deals further with excavations undertaken by the late Mr J. L. Starkey and others at a mound known as Tell el Dawir about half way between Jerusalem and Gaza. Total expenditure by the Trustees on the Leachian expedition including costs of publication, has amounted to £35,496. During the period 1956–58 grants made in aid of research in human and animal medicine and the contributory sciences have totalled £925,357. In making these grants the Trustees have followed their previous policy of supporting enterprises the merits of which were endorsed by the best available scientific opinion but which had not hitherto received the help they needed. Priority was given to tropical medicine pharmacology, pharmacy, therapeutics, veterinary medicine and the history of medicine. The report contains a full list of research grants and of travel grants during the period. Travel grants were made to 167 research workers, expenditure increasing from £11,410 in 1955–56 to £20,922 in 1957–58 and in addition five block grants were made to the organizing committees of international congresses or of smaller specialist symposia abroad, bringing the total expenditure to £42,175 on 257 persons in the period. The Trustees have also instituted a system with the Carlsberg Foundation of

Carlsberg Wellcome Travelling Research Fellowships to encourage friendly co-operation on an exchange basis between Danish and British research workers in sciences bearing on human and animal medicine and two fellowships were awarded in each of the academic years 1957–58 and 1958–59. Capital grants for building projects during the period amounted to £543,509, with a further £115,160 to assist medical research libraries and museums which included some building projects, and a further £171,065 allocated for expenditure on major items of research equipment. In support or endowment of senior research posts the Trustees allocated £72,983, and to various grants for research expenses and assistance, £25,197. New grants totalling £3,932 were made for work in the history of medicine and £957 to assist other scientific publications. A grant was made to the Royal College of Physicians to cover the expected cost of producing a new edition of the 1923 Harvey film, by the use of colour photography, synchronized sound track, animated diagrams and other appropriate improvements of cinematographic technique.

English Rural Life

THE Report of the Museum of English Rural Life for 1958 (University of Reading Museum of English Rural Life—Report 1958 Pp 24 Reading The University, 1959 1s) is far from formal for it includes in fact is mainly devoted to a summary of the principles of display in a museum. This part is contributed by Miss Margaret Fuller and Mr C. A. Jewell and is of interest and value to all museum curators especially those who deal with the difficult problem of exhibiting folk life material. In this report the policy of the Museum in relation to other regional museums is more clearly defined than it has been in the past and it is noted that it states its major task to be the formation of a national archive of information on all aspects of country life. It is hoped that in the future a considerable proportion of the objects in the Museum will be available to supplement other collections or to form the nucleus of new folk sections.

Genetical Effects of Population Subdivision

P. A. P. MORAN has advanced a theory relating to some genetical effects of population subdivision (*Australian J. Biol. Sci.*, 12, 2, 100 (1959)). The genetical effects of the subdivision of a population into partially isolated subgroups are considered in two particular cases. In the first a probability model is studied in which the subpopulations are of finite size with migration between them. In the absence of selection the asymptotic rate of progress to homozygosity is shown to be very little affected by the subdivision. In the second case a deterministic model is studied in which there are two subpopulations in which selective forces are equal and opposite. A stable dimorphism is then shown to exist if there is any small amount of intermigration.

Fine Structure in Cells

G. SUTTERFIELD, H. STERN and F. B. JOHNSTON have given an account of the fine structure in cells of pea and wheat embryos, based on observations using phase contrast and electron microscopes (*Canadian Journal of Botany* 37 65 (1959)). The aim was to provide a basis for relating biochemical data on isolated cell fractions with the cytological structure *in situ*. Pertinent observations include the following:

The nuclei of all cells were similar, showing nuclear membranes, chromosomes, and prominent nucleoli. The cytoplasm contained highly developed structures which presumably reflected the incipient growth condition of the cells. Several cytoplasmic components were common to both embryos: small dense granules, endoplasmic reticulum, mitochondria, proplastids, amyloplasts, irregular bodies, plasma membranes, and plasmodesmata. The small dense granules, presumably ribonucleoprotein particles, occurred profusely, both free and in association with extensively developed endoplasmic reticulum. These particles are probably responsible for the microsomal fractions obtainable from embryos and seedlings. The mitochondria were usually relatively small (0.25–0.5 μ diameter) although groups of very long (5 μ) ones were occasionally found. Bodies resembling mitochondria in size and shape, but lacking cristae, were present and represent either immature mitochondria or proplastids. Reserve material occurred as starch in structurally complex amyloplasts and possibly as protein in the irregular bodies. In addition to these structures cells of the wheat embryos remote from the meristems contained prominent cytoplasmic bodies classified as 'dense' and 'thick-walled'. The dense bodies probably represent stored lipids while the significance of the thick-walled bodies, which showed a variety of forms, is unknown.

Rafflesia in Sumatra

AMONG the genera of plants which might well be described as wonderful, if not odd, *Rafflesia* must surely be accorded a leading place. Some thirteen species were recorded by Koorders in 1918 for the whole of the Malaysian region, but it now appears that some of this investigator's views may require revision. W. Meijer (*Ann. Bogor. Bot.*, 3, 1, 33 (1958)) has now added further information on *Rafflesia arnoldii* as observed by himself and colleagues in West Sumatra. From an examination of the literature and the material preserved in the Herbarium Bogoriense, as well as from his own observations, he has concluded that the *Rafflesia* species in question is identical with the original *R. arnoldii* of Robert Brown (1822) and that it occurs in both Central and South Sumatra. Its taxonomic position is discussed, and the author points out that *R. tuan-mudae* Becc. from Borneo is very closely related to, and may even be conspecific with, *R. arnoldii* R. Br., and that the key given in Koorders's monograph is incorrect as to the distinction between these two plants. Some information concerning other *Rafflesia* species occurring on Sumatra is also given. Observations on the growth-rate, mortality of the buds, and the possible mode of distribution of the seeds are recorded. It is now estimated that the entire cycle from seed to seed takes approximately 4½–5 yr.

Soil Basidiomycetes

J. H. WARCUP has contributed the results of an investigation on the isolation of basidiomycetes from the soil (*Trans. Brit. Myc. Soc.*, 42, 1, 45 (1959)). Whereas extensive series of dilution and soil plates from wheat-field and pasture soils failed to reveal these fungi, they were isolated from roots, and from hyphae, rhizomorphs, and sclerotia picked out from soil. Over a three-year period, no basidiomycete fructifications were found in the wheat-field although isolations from soil and roots showed that the field had an abundant and varied population of basidiomycetes. While fructifications were obtained from

the pasture, the species thus seen fruiting were different from those isolated from soil and roots, indicating that the population was more varied than the fructifications alone would suggest. Some of the basidiomycetes were induced to form fructifications in culture.

Histological Localization of Peroxidase

D. S. VAN FLEET (*Canadian J. Bot.*, 37, 3, 449 (1959)) has observed that peroxidase is detectable in all tissues but is most reactive in the basophilic cells of the histogens. Oxidation of applied phenols and aminophenols by peroxidase produces quinones and quinonodimines that are adsorbed by nucleic acids and other basophilic substances in the formative centres of primordia. Localized reactions for peroxidase occur in the axils of leaf primordia prior to bud formation and on the surface of apical meristems in a spiral pattern marking the points for the future development of leaf primordia. Peroxidase is detectable in advance of or accompanying cell division and declines after the division phase; decline of peroxidase at the end of the division phase is related to the increase of phenols, naphthols and phenolases. Peroxidase declines in all tissues with the exception of the phloem, a continuous peroxidase system in the phloem connects primordia with adult tissue. The hypothesis is offered that the cellular units of the phloem peroxidase constitute a continuous system between primordia and adult tissue and are functional in catalysing the reduction of hydrogen acceptors essential to cell division and the initiation of primordia.

Oxidation of Krebs Cycle Acids by Apple Tissue

M. D. HATCH, J. A. PEARSON, A. MILLER and R. N. ROBERTSON, in a study of the oxidation of Krebs cycle acids by tissue slices and cytoplasmic particles from apple fruit (*Australian J. Biol. Sci.*, 12, 2, 167 (1959)), point out that it has hitherto been difficult to demonstrate the Krebs cycle in either cytoplasmic particles or tissue slices obtained from apple fruit. In the present investigation, evidence was obtained for the operation of the classical Krebs cycle–cytochrome oxidase respiratory system in cut tissue and mitochondria from Granny Smith apples. The respiration of cut tissue increased when either citrate, α -ketoglutarate, succinate, malate, fumarate, or pyruvate were added. Both the endogenous and acid-stimulated respiration were inhibited by malonate, cyanide, and azide. The rapid oxidation of Krebs cycle acids by cytoplasmic particles from apple flesh was also demonstrated. These particles showed cytochrome oxidase activity and contained a succinoxidase system dependent on cytochrome c.

Radiation in Industry

ARTHUR D. LITTLE, INC., undertook during 1958 a study of the anticipated need for high-level radiation sources and their potential uses in industry, on behalf of the CEM group of companies (Emerson Radio and Phonographic Corporation, General Airline and Film Corporation, and Revere Copper and Brass, Inc.) and the General Electric Company's Hanford Atomic Products Operation. A summarized version of the firm's report was given by S. E. EATON and M. MICHAELIS at the seventh annual conference of Atomic Energy in Industry (Radiation: a Tool for Industry, Pp. 1+28, Cambridge, Mass., Arthur D. Little, Inc., 1959), held by the National Industrial Conference Board, Inc., at Cleveland, Ohio, during

April 8-10, 1959. The study was restricted to a survey and analysis of the available technological data and consisted of an examination of some 2 500 articles published during the past ten years and a series of some 330 interviews with leading workers in the field. The pattern of current industrial activity in the applications of penetrating high intensity ionizing radiations, present-day radiation costs, and radiation applications to chemicals and petroleum to polymers, to pharmaceutical products, medical supplies and food, to power sources, and to miscellaneous substances such as semiconductors are separately discussed. Much basic work has been done on relatively simple systems, but more research on basic reaction mechanisms and more and better research equipment are required. There is a considerable lack of knowledge both among industrial scientists and by the general public on the subject of radiation, its benefits, and the safeguards against its possible hazards. Future long term research on the effect of radiation on systems held at very low temperatures and very high pressures, the development of new techniques in solid catalyst activation, and the study of the usefulness of low-energy radiation in the 1-1,000 eV range, are some of the recommendations in the report. It is emphasized that work up to date has been largely empirical, that possible unique features of radiation applications have not yet been fully explored and that even radiation engineering is relatively undeveloped and radiation economics uncertain.

Nobellium Research

In 1957 P. R. Fields and others reported the production at Stockholm of an isotope of element 102 in experiments in which osmium targets were bombarded with cyclotron accelerated $^{12}\text{C}^{+}$ ions (*Nature* 180, 1010 and 1012 1957). Two other groups have since reported experiments on the production of element 102. At Berkeley A. Ghiorso *et al.* bombarded curium with carbon 12 and carbon 13 ions accelerated in *Hilac*, but did not observe the 102 isotope reported by Fields *et al.* They detected and identified the presence of the isotope $^{244}\text{102}$ which has a half life of three seconds. In Moscow, G. N. Flerov and co workers, by bombarding plutonium 241 with $^{16}\text{O}^{+}$ ions, observed a short lived product emitting long range alpha particles with an energy of 8.8 ± 0.5 MeV which they ascribe to an isotope of element 102. Because of the negative results at Berkeley Fields and his co workers have recently made a thorough re-examination of their experimental data and their comments and discussion on the Berkeley and Stockholm experiments are given in a paper in the *Arkiv för Fysik*, 15, 225 (1959). They conclude that though their earlier mass assignment made in 1957 seems now less certain, nevertheless their re-examination has not led to any new conclusions regarding the interpretation of their results. It is felt that judgment on the discovery of the element 102 should be reserved until additional experimental studies, including the properties of neighbouring nuclides, have been carried out.

Borden Award of the Nutrition Society of Canada

The Nutrition Society of Canada has announced that the Borden award of the Nutrition Society of Canada will be given annually in recognition of outstanding research work done by one of its members. The first award will be made in June 1960. The

recipient of this award which has been presented by the Borden Company Foundation, Inc., must be under the age of forty years and must have published the meritorious work within the preceding three years. It is hoped that this award will further encourage research activities by younger members of the Society.

Lady Tata Memorial Trust

The Trustees of the Lady Tata Memorial Trust on the recommendation of the (European) Scientific Advisory Committee have made the following awards for research on leukaemia and allied diseases in the academic year beginning October 1 1959. *Grants for Research Expenses*: Dr M. Bessis (France), Centre National de Transfusion Sanguine, Paris; Dr B. M. Braganza (India), Indian Cancer Research Centre, Bombay; Prof G. Klein (Sweden), Karolinska Institute Stockholm; Dr J. Pontén (Sweden), Pathology Institute, Uppsala; Dr M. Simonson (Denmark), Institute of Pathological Anatomy, Copenhagen; Dr A. E. Stuart (Scotland), Department of Pathology, University of Edinburgh. *Scholarships*: Dr J. Hastrup (Denmark), Institute of General Pathology, Aarhus; Dr E. Kelenyi (Hungary), Postgraduate School of Medicine, Budapest; Dr P. A. Pillai (India), Centre de Microscopie Electronique, Lausanne, Switzerland.

Paul Instrument Fund Awards

Awards by the Paul Instrument Fund Committee of the Royal Society have been made as follows: £1,000 to Dr H. B. Barlow, assistant director of research, Department of Physiology, and Mr P. E. K. Donaldson, technical officer, Physiological Laboratory, Cambridge, for the development (a) of a device for automatically improving coding of messages and (b) of a diffused storage sequence engine, the object being to advance knowledge of the operation of comparatively simple assemblies of nerve cells by making instruments which perform the same task as such assemblies. £600, in supplement of a previous grant, to Dr E. T. Hall, senior research officer at the Research Laboratory for Archaeology and the History of Art, Oxford, for improvements to an apparatus with which magnetic measurements may be made with the view of dating archaeological material. £2,000 to Dr H. Motz, reader in engineering science, University of Oxford (in association with Prof G. B. Walker, professor of electrical engineering, Essex College, Assumption University, Windsor, Ontario) for the construction of a linear accelerator working at 10 cm (*J* band). £5,500 to Prof R. O. Rodman, professor of astrophysics in the University of Cambridge, for the construction and testing of a thin astronomical mirror of plate glass and of a new type of support system. £5,900 to Dr P. M. B. Walker, Royal Society Research Fellow, Department of Zoology, Asbworth Laboratory, University of Edinburgh, for the construction of a new microspectrophotometer that will integrate over a defined but irregular area which can be altered quickly and easily.

Grant for the Massachusetts Institute of Technology

Dr JULIUS A. STRATTON, president of the Massachusetts Institute of Technology, announced recently that the Institute had received a gift of

2,527,500 dollars (about £900,000) from Mr and Mrs C H Green of Dallas, Texas. This represents the March 31 market value of 30,000 shares of stock of Texas Instruments Inc., in which form the gift was made. The money will be used to construct a multi-story building on the Institute site, and will be a centre for the study of Earth sciences. Laboratories for research work in geophysics, meteorology, oceanography and related fields will form an important part of the new building.

University News:

London

DR P GROOTENHUIS, lecturer at the Imperial College of Science and Technology, has been appointed to the University readership in mechanical engineering tenable at that College. The title of reader in sociology in the University of London has been conferred on Mr T B Bottomore, in respect of his post at the London School of Economics and Political Science. The title of professor emeritus in the University has been conferred on Prof R J S McDowall on his retirement from the Halliburton chair of physiology at King's College, Prof Margaret M A Murray on her retirement from the chair of physiology at Bodford College, Prof J H Woodger on his retirement from the professorship of biology at the Middlesex Hospital Medical School, and Prof H J Collins, on his retirement from the Chadwick chair of civil engineering at University College.

University College of Rhodesia and Nyasaland

MR W LLOYD JENKINS has been appointed lecturer in the Department of Chemistry with responsibility for teaching agricultural chemistry. Previously he was a lecturer in agricultural chemistry in the University College of Wales, Aberystwyth.

The Night Sky in October

NEW MOON occurs on Oct 2d 12h 31m UT, full moon on Oct 16d 15h 58m, and new moon on Oct 31d 22h 41m. The following conjunctions with the Moon take place: Oct 6d 00h, Jupiter 4° S; Oct 8d 05h, Saturn 5° S; Oct 28d 14h, Venus 0° 9' N. In addition to these conjunctions with the Moon, Venus is in conjunction with Regulus on Oct 1d 08h, Venus being 5° 7' S, and Mercury with Spica on Oct 4d 09h, Mercury being 2° 1' N. There will be a total eclipse of the Sun on October 2, visible as a partial eclipse at Greenwich. The path of totality begins at sunrise on the eastern seaboard of the United States, crosses the North Atlantic, Canary Islands and North Africa, ending in the western Indian Ocean at sunset. The partial eclipse which will be seen at Greenwich begins at 11h 01m, reaches its greatest magnitude of 0.33 at 11h 58m and ends at 12h 56m. The eclipse belongs to a series which began in 1599. Mercury is too close to the Sun for observation. Venus is a morning star, rising at 2h 55m, 2h 30m and 2h 35m on October 1, 15 and 31, respectively. Its stellar magnitude is approximately -4.3, greatest brilliancy is reached on October 8. Its distance increases during the month from 36 to 55 million miles and the visible portion of the apparent disk increases from 0.211 to 0.443. Mars is too close to the Sun for observation, conjunction being on October 29. Jupiter is also too close to the Sun for observation. Saturn sets at 21h 20m, 20h 25m and 19h 30m on October 1, 15 and 31, respectively. Its stellar magnitude is +0.8, it

remains in Sagittarius. Occultations of stars brighter than magnitude 6 are as follows, observations being made at Greenwich: Oct 10d 20h 13.4m, τ Cap m (D); Oct 17d 20h 04.4m, ξ Ari (R); Oct 20d 23h 35.1m, 318 B Tau (R); Oct 21d 23h 38.6m, 130 Tau (R); Oct 28d 4h 22.0m, 58 Leo (R). D and R refer to disappearance and reappearance, respectively. The Giacobinids are active on October 9 and the Orionids during the third week of the month, conditions for both are unfavourable.

Announcements

LORD NETHERTHORPE, president of the National Farmers' Union, and Prof F W Rogers Brainbell, professor of zoology in the University College of North Wales, Bangor, have been appointed to fill vacancies in the membership of the Agricultural Research Council caused by the retirement of Sir Solly Zucker and Mr Frank Rayns.

DR A G OOSTON has resigned from the chairmanship of the Editorial Board of the *Biochemical Journal* and the Committee of the Biochemical Society has appointed Dr W V Thorpe as his successor. Correspondence and communications should still be sent to the Secretary to the Editorial Board, Lister Institute of Preventive Medicine, Chelsea Bridge Road, London, SW 1.

THE following officers of the Association of Consulting Scientists have been elected: *Chairman*, Dr J G Davis; *Hon Treasurer*, Dr G W Ferguson; *Hon Secretary*, Mr W H Stevens, 15 Hawthorne Road, Bromley, Kent.

A MEETING will be held on October 31 at the University of Nottingham with the object of forming a Society for Forensic Science. Further information can be obtained from Mr S S Kind, 18 Hall Lane, Harrogate, Yorkshire.

THE eighth German Plastics Convention will take the form of an International Symposium on the Ageing of Plastics, it will be held during October 19-21 at Dusseldorf, Germany. Further information can be obtained from the Arbeitsgemeinschaft Deutsche Kunststoff-Industrie, Frankfurt (Main), Karlstr 21.

THE German Society for Electronmicroscopy is holding a conference on various aspects of electronmicroscopy at the Departments of Pathology and Anatomy, Albert-Ludwigs-University, Freiburg im Breisgau, Germany, during October 18-21. Further information can be obtained from Tagung der Deutschen Gesellschaft für Elektronenmikroskopie e V Pathologisches Institut der Universität, Freiburg, Albertstr 19.

THE City of London College, in collaboration with the Plastics Institute, has arranged a series of eight lectures on plastics which will be given on successive Mondays at the College, commencing on October 5. Further information can be obtained from Mr A Fawthrop, head of the Department of Shipping and Commercial Products, City of London College, London, EC 2.

ERRATUM The author of the communication "Appearance of Granules in the Cytoplasm of Tumour-cell Cultures in Contact with Lysozyme" in *Nature* of July 18, p 202, is Mrs Dircce Babudieri Callerio, and not Prof Carlo Callerio as printed.

FLUCTUATION PHENOMENA AND STOCHASTIC PROCESSES

THE theory of probability developed as a branch of pure mathematics. Its applications to physics have now become so widespread that there is scarcely a branch to which it does not contribute significantly. During the nineteenth century the establishment of the statistical nature of the second law of thermodynamics, the resolution of the irreversibility paradox, and the development of the powerful technique of statistical mechanics were all the result of applying statistical methods to an atomic population. In the twentieth century the wave particle paradox was solved by rooting atomic physics in the theory of probability. At a less fundamental level, Brownian movement, diffusion and radio noise are physical phenomena the character of which is essentially stochastic, and radio wave propagation, sea waves, nuclear reactors and polymer physics are examples of fields in which stochastic problems have recently attracted considerable attention.

The apparatus of the mathematician has been accepted with gratitude by the physicist generating functions and characteristic functions for manipulating probability distributions, generalized Fourier analysis introducing autocorrelation functions, and leading to the Wiener-Khinchin theorem for fluctuation phenomena stationary in time. In return the physicist has continually thrown up a variety of novel problems to challenge the ingenuity of the mathematician and maintain his interest.

The two day conference of the Physical Society on "Fluctuation Phenomena and Stochastic Processes", held at Birkbeck College on March 19 and 20, attracted research workers in many different fields. Altogether, twenty nine papers were presented most of the participants were British, although contributions also came from the United States, Canada and Norway.

In his opening remarks of welcome, Prof J D Bernal (Birkbeck College London) pointed out that physics had learnt to deal adequately with the completely regular, and the completely random, it was the partially regular which still awaited treatment. The nature of the liquid state, and biophysical problems connected with the structure of large molecules, were important examples of this.

In the opening paper Prof M S Bartlett (University of Manchester) reviewed the various types of statistical fluctuations which occurred in physics, and attempted to classify them in order of relative size. In spite of the existence of occasional abnormal fluctuations, macroscopic averages in classical statistical mechanics had a 'stability' resulting from the large number of component systems involved. The measurement of time and space averages for phenomena such as turbulence and random surface waves, on the other hand, made use of the ergodic properties of some stationary processes. A fairly general 'weighted sum' type of process occurring in noise and Brownian motion theory was defined, together with the conditions for statistical 'stability'. Finally there was the class of possibly exponentially increasing and unstable multiplicative (branching) processes such as nuclear cascades.

Dr R Furb (Birkbeck College) gave a comprehensive paper entitled "Fluctuations of Macroscopic

Parameters". Macroscopic parameters ξ_i were operationally defined in finite regions Δs , of space and finite intervals Δt , of time of such magnitude that irregular fluctuations could be observed superimposed over the regular quasi continuous functions $\xi_i(r, t)$. The theory of these fluctuations was mainly concerned with the determination of the second moments of the temporal fluctuations of the parameters ξ_i in a fixed Δs , and of the spatial fluctuations in one and the same Δt . It was a characteristic feature of the theory that these moments could be expressed in terms of the macroscopic functions $\xi_i(r, t)$, and that only some very general statistical properties of the random molecular processes responsible for the fluctuations needed to be known.

In the temporal problem the correlation functions of the type $c_i(\tau) = \langle \xi_i(r) \xi_i(r + \tau) \rangle / \langle \xi_i(r) \rangle^2$, could be calculated by making use of a generalized 'Langevin equation', in the limiting case of $\tau = 0$ the second moments $\langle \xi_i^2 \rangle$, might be obtained under conditions of statistical stationarity from statistical mechanics. This latter procedure could be applied to the problem of fluctuations of strain and stress in crystalline solids.

In the problem of spatial fluctuations the same method of statistical mechanics could be used for evaluating the spatial correlation products $\langle \xi_i(x) \xi_j(x + \zeta) \rangle$, of two parameters in two regions Δs_1 and Δs_2 , in a homogeneous medium separated by a distance ζ under conditions of 'quasi-stationarity', that is, when in spite of the finite speed of propagation of the interaction processes the values $\xi_i(x)$ and $\xi_j(x + \zeta)$ could be assumed to be simultaneous to a sufficient degree of approximation. This method could be used to obtain formulae for the fluctuations of electric charge and potential in a discontinuous system of conductors and had been applied by E Morris to the problem of fluctuations of surface charge density on the surface of a single continuous conductor and the fluctuations of potential on and outside its surface.

Finally, the general problem of spatial fluctuations could be reduced to that of temporal fluctuations in such cases where the relevant Langevin equation had the character of a wave equation. This method was used by M N Moore for the solution of the problem of spatial fluctuations of strain and stress in crystalline solids.

Several papers dealt with the mathematical properties of stochastic functions and with their application to the analysis of experimental data. Mr D G Brannan (Massachusetts Institute of Technology, Lincoln Laboratory) in a paper entitled "A New Approach to Certain Types of Random Functions" developed *ab initio* a theory of a class of stochastic processes which he hoped would have application to certain types of physical problem. Mr M B Priestley (University of Manchester) considered the problem of detecting a signal containing several harmonic components in the presence of background noise. When the noise had a uniform spectrum the appropriate quantity for picking out the harmonic terms was the periodogram. But when the spectrum of the noise was non uniform this could no longer be used and he proposed a method of analysis based on the

tail of the auto-correlation function, he also showed how a significance test could be constructed.

Mr B Landmark (Norwegian Defence Research Establishment) dealt with the provision of a stringent test for the Gaussian character of a given noise signal. An amplitude test was usually insufficient, and he suggested using the simultaneous variations in amplitude and phase. This had been applied experimentally to the scattering from ionospheric clouds¹, and the results were in good agreement with those to be expected for Gaussian noise.

Dr. L. Mandel (Imperial College of Science and Technology, London) gave an interesting example of a problem in which the approach of the quantum theory produced a substantial simplification. The distribution of the integral, E_T , over a time interval T of the square of random noise was quite complicated, and some of its properties had been deduced by Rice². If we interpreted the noise as arising from an electromagnetic wave, E_T was proportional to the energy contained in a length cT of the wave train. Bose-Einstein statistics could be applied to the photons in this region, and the resulting probability distribution could be determined more readily.

The statistics of radioactive decay was the subject of a communication by Mr A C Hughes. He was concerned with testing fluctuation theory for short-lived substances, that is, those with half-lives short compared with the time of observation. Experiments had been performed with an isotope of rhodium (half-life 44 sec), and two isotopes of silver (half-lives 24 sec and 2.3 min), the agreement with theory was good.

Dr M N Moore (Birkbeck College) spoke on the "Stochastic Kinetics of Nuclear Reactors". It could be shown that the square of the modulus of the reactor transfer function was proportional to the Fourier transform of the auto-correlation function for power noise in the reactor. Since the power noise represented the response to the minimum power input signal, measurements of transfer functions based upon reactor noise were of all possible measurements least subject to non-linear distortion. By performing the experiment at various power-levels and temperatures, it was possible to measure both power and temperature coefficients³.

Some examples were given of new problems in probability which had been suggested by physical phenomena. Prof C Domb (King's College, London) said that if one wished to understand what was happening in a regular solution, one must study its fluctuation properties, or the distribution of clusters of different sizes and shapes as a function of temperature. Even for a purely random mixture this was very difficult, although one could readily establish a difference in behaviour in one, two or three dimensions. Thus for a 50:50 mixture if one considered clusters of up to 5 atoms, 88 per cent of the total number were accounted for in one dimension, 17 per cent in two dimensions and only 2 per cent in three dimensions. A critical probability entered in these problems in the same manner as those studied by Hammersley⁴.

Dr M E Fisher (King's College, London) discussed the shapes and sizes of polymer and polyelectrolyte molecules which seriously affected properties like viscosity. We should be greatly assisted in this field by a knowledge of the properties of non-intersecting random walks on lattices. These walks were non-Markovian and their behaviour probably differed essentially from Markovian walks. The only property

which had been rigorously established⁵ was that C_n , the total number of walks of n steps, was asymptotically of order μ^n . Some conjectures on the value of μ for a quadratic lattice had been rigorously proved⁶. The subject suffered seriously from a lack of theorems of the 'central limit' kind. Dr M F Sykes (King's College, London) dealt with methods for the practical determination of parameters in self-avoiding walks. Monte-Carlo methods had been used extensively by Wall and his collaborators⁷, but Sykes and his colleagues had preferred to determine the properties exactly for finite values of n , rather than to attempt asymptotic extrapolation. When n was larger than about 10, irregular variations were small, and one could put forward the results with confidence. He estimated that for a quadratic lattice $c_n \sim n^{1.5} \mu^n$, where $\mu \approx 2.640$ (with a probable error $< \frac{1}{4}$ per cent). Also there was strong evidence that if p_n is the number of simple closed polygon walks of n steps, then $p_n^{1/n} \rightarrow \mu$.

Mr J M Hammersley (Atomic Energy Research Establishment, Harwell) spoke on "Percolation Processes"⁸. These differed from diffusion processes in that the random mechanism was in the medium instead of the fluid. Practical examples of percolation processes were molecules penetrating a porous solid, or disease infecting a community. The processes could be studied in crystals or mazes, and the mathematics was more difficult than that of diffusion processes. It was possible to show rigorously that critical probabilities existed for crystals below which, for example, a fluid starting in one part of the medium would not spread to infinity. Upper and lower limits had been established theoretically for these probabilities, and Monte Carlo methods had been successfully used to estimate them.

It was not surprising to find several papers devoted to the random walk problem and Brownian movement. Dr P H Roberts (King's College, Newcastle) spoke on the "Random Walk on a Sphere"⁹. He was concerned with the geological problem of the path of the Pole as indicated by rocks. Other work in this field had assumed a lattice model, and a planar distribution¹⁰. With the mathematical help of H D Ursell, he had used the correct distribution for a sphere, which, incidentally, differed appreciably from the distribution given by R A Fisher¹¹.

The effect of persistence on a random walk was discussed by Mr A J Allnut. In problems such as multiple scattering in foils the assumption that all directions of scatter were equally probable after collision was invalid, it was necessary to take into account persistence in the initial direction, and formulae for the mean and mean square deviation could readily be derived. Mr J C Barton (Northern Polytechnic, London) described an experimental method of simulating a one dimensional random walk. This was a problem in which an analogue computer could be of value and could provide information on first passage times for a random walk with persistence¹². (In the discussion Prof Bartlett pointed out that theoretical formulae for first passage times were available for all Markoff processes.)

Dr A R Stokes (King's College, London) in his paper on "Light Scattering by Semi-stiff Chain Molecules" referred to a different application of an analogous problem. The distribution of the end-to-end distance of a flexible chain was Gaussian, stiffness in the chain restricted the freedom of the angle between successive links, and modified this distribution, thus influencing the light-scattering

properties. The modified distribution had been calculated by Daniels¹⁰, but he had found a simpler approach by using the Fourier transform of the end to end distance. The results could be expressed in a form suitable for practical calculation.

The Brownian movement of non linear systems was discussed by Dr D K C MacDonald (National Research Council, Ottawa). Many problems in this field still awaited solution. Some results of his own approach¹¹ had been substantiated by R O Davies¹², although there was some disagreement with van Kampen¹³, who maintained that the distribution of fluctuations was Gaussian even for non linear systems. Dr MacDonald mentioned that he had corresponded with Einstein, who agreed that the statement in his early work on the Gaussian nature of the distribution needed reconsideration.

Dr A Suddaby (Sir John Cass College, London) discussed the relation between the microscopic theories of transport processes developed by Kirkwood, and the macroscopic theory of Brownian movement. In the course of his development, Kirkwood introduced a friction constant β which was an integral up to time τ of the correlation of the total force on the particle at different times. The analogous constant in Brownian movement theory was determined by the correlation of the fluctuating force in the Langevin equation. These two values could be shown to agree provided $\beta \ll 1$.

Dr E R Wooding (University of Sheffield) presented a paper on "Recombination in a Plasma as a Stochastic Process". The rate at which ions of opposite charge diffused together was obtained by applying Kramer's method to solve Smolouchowski's equation for diffusion in a field of force. Charge transfer was assumed to occur after the ions approached to within a distance where they could enter a bounded orbit. An ion or atom in the vicinity of an orbit influenced the recombination coefficient. The resulting function was dependent on the degree of ionization, but was similar to that obtained by Thomson¹⁴ at low pressures, and changed to Jaffo's relationship¹⁵ at high pressures if the ionization was low.

Dr G Wylie (University of Glasgow) discussed the Brownian motion of spin systems. There were two sources of interest in this problem, its neatness as a model for irreversible processes in quantum mechanics, and the experimental interest in nuclear magnetic resonance experiments. If one focused on individual spins, relaxation times were of the order of milliseconds, whereas for the whole spin system they ranged up to hours. By manipulating electromagnetic fields the spin system could be thrown into conditions far from the Boltzmann distribution. The fluctuating interaction between spins revealed itself in the shape of the magnetic resonance absorption line.

A group of papers was concerned with stochastic problems arising in radio physics. Mr J A Ratcliffe (University of Cambridge) gave an introductory talk and discussed some problems associated with the Fresnel diffraction patterns formed by an assembly of random irregular diffracting screens. It was well known that, if the correlation function $\rho_f(\xi)$ of the complex amplitude $f(x)$ over a one dimensional diffracting screen was defined as $\langle f(x)f^*(x+\xi) \rangle_{\text{screen}}$ and if $g(x)$ was the complex amplitude in the diffraction pattern over any plane parallel to the screen, then with certain reservations $\rho_g(\xi)$ was equal to $\rho_f(\xi)$. If the screen

was statistically stationary over x and if the correlation function $r_f(\xi)$ was defined as $r_f(\xi) = \langle f(x_1)f^*(x_1+\xi) \rangle$ evaluated at two fixed points x_1 and $(x_1+\xi)$, then it was also true that $r_g(\xi) = r_f(\xi) = \rho_f(\xi)$. If, however, the screen was not statistically stationary the last relation was not necessarily true.

Mr Ratcliffe considered particularly the non stationary case when the screen $f(x)$ could be described as an assembly of infinitely long random screens placed, in succession in front of an aperture of finite width. He suggested that this simple example represented approximately the problems of the diffraction of (a) radio waves radiated from a radio star with a sharp boundary, (b) light waves radiated from a source of light placed behind a slit or (c) radio waves reflected from an irregular meteor trail of limited length. He stated that, if the limiting aperture subtended less than the first Fresnel zone at the observing plane then $r_g(\xi)$ was determined not by the fine structure in the screen but by the aperture bounding it. If however, the aperture subtended a large number of Fresnel zones then $r_g(\xi) = r_f(\xi)$ and was determined by the fine structure in the screen.

Mr S A Bowtell (Pennsylvania State University) discussed the scattering of electromagnetic waves from a continuous medium containing three-dimensional random inhomogeneities of refractive index. He had derived the form of the emerging angular power spectrum when the scales of the inhomogeneities were different in the three space directions. Contrary to previous results¹⁶, he had found that the medium could not be analysed as a series of superposed thin phase screens, spaced in the propagation direction, and with independent phase profiles.

Mr M L V Pittaway (University of Cambridge) was concerned with reflection from an irregular medium. Before proceeding to a three-dimensional solution for irregularities he thought one should obtain a solution for a horizontally stratified ionosphere¹⁷ and treat the irregularities as a small perturbation. The power spectrum of the scattered wave could then be expressed as an integral in terms of the stratified solution. Dr B H Briggs (University of Cambridge) dealt with the experimental problem of specifying the pattern on the ground (including time changes and movements) formed by reflection from or transmission through, an irregular ionosphere. He defined parameters which could be used to specify this pattern, and which could be deduced from observations at a few points on the ground¹⁸. As an example, he considered the application to radio star scintillations. Mr R P Mercier (University of Cambridge) discussed theoretical aspects of radio wave fading. A scalar wave with random variations of amplitude and phase across the wave front was taken as a simple model. It was assumed that the in phase and quadrature components of the fluctuating part of the field were normally distributed, and a parameter was introduced to specify the intrinsic correlation of the fading. Various properties of this parameter could be derived, and used to interpret fading from the ionosphere.

"Coherence Properties of Partially Polarized Light" was the subject of the paper by Dr E Wolf (University of Manchester). Observing that the usual definition of Stokes parameters of a quasi monochromatic plane electric wave was not unique an experiment was analysed which led to a unique

coherency matrix and to a unique set of Stokes parameters. The degree of polarization of such a wave was also equal to the maximum value of the degree of coherence which existed between the components of electric vibrations in orthogonal directions in the wave front. This suggested a new method of measurement of the degree of polarization, based on interference experiments.

Prof E G Richardson (King's College, Newcastle) referred to experiments on the propagation of sound waves in a fluid having random variations in either density or momentum, whereby the amplitude and relative phase of the signal picked up after transmission through the medium fluctuated in time. The former type occurred near the critical point of a fluid or of a mixture of liquids, the latter in the atmosphere or in the wake of an obstacle or, again, in a boundary layer. Analyses of such measurements were presented. In the case of the liquid mixture a correlation was sought between the pattern of the scattered radiation and the mean size of the clusters which formed at the critical point. As an example of the second type, frequency spectra of the modulations of the sound signal transmitted afloat the wake of a cylinder involved the discerning of peaks in the spectrum against the background of fluctuation 'noise' in the general flow.

Dr M S Longuet-Higgins (National Institute of Oceanography) discussed "Sea-Waves as a Stochastic Process". He showed a typical record of pressure at a fixed point on the sea bed which agreed closely with a Gaussian distribution. Non-Gaussian features usually appeared when the waves were steep and near the point of breaking, or in shallow water. To describe the sea surface a random process two spatial dimensions and one of time were needed, the practical problem for wave forecasting was to relate this to winds and other relevant factors. Dr Longuet-Higgins also listed a number of properties of a Gaussian surface which might be of use in determining the spectrum, these included wave slopes¹⁹, 'specular points' and 'twinkles'²⁰.

The final paper was given by Prof E W Montroll (University of Maryland) on a stochastic treatment of traffic flow. Experimental data indicated that the acceleration of a car in a line of traffic at time t was proportional to the velocity difference between itself

and its neighbour at time $(t - \Delta)$, where $\Delta \sim 1.5$ sec and the proportionality constant²¹ was 0.37 sec^{-1} . Theoretical investigation showed that the motion became unstable when the product of lag time and proportionality constant exceeded $1/2$. Thus the experimental data showed that driving was usually on the verge of instability. 'Acceleration noise' was put forward as a parameter which would characterize the driver-car-road complex under various conditions²². Reasonable agreement was obtained with traffic flow measurements²³.

The conference was organized at the suggestion of Dr Firth, who is to be highly commended on his initiative. The one hundred participants would undoubtedly wish to express their thanks to him, to Birkbeck College, and to the Physical Society for the excellent arrangements. C. DOMB

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BIOMECHANICS

ON April 17 the Institution of Mechanical Engineers held a symposium on "Biomechanics" with the purpose of bringing medical men and engineers into closer contact.

Biomechanics, in its broadest sense, may be defined as the branch of science which applies the principles of mechanics and the techniques of engineering to the human body in the process of its repair, and in the field of man-machine relationship, where man is the essential link in operating these machines.

The symposium was opened by the President of the Institution and the papers and discussion were presented under the chairmanship of Prof S J Davies. In the opening paper on the importance of biomechanics as a service to man, illustrated by a

discussion of problems in metallic osteosynthesis, J M Zarek, from King's College, London, gave a brief account of the nature of biomechanics as a new field of endeavour in which some of the engineering knowledge may be of direct use to the medical man. The man-machine relationship was only mentioned, as this aspect of biomechanics appears to be already well appreciated by the engineers and was not dealt with at the symposium in detail. After discussing the scope of biomechanics, the general history and current British activities in this field were reviewed. Problems of bone repair were considered at length and the work in the Civil Engineering Department at King's College, London, on the stress/bone formation relationship and the behaviour of metals in the human body were discussed.

In the second paper, R I Tanner, from the University of Manchester, presented a paper on some tests on 'Fluon' as a material for artificial animal joints in which results of artificial hip joint friction and wear are given. They are based on the results obtained by means of simple pendulum apparatus which provides a reasonable approximation to the walking motion of a normal person.

A critical review of published work on the nature of lubrication in animal joints was given by John Charnley from the Department of Orthopaedics at Manchester. Further, some of the experiments which have been accepted in support of the theory of hydrodynamic lubrication have been repeated by him to show that the lubrication of animal joints is almost certainly a boundary phenomenon. Charnley emphasized that the coefficient of friction of animal joints reaches a very low figure and surpasses in slipperiness any combination of sliding surfaces known to engineering.

A paper on the provision of workable substitutes for missing or defective limbs was presented by D S McKenzie and Brig N A M Swettenham, from the Limb Fitting Centre Ministry of Health, Rom Hampton.

Limb fitting has been essentially a craft until quite recently, and many ideas current in the last century exist materially unchanged to-day. This situation is now changing as a great deal of research work on artificial limbs with emphasis on fundamental studies is in progress. Some of the problems here are very complex. The prosthesis has to replace a human component but it does not necessarily follow that its mechanical design should copy that of the part it replaces. Amputation often changes the pattern of muscular control and weight bearing. The paper also described some of the features governing the construction of artificial limbs. Each case has to be treated individually and *ad hoc* modifications have to be made to suit individual needs. In a research field of this nature it is difficult to prove that a proposed change has merit, and evaluation techniques still require much development. Some devices evoke general acceptance but more often individual responses vary and the type of case for which the new idea is best suited must be discovered. Only users can supply the final answer but they cannot give up unlimited time to experimentation. Objective testing is therefore necessary to eliminate obvious flaws and shorten user trials.

Following the presentation of the papers a film entitled "Late Results of Four Massive Internal Prostheses" was shown by A C Bingold and W G France. Here the authors gave an excellent picture of how, through the co-operation of surgeons with engineers, instead of amputation, limbs can be saved and restored to their normal use.

The success of the symposium, I think, was reflected in the very interesting discussion which followed and well exceeded the time limit allocated for this purpose.

The Institution was honoured by the presence of Sir Harry Platt, of the Royal College of Surgeons who, in opening the discussion, stressed the importance of interdisciplinary work between the medical men and engineers. He said that the symposium had clearly demonstrated that some of the surgical techniques now in use are so complex that it is impossible for one profession only to solve the problems involved.

Dr F C Harper of the Building Research Station showed a film and some results obtained in the course of studying the forces exerted by the human foot in walking, the emphasis there being on the wear resistance of floor surfacing materials.

Dr J D Moreland and Mr S J Thurlow, of the Road Research Laboratory, discussed their investigations into the problems connected with road crash injuries.

Mr E H J Smyth, an orthopaedic surgeon from the Southampton and Isle of Wight Hospital Group, presented in a very interesting manner his views on the functional significance of the formation of trabeculae in the neck of the femur.

Finally because of shortage of time, after a number of speakers discussed a variety of subjects of their own interest, the authors of the papers answered various points raised in the discussion very briefly.

In conclusion the large attendance and the discussion were an indication that the Institution of Mechanical Engineers had organized a successful symposium which from the 'mixed' audience indicated the growing affinity between engineering and medicine in the process of alleviating human suffering.

The Institution of Mechanical Engineers will shortly publish the proceedings of the symposium which will include the discussion and communications.

J M ZARPK

INTERNATIONAL STARCH CONVENTION, 1959

THE ninth annual Starch Convention, which took place at the Cereal Research Station Detmold, Germany, during April 21-23 was attended by 360 chemists from seventeen nations. The papers which were read to the meeting were divided into four sessions, on research and analysis, starch manufacture, starch fractions and derivatives and on industrial applications.

The opening address was delivered by T J Schoch (Argo, Illinois), whose theme was the application of modern methods of starch chemistry to characterizing its useful properties. Waxy sorghum starch, which is comprised wholly of amylopectin, can be given some of the characteristic properties of corn starch by

cross linking the polysaccharide chains with phosphorus or chlorhydrin or fatty acid groups. The amount of cross linking agent required to achieve this result is only 1 part per 1,000 parts of starch. Thus waxy starches, which normally give rise to fluid pastes are deprived of this property and become 'short'. Simultaneously their resistance to shear increases greatly. Another result is that such starches lose the property of gelatinizing in water at a precise temperature and instead show a gradual increase in solubility with rising temperature. Cross linking also results in a marked improvement of resistance to freeze thaw cycles which has important implications for the food industry.

Improved freeze-thaw characteristics show as a lower rate of sedimentation after freezing, and better gloss and transparency of the paste.

The new properties of amylopectin obtained by cross-linking can be explained by a greatly reduced rate of retrogradation and greater internal rigidity of the starch molecule. The technique of cross-linking can be extended to dextrines, which are used as moistening gums on envelope flaps and labels. The deterioration of such gums on ageing has been shown to be due to retrogradation of the dextrine in the presence of small amounts of water. By using the hydroxyethyl derivative of dextrines for gumming purposes, the ageing characteristics of flap gums can be largely avoided. Finally, Dr Schoch explained how starch films, which have been laid down by slow evaporation of water, have a greatly increased resistance to water when compared to quickly dried films. This again can be shown to be due to retrogradation taking place during the slow drying of films.

Prof M Samec (Ljubljana, Yugoslavia) described how the bursting and tear strength of paper can be markedly improved by using a starch size which has been previously irradiated with cobalt-60. This process might become of great importance if the cost of the radioactive material would be reduced in the future.

The use of starch as sizing agent in the paper industry was described by J Seaman (Slough, Bucks). A beater size should preferably be a potato starch soluble in cold water, of which 5 per cent w/w is added to the paper pulp. Such starches are manufactured by passing a slurry containing starch and borax over steam-heated drying rolls. The product when re-dissolved has pH 8.5 at 5 per cent concentration. For surface sizing it is advantageous to use an oxidized starch, which is manufactured by treating potato starch with sodium hypochlorite. The material has to be cooked with water before use to give a size having pH 7.5 at 15 per cent solid-content. For paper coating, white potato dextrine (1 part) is added to china clay (5-6 parts) and the mixture made up with water to a slurry having a solid content of 50 per cent.

When selecting dextrines for coating purposes, it is essential to choose one with a maximum rate of set back to enable the coating to set on the surface of the paper as rapidly as possible.

Prof M Mautner (Zagreb, Yugoslavia) described a new method for the continuous production of

glucose by the acid hydrolysis of starch. The starch slurry is first treated with hydrochloric acid and is then passed into a conical chamber, which rotates very quickly about its long axis. The chamber is heated externally by steam and is provided with an inlet at the wide end and an outlet at its apex. Ungelatinized starch particles are forced by centrifugal force to the walls of the chamber, where they gelatinize instantly. In so doing their specific gravity is reduced and they are replaced by further ungelatinized granules. The chamber has a peripheral speed of 30 m/sec and it can deal with $2\frac{1}{2}$ tons of raw starch per hr. After leaving the chamber the starch paste is fed into a series of flat, box-like heat exchangers, where the final conversion of starch to glucose takes place. It is estimated that the total time required for conversion is only 18 min.

At the Convention a total of twenty-two papers was read and they will be reprinted in full in the journal *Die Stärke*.

The actual Convention was followed during April 24-25 by the first meeting of the International Standards Organization Technical Committee No 93, which has been set up to establish international recommendations for analysis of starch, including its derivatives and by-products. There were 65 delegates present from Czechoslovakia, Denmark, Eire, Finland, France, Germany, Hungary, Italy, India, The Netherlands, Norway, Switzerland and the United Kingdom. The chair was taken by Prof. K. Heyns (Hamburg), the secretariat being held by the German Standards Association. The British side of the work is in the hands of the British Standards Institute Committee on Analysis and Testing of Starch Products, ten members of this committee—representing manufacturers and users of starch and associated products, research interests and Government departments—were present. The work already done by the British Standards Institute Committee enabled the British delegation to give a strong lead at these inaugural discussions of the International Standards Organization and many of the United Kingdom proposals were adopted.

It was agreed that the scope of the new International Standards Organization committee should cover terminology, methods of sampling, methods of analysis and examination of starch, its derivatives (including hydrolysis products and dextrines) and its by-products.

E. Dux

THE EDUCATION OF TECHNOLOGISTS

THE presidential address to the Institution of Metallurgists, delivered by Prof A. J. Murphy on May 12, covered a field involving not only the metallurgist but also the technologist in general, and in no small measure the pure scientist as well.

After dealing with matters of a more or less domestic nature, Prof Murphy turned his attention to the general background desirable in the training of the technologist. From this the following has been extracted:

Sooner or later in any discussion on the education of scientists and technologists the remark will be made "What a pity it is that you cannot give your bright young technical men some sense of cultural

values". Often this can be recognized as the defensive manoeuvre of a dyed-in-the-wool classicist, who, in an age of automation, atomic energy and satellites, sighs for the day when he could with impunity, and publicly, dismiss science as something they used to call "stinks" at school.

But there is more in it than that. It must be admitted that far too many technically competent men are distressingly inept in communication by speech and writing. This is very regrettable. The blame rests primarily on the schools—of that I do not have the slightest doubt. I do not believe that any reasonably intelligent boy who had been properly taught the elements of English grammar and syntax could perpetrate the mangled compositions which

one encounters alike in Ph.D. theses and the scripts of technical representatives. As for some of the efforts at reported speech which one receives from secretaries of technical committees one can only regret that the writers have not been able to experience the intellectual satisfaction to be gained from a proper appreciation of the sequence of tones. The Institution of Metallurgists is trying to do something toward remedying this state of affairs by requiring the demonstration of at least a modest competence in the use of the English language as part of the qualification of a metallurgist. We must hope that by gradual seepage down the line this measure will encourage the schools to increase their efforts in teaching English for use.

We are all fully persuaded that premature and immoderate specialization can produce monsters. Once such damage has been done there is not much hope for rescue operations conducted in university faculties of science and engineering or in technical colleges. Again I think we must look to the schools for salvation. An awareness of what goes on outside his specialization ought to have been gained in the technologist's school days. Special lectures of one hour a week in the liberal arts, isolated from the technological course make no appreciable impression on deficiencies in this respect which the student has brought with him to the university or technical college.

Somehow time must be found, or regained, in the schools for these opportunities to taste the many savours which go to make a full life. The late Prof Samuel Alexander said that liberality was the spirit of pursuit, not a choice of subject. Sir Eric Ashby in a series of stimulating papers and lately in his book 'Technology and the Academics' has denied that technology and culture are antitheses and has urged that technology properly taught can provide a path to culture through a man's specialization and not by bypassing it. In this respect technology has the advantage over pure science in its opportunities for developing cultural appreciation, since applied science necessitates contact with one's fellow men outside one's specialization. If the technologist is to achieve the successful application of his

science he must study his fellow man in order to understand his desires, his fears and his needs.

To the man whose training has been along the route of an apprenticeship and a Higher National Certificate qualification corporate membership of a professional institution opens a door to promotion to positions of major responsibility which otherwise would remain closed. Much could be written about our neglect during the thirty years or so before and after the beginning of the century, to appreciate the immensely valuable national asset which we possessed in this type of man and we may yet have cause to regret our improvidence. Apprenticeship in the engineering and metallurgical industries fell into sad disrepute in those days. Less and less did it serve as a springboard for advancement to executive appointments save for men of exceptional ability whom no system however bad could have held back more and more it became merely a procedure for instilling into the youngster the minimum technical knowledge which operative employment required. In our time we see a new approach. Positive action is taken to encourage and help the young man in industry to broaden his educational horizon and to aim at the most ambitious target which his intellectual ability brings within his scope.

It is a good thing from time to time to count one's blessings. It adds zest to the enjoyment of good times and it helps to keep one's sense of proportion when things are not going so well. Sometimes a piece of good fortune is too obvious to be overlooked. There are also those blessings which become evident only after a little reflection. In this category comes the privilege which we enjoy in a calling in the absorbing world of science and technology. It is indeed a happy circumstance for us that we make our livings by engaging in an occupation which commands our great interest, even apart from the tangible rewards which economic necessity compels us to exact. When we contemplate the lot of many of our fellow citizens who must earn their daily bread by the performance of ineffectually dull chores, then surely we cannot deny the boon with which by contrast we are favoured.

VISUAL ILLUSTRATION OF UNIVERSITY LECTURES

AT the annual general meeting of the British Universities Film Council held at University College Cardiff, on May 8 and 9, one session was devoted to a discussion under the chairmanship of Prof G. E. H. Foxon, on the problems of illustrating university lectures by film and related techniques. It was attended by several guests as well as the representatives of the universities on the Council.

Opening the discussion, the guest lecturer Mr C. L. Engel of the Department of Medical Illustration Guy's Hospital Medical School and editor of *Medical and Biological Illustration* took as his subject 'The Lecture Theatre of the Future'. He pointed out that considerable information was now available on several matters influencing design of lecture theatres, including the visibility of blackboards and of projection screens of different materials. The value of the 'recessed' type of screen was particularly stressed as it allows of sufficient illumination

in the theatre for note taking without impairing the quality of the projected image. Methods involving complicated arrangements of projection are usually considered unsuitable for university use because they upset the speed of the lecture and come between the lecturer and his audience by interposing another person as projectionist. Several devices to overcome this trouble were demonstrated, including first a projector for 2 in. x 2 in. slides with automatic slide change and change of focus; and secondly the prototype of a magazine loading projector for loop films. The details of operation of this loop projector were demonstrated in close up by closed-circuit television (with apparatus kindly lent by the Marconi Wireless and Telegraph Company) thereby showing another method of lecture illustration. Mr Engel concluded by pointing out the need for a magazine loading one projector operated by the lecturer by remote control so that the film sequence could be

introduced precisely when required and, if necessary, repeated

Mr C J Duncan (University of Durham, King's College, Newcastle upon Tyne) said that the normal 'instructional film' with its elaborate production, titling and sound commentary was quite unsuited to the university lecture, what is required is a short piece of film which illustrates only the essential event in which the movement being dealt with occurs. As an example, Mr Duncan demonstrated how, in describing a piece of apparatus, its components could all be shown by slides, thus enabling the speed of explanation to be varied on different occasions and the moving sequence showing the apparatus in use could be projected at the appropriate moment. This method is of value in that it avoids the necessity of producing a complete film with all the necessary editing and titling, and so is much less expensive than an instructional film, also it is much more flexible and any subsequent modification of the apparatus or technique being demonstrated merely necessitates the substitution of a small piece of film and not the production of a completely new full-length film. These short films lasting some 15-20 sec can be called 'moving diapositives', and if several are joined together by short lengths of blank film, during which the projector is stopped, several such short sequences can be shown in one lecture without re-threading the projector and thus disturbing the lecture.

Prof H I Stonehill (Royal Military College of Science, Shrivenham) reviewed the use of television as a medium of instruction at college- and university-level in the United States, emphasizing how much this method was being employed there for instruction at all levels. In discussing in more detail its use in universities an account of some assessments of its value was given, apparently, results so far indicate that students 'attending' lectures by television do as well in tests as those actually present in the lecture room. Some students were reported to prefer television lectures because, when concentrating on the screen, they had less difficulty in preventing their attention from wandering than when in a large audience.

Mr A. M. P. Brookes (Cambridge) described experiments now going on in the Engineering Labor-

atories at Cambridge where, on account of large numbers, some students were 'attending' the lectures in an adjacent room to which the lecture was televised. The lectures involved were those given by Mr Brookes himself, and he told of the first attempt and the modifications in technique that had been made in succeeding lectures. Small television cameras can be set up in the lecture room without waste of space, so sited that they cover the movements of the lecturer and show the blackboards clearly. It is important that the lecturer should appear in the picture in reasonable proportion when seen against the blackboard, close-ups which tend to turn the lecturer into a 'television personality' are to be avoided. The necessity for keeping in view of the television cameras does tend somewhat to limit the movement of the lecturer on his rostrum. It is of great importance that the camera covering any one blackboard remains in use long enough for students to copy any diagram or note which it is expected they shall copy. At present, Mr Brookes and his colleagues are learning by trial and error, but inspection of students' note books indicates that those receiving the lecture by television make as full notes as those in the lecture room.

During a general discussion which followed, Mr Brookes, with the aid of the equipment present, gave a demonstration of 'blackboard work' by television.

This session covered a wide field, and while little summary is possible, attention may be directed to the point made by several speakers that films and television are so well adapted to mass instruction that their possible uses at university-level tend to be overlooked. This is particularly so with films, for although instructional films have been available for many years, suitable film illustration for a university lecture is hard to come by. This, as has already been suggested, is because instructional films are produced as complete entities. There is a need for the provision of short lengths of film illustrating those particular points, which are found in several sciences, when movement plays such an essential part that it cannot be illustrated by other means. Whether this can be done on a commercial basis or whether such sequences, perhaps produced in the course of research, can be exchanged between university departments remains to be seen.

G. E. H. FOXON

THE HALDEN (NORWAY) REACTOR

THE boiling heavy-water reactor of the Norwegian Institutt for Atomenergi at Halden, which is to be used for a joint programme of research and experiment organized by the Organization for European Economic Co-operation, European Nuclear Energy Agency, was successfully operated for the first time on June 29, 1959. The reactor, moderated and cooled with heavy water and fuelled with natural uranium, is located in an excavation in a rock near the paper and pulp factory Saugbrugsforeningen in Halden, 120 km south of Oslo. It is the first boiling heavy-water reactor in the world, and the first boiling-water reactor in Europe. Besides its main function as a power demonstration reactor for studying problems associated with boiling heavy-water reactor systems, the installation will also produce some 15 tons per hour of process steam in the secondary light-water circuit. Eventually this

steam will be used in the paper factory and it is believed that this will be the first nuclear process steam installation.

The reactor was designed at the Netherlands-Norwegian Joint Establishment for Nuclear Energy Research, Kjeller, and was built by the Norwegian Institutt for Atomenergi. The main sub-contractors were the Kvaerner-Myhren, Thune Combino (mechanical installations), the Chr Michelsens Institutt (control and instrumentation), Hoyer Ellefsen (civil engineering work), the UK Atomic Energy Authority (fuel), and the US Atomic Energy Commission (heavy water). The total cost of the plant, including heavy water and the first uranium fuel load, was 3.5 million dollars.

The Organization for European Economic Co-operation Agreement concerning the reactor was signed in June 1958 by Austria, Denmark, Euratom

(representing Belgium, France, Germany, Italy, Luxembourg and the Netherlands) Norway, Sweden, Switzerland and the United Kingdom. It provides for a joint programme, budget and staff for research and development work with the reactor for a period of three years. Through agreements with the Institut for Atomenergi, the United States and Finland are also associated with the reactor project. At present, a professional staff of thirty recruited from the participating countries, is attached to the project. During the next six months the reactor will be operated at low power levels to enable fundamental reactor physics experiments to be performed. After

this period the power level will be increased gradually up to the design power of 10 MW thermal energy.

The reactor plant will be officially opened by H.M. King Olav on October 10.

The Halden Reactor Project is one of several joint undertakings sponsored by the European Nuclear Energy Agency of the Organization for European Economic Co-operation, others are the 'Eurochemie' company for the chemical processing of irradiated fuels (established by an international convention signed in December 1957) and the Dragon high temperature gas-cooled reactor project, work on which began last April.

THE DANISH ATOMIC ENERGY COMMISSION

THE report on the activities of the Danish Atomic Energy Commission* for the period April 1, 1957, to March 31, 1958, deals mainly with the erection of the Riso Research Establishment and the three reactors DR1, DR2 and DR3 and the work of the six departments of the Establishment. The membership of the Commission remained unchanged during the period under review and Prof Niels Bohr continued to act as chairman. The total cost of the Establishment was originally estimated at about 100 million kroner. The expenditure so far, including that estimated for 1958-60, is about 90 million kroner, of which about 60 million kroner is for expenditure on buildings and the remainder for the three reactors and the requisite technical and scientific equipment. On March 26, 1958, the Finance Committee authorized an additional expenditure of up to 2.5 million kroner on a linear accelerator to be used for experiments on the preservation of food and for other irradiation experiments.

On August 15, 1957 the first of the three reactors began to operate and by September the chemical, reactor engineering, electronics and physics laboratories together with the administration building were completed and in use. Then followed the health physics department, the library and the canteen and early in 1958 the agricultural department, the lecture hall and the buildings to house the DR2

reactor group were completed, leaving only the buildings for the DR3 reactor to be erected. A detailed map attached to the report shows the complete layout of the Establishment.

In the physics department one group has been working on the construction of a laboratory for investigations of beta and gamma ray activities, another group with neutron spectroscopy and a third group with solid state physics, particularly the study of the effects of radiation damage to metals and graphite. A study has also been made of the literature on deuterium fusion and of the theoretical aspects of the utilization of the energy from deuterium fusion. The electronics department has undertaken active research on scintillation counters and on the development of a reactor simulator. Two study groups were formed in the reactor engineering department. The first was engaged in drafting a project for a heavy water moderated power reactor with an organic cooling medium and the second for a high temperature gas cooled reactor.

A section of the report is devoted to the International Atomic Energy Agency, and to regional co-operation in Europe, including the Organization for European Economic Co-operation and Euratom. The report also gives details of geological surveys in Greenland, relations between the Commission and commerce and industry, educational activities which included experimental reactor courses with DR1 and lecture courses at the Technical University of Denmark and general information services.

* Report on the Activities of the Danish Atomic Energy Commission for the period from 1 April 1957 to 31 March 1958. Pp 62 (Copenhagen: Danish Atomic Energy Commission 1958).

ATOMIC POWER CONSTRUCTIONS, LTD

ATOMIC POWER CONSTRUCTIONS, LTD, 28 Theobalds Road London, WC1, which was formed in December 1956, is carrying out extensive research and development in connexion with the national nuclear power effort. The research programme is concentrated at the company's laboratories at Heston, Middlesex, and a booklet* recently prepared gives a survey of the problems being tackled. In the Calder Hall type of reactor the uranium is arranged in a pattern of vertical rods embedded in a large cylindrical 'core' of graphite. The heat generated in the rods is carried away by blowing carbon dioxide gas past them and in order to economize in pumping power the reactor designer puts the

whole of the carbon dioxide gas circuit under a pressure of some 20 atmospheres. Consequently the core and uranium must be enclosed in a pressure vessel.

Most stringent precautions must be taken against failure of the pressure circuit in which the carbon dioxide circulates, and a major part of the work undertaken by Atomic Power Constructions, Ltd is concerned with proving the materials and fabrication techniques which are used in the construction of the pressure vessel. An important problem is creep of the steel to be used for the pressure vessel and for the heat exchangers and in order to acquire the necessary information sufficiently quickly an air conditioned creep laboratory containing a battery of seventy creep machines has been set up. The strain ageing of steels at elevated temperatures would

* Research and Development at the Heston Laboratories of Atomic Power Constructions, Limited. Pp 10 (London: Atomic Power Constructions Ltd 1959).

ability and welding techniques for use with selected steels, and the chemical compatibility of the various materials used in the reactor with the carbon dioxide coolant gas, are some of the other problems being investigated by the Metallurgical Division. A considerable expansion in facilities is planned during 1959, and additional long-term researches relating to uranium, magnesium and the weldability of steel will be started. The design of the best heat transfer surface for the fuel elements is at present largely empirical and at the Heston Research Laboratories two experimental rigs are provided for experimental tests. In both, the fuel element can be placed in a

working section and the heat developed in the uranium simulated by an electric heater. Facilities for basic studies in heat transfer and in other design problems have also been set up, and these facilities comprise a flow visualization rig and associated equipment in which water replaces the pressurized carbon dioxide as the working fluid.

Crompton Parkinson, Ltd, the Fairey Aviation Co., Ltd, International Combustion (Holdings), Ltd, Richardsons Westgarth and Co., Ltd, and Nuclear Civil Constructors (Trollope and Colls, Holland and Hannen, and Cubitts) form the five member companies of Atomic Power Constructors, Ltd.

COFFEE RESEARCH IN THE BELGIAN CONGO

TWO investigations of a fundamental character on the genus *Coffea* have recently been published by the Institut National pour l'Étude Agronomique du Congo Belge, (i) *Recherches sur l'Autostérilité du Caféier Robusta (Coffea canephora* Pierro) by M. Devreux, G. Vallaeys, P. Pochot and A. Gilles (No. 78, 1959, Pp. 44+8 plates, 40 francs), (ii) *Recherches sur les Affinités Chromosomiques dans le Genre Coffea* by J. Bouharmont (No. 77, Pp. 94+2 plates, 70 francs). The self-sterility of Robusta coffee has been known in a somewhat confused way for many years, but no convincing demonstration of this phenomenon has previously been presented. This information is important in preparing a rational programme of selection. The investigators of the work indicated above have now shown, under strictly experimental conditions, that this variety is quite self-sterile. As a result of many controlled self-pollination experiments, using 19 clones and based on a very large number of flowers, for example, more than 15,000 in one instance, an extremely small number of fruits has been obtained, the highest percentage not exceeding 0.24. By contrast, when the flowers of the same clones were subjected to cross-pollination, a number of ripe fruits, 30–40 per cent, was obtained. The self-sterility is not attributed

to defects in floral structure or in micro- or macro-sporogenesis but to anomalies in the formation and growth of the pollen-tubes. In no case were these able to traverse the style. While a genetical explanation in terms of incompatibility may be advanced, validation has still to be obtained.

Observations on the chromosome numbers of thirteen species of *Coffea*, including all the well-known species such as *C. arabica*, *C. liberica*, *C. stenophylla*, etc., have shown that all those examined are diploid with 22 chromosomes, except *C. arabica* which has 44. Certain hybrids are diploid and others tetraploid. The nuclear behaviour at mitosis is apparently identical in all the species. Measurements of chromosome lengths show that these are all much alike. It is considered that these comparisons by measurement confirm the close systematic relation of certain species, but it does not enable a general classification of the genus to be established. An average idiogram of the African *Coffea* has been prepared. The author concludes that the genus is a very homogeneous one, and that the species investigated are closely related from the cytological point of view. Lastly, this investigation has yielded no evidence of difficulties in obtaining interspecific hybrids.

BOTANY IN SCOTLAND

AN agreeable and very well-deserved tribute has been paid to Prof. J. R. Matthews, regius professor of botany in the University of Aberdeen, by his friends, past and present colleagues and former students, on the occasion of his seventieth birthday. During his twenty-five years as regius professor he has greatly increased the stature of his Department, has helped the cause of botanical science by his work on the councils of various societies and has made many valuable contributions to botany, especially in the field of research relating to the origin and distribution of the British flora. The presentation volume under consideration has been printed for the Botanical Society of Edinburgh and appears as a special number of the *Transactions* (38, March 1959, 15s). There is a foreword by H. R. Fletcher, and, as might perhaps be expected, a number of the articles relate to the ecology of Scottish plants. But there are also some contributions dealing with other aspects of botanical science, for example, "Some Fundamental Considerations on the New Morphology", by H. J. Lam, "Peristome Teeth and Spore Discharge in Mosses", by

C. T. Ingold, a biographical essay on "The Rev. John Walker (1731–1804)—a Notable Scottish Naturalist", by G. Taylor, of the Royal Botanic Gardens, Kew, and J. Grant-Roger has contributed a useful article on the "Conservation of the Scottish Flora".

Further evidence of the work of this distinguished and active botanical society has also been published (*Trans.*, 37, Part 4, 1959). This is devoted entirely to various aspects of Scottish botany. Thus there are floristic studies of a number of different regions, sometimes combined with geological observations. D. Ratcliffe has contributed an article on the "Habitat of *Koenigia islandica*", and D. G. Downie on "*Rhizoctonia solani* and Orchid Seed". There is a special cryptogam section by D. M. Henderson and an alpine section by D. Grant-Roger. There is also a useful general article dealing with botanical research in Scotland. This gives a brief account of the activities of the main research institutes, including those devoted to marine biology and nature conservation, but it is not concerned with university departments of botany.

HABIT OF ICE CRYSTALS GROWN IN HYDROGEN, CARBON DIOXIDE AND AIR AT REDUCED PRESSURE

By A. P. van den HEUVEL and DR. B. J. MASON

Imperial College of Science and Technology London

ICE crystals grown from the vapour in air at normal atmospheric pressure show a remarkable variation of crystal habit with temperature. This has been closely investigated by Hallett and Mason¹ by growing crystals on a thin fibre running vertically through the centre of a diffusion cloud chamber in which the vertical gradients of temperature and supersaturation were accurately controlled and measured. The results of many experiments covering a temperature range of 0° to -50° C and supersaturations varying from a few per cent to about 300 per cent (in very clean, droplet free air) consistently showed the crystal habit to vary along the length of the fibre in the following manner: 0° to -3° C, thin hexagonal plates, -3° to -8° C, needles, -5° to -8° C hollow prisms, -8° to -12° C hexagonal plates, -12° to -16° C, dendritic stellar crystals, -16° to -25° C, hexagonal plates, -25° to -50° C, hollow prisms. These changes of habit were controlled almost entirely by the temperature, the supersaturation influencing only such secondary features as the growth rate and the onset of dendritic and needle growth. Similar conclusions have been reached by Kobayashi.²

In attempting to account for these changes of habit, considerable interest is attached to recent reports by Isono *et al.*^{3,4} that they are further modified if the crystals are grown in an atmosphere of hydrogen instead of air, but that little change is effected by replacing air with carbon dioxide. In particular, Isono found that crystals grown in a water saturated air at -7° C developed preferentially along the *c* axis to form hexagonal prismatic columns but, in hydrogen, the growth rates in the *a* and *c* directions were approximately equal. Furthermore, needle like crystals grown in air thickened, and skeletal growth was suppressed when the air was replaced by hydrogen. Crystals grown at -10° C in air took the form of thin hexagonal plates, but those grown in other wise similar conditions in hydrogen developed as thick plates and short hexagonal columns.

In general the effect of hydrogen was to produce more nearly isotropic growth and isometric crystals changes which were attributed to the high diffusion coefficient of water vapour in hydrogen, it being 3.4 times that in air. The fact that crystals grown in carbon dioxide were very similar to those grown in air at the same pressure was taken to be consistent with the diffusivity being only 0.7 times that in air.

If the rate of diffusion of water vapour were an important factor in controlling crystal habit, very similar results to those obtained in hydrogen should be obtained in air at reduced pressure since the diffusivity is inversely proportional to the air pressure. Indeed, Kobayashi² and Isono⁴ report that reduction of the air pressure does influence the shapes of crystals grown in both diffusion and mixing cloud chambers.

Isono found that his results obtained at -7° and -16° C in hydrogen were reproduced in air at pressures of 80-30 mm. mercury. Kobayashi reports that the hexagonal plates and dendritic crystals found at temperatures between -10° C and -20° C in air at normal atmospheric pressure persist if the pressure exceeds 300 mm, but at less than 100 mm pressure, they are entirely replaced by hexagonal columns, often with hollow cavities and, at less than 70 mm pressure, by short solid columns which now occur at all temperatures between 0° C and -30° C. Unfortunately, under the conditions of the experiment, the total pressure could not be lowered without also lowering the supersaturation of the vapour, and Kobayashi attributes the formation of solid prismatic columns at low air pressures to the slow growth conditioned by the low supersaturation. He supports this view by recording that in air at normal atmospheric pressure only solid columns are obtained in

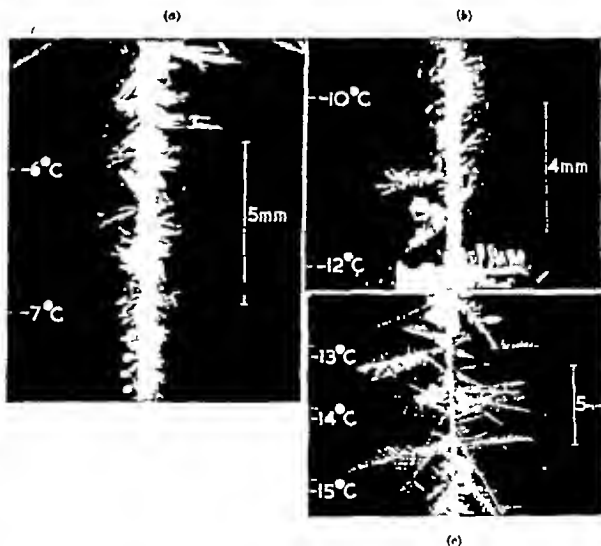


Fig. 1 Ice crystals growing in an atmosphere of hydrogen on a fibre suspended in a diffusion cloud chamber

a Needles and hollow prisms in the temperature range -5 to -7.5° C b plates between -9 and -12° C c dendrites between -12 and -16° C



Fig 2 Crystals grown in air at 80 mm. mercury pressure. The sequence is plates → needles → hollow prisms → plates → dendrites → plates as the temperature varies from 0° to -20° C

the temperature range 0° to -30° C providing the supersaturation does not exceed 7 per cent with respect to ice

Because the results of these Japanese experiments in hydrogen and in air at low pressure, if confirmed, might throw new light on the mechanism responsible for the remarkable habit changes in ice, similar investigations have been made by us

The crystals were grown, in aerosol-free air, in the diffusion cloud chamber described by Hallett and

Mason¹. They were supported on a fine fibre along which the temperature varied from 0° to -50° C, and the supersaturation could be varied and measured over a wide range. In a chamber filled with hydrogen at atmospheric pressure, the crystals exhibited the same variation with temperature as listed above for crystals grown in air (Fig 1). No differences were observed except that the crystals grew much faster in hydrogen, in conformity with the diffusion coefficient of water vapour being 3.4 times that in air, and the thermal conductivity, which controls the rate of dissipation of the latent heat of crystallization, being about seven times greater.

Crystals were also grown under reduced air pressures of 300, 150, 80, 40 and 20 mm mercury, the pressure never varying by more than 1-2 mm during the course of any one experiment. Again, as shown in Fig 2, the habit varied with temperature in a manner identical to that observed at normal atmospheric pressure and dendritic forms could always be produced between 0° C and -3° C, and also between -12° and -16° C, at high supersaturations.

Crystals were grown under low supersaturations at atmospheric pressure between two parallel sheets of ice maintained at slightly different temperatures. This arrangement allowed the temperature and supersaturation to be accurately determined. Under supersaturations not exceeding 5 per cent with respect to ice, plate and sector-plate crystals appeared in the temperature range -10° to -15° C and therefore the experiments provided no support for Kobayashi's claim that only solid prismatic columns occur at all temperatures between 0° C and -30° C at such low supersaturations.

Summarizing, we have been unable to confirm that the habit of ice crystals grown from the vapour is essentially modified by growing them in either hydrogen or in air at reduced pressure, although their growth-rates are affected in the sense one would expect from the manner in which the diffusivity and thermal conductivity of the environment would influence the fluxes of water vapour and heat.

We are unable to offer an explanation of the results obtained by the Japanese workers except to suggest that, perhaps, their apparatus may have been contaminated with small traces of foreign vapours such as are known² to affect markedly the ice crystal habit even though present in only very small quantities.

¹ Hallett, J., and Mason, B. J., *Proc Roy Soc. A*, 247, 440 (1959)

² Kobayashi, T., *J. Met. Soc. Japan*, 36, 193 (1959)

³ Isono, K., Komabayashi, M. and Ono, A., *Met. Papers Geophys. Inst. Tokyo Univ.* 8, 327 (1955)

⁴ Isono, K., *Nature*, 182, 1221 (1958)

⁵ Hallett, J., and Mason, B. J., *Nature*, 181, 407 (1958)

CELL-WALL MUCOPEPTIDES OF *STAPHYLOCOCCUS AUREUS* AND *MICROCOCCUS LYSODEIKTICUS*

By H. J. ROGERS and H. R. PERKINS

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A CONSIDERABLE number of recent studies have been concerned with the superficial layers of micro-organisms. In particular, insoluble material which is resistant to the action of several proteolytic enzymes and nucleases has been isolated. The morphology of this material is such that it may be regarded as consisting of the cell walls. Lysozyme-

sensitive micro-organisms yield walls which are dissolved by lysozyme. In Gram-positive species the material has a relatively simple overall chemical composition compared with that of the cytoplasmic proteins, and its biosynthesis is inhibited by antibiotics such as penicillin and bacitracin. Elucidation of the more detailed chemistry of the structure and

biosynthesis of the cell wall holds, therefore, the hope of a further understanding of the mode of action of antibiotics. The purpose of the present article is to discuss some recent observations made in these laboratories and elsewhere in relation to concepts about the structure and biosynthesis of the cell walls of in particular, staphylococci and micrococci.

The work of Salton¹ and Cummins and Harris² firmly established that a large proportion of the substance of cell walls of representative strains of several species of Gram positive cocci, other than some streptococci, consists of a limited number of amino acids, two amino sugars and sometimes one or two hexoses, these component substances were detected on paper chromatograms of acid hydrolysates of the wall structures. The name mucopeptide³ has more recently been proposed to describe the group of polymeric substances containing these compounds. The earlier work was not designed to give an exact indication of the quantitative interrelationship between the components or to express any attitude towards the number of polymers combined to give the final insoluble wall structure. Suggestions of possible heterogeneity at the polymer level were, however, contained in the earlier work of Mitchell and Moylo⁴, who had isolated from a cell fraction they called "cell envelopes" polyol phosphate compounds. Cell walls prepared by the Salton and Horne⁵ method were known to contain small amounts of phosphorus, and later Baddiley⁶ and his colleagues first obtained substances which they called teichoic acids from *Lactobacillus arabinosus*. One component of teichoic acid associated with the wall structure was polyribitol phosphate carrying in covalent linkage either glucose or N acetylglucosamine (to which, in turn, alanine was bound in ester linkage. This type of substance was shown to be present in cocci⁶. Its amount varied from negligible quantities in walls from *Micrococcus lysodeikticus* to about 30 per cent in the strain of staphylococcus wall examined. These quantities were deduced from the phosphorus contents of the walls—only a small proportion of the calculated material is recorded as having been isolated. Mitchell and Moylo⁴ have recently shown that their polyol phosphate also contains ribitol phosphate. The presence of substances of this type which can be extracted by cold trichloroacetic acid may explain the report⁶ of the presence of components soluble in trichloroacetic acid and in water in frozen dried wall preparations.

The homogeneity or heterogeneity of the structure remaining (that is, the mucopeptides) after the removal of teichoic acid is still unjudged. Examination of the concentration of amino-acids in the mucopeptides from various strains of staphylococci and micrococci shows that considerable differences in the molecular proportions occur. Moreover, the ratios for most of the strains do not fit any simple pattern. Even if the small amounts of alanine present in the teichoic acid in walls from some strains cause some distortion of the values for the concentration of this amino-acid in the mucopeptide, such considerations do not apply to the other amino-acids. Park and Strominger⁷ have suggested that a uridine-muramic acid peptide originally isolated by Park⁸ from penicillin treated staphylococci may be a biosynthetic precursor of mucopeptide. This peptide had its amino-acids (alanine, glutamate and lysine) in simple molecular proportion and resembled in this respect the wall mucopeptide. If this compound should eventually prove to be a precursor then presumably

Table 1 AMINO-ACID COMPOSITION OF CELL WALLS EXPRESSED AS MOLAR RATIOS (GLUTAMATE TAKEN AS 1.0) IN SEVERAL STRAINS OF STAPHYLOCOCCI AND MICROCOCCI

| Strain | Glutamate | Alanine | Glycine | Lysine | Ref |
|-------------------------|-----------|---------|---------|---------|--------------|
| 524/SG | 1.0 | 1.8 | 3.2 | 0.6 | 8 |
| H | 1.0 | 3.2-3.7 | — | 0.0-1.2 | 9 |
| Duncan | 1.0 | 2.8 | 6.3 | 1.0 | 23 |
| 11 | 1.0 | 1.4 | 0.45 | 0.5 | Present work |
| Oxford | 1.0 | 1.9 | 4.9 | 1.0 | Present work |
| <i>M. lysodeikticus</i> | 1.0 | 1.0-2.5 | 1.2-1.6 | 1.0 | 13 |

Cell walls prepared by the Cummins and Harris method, hydrolysed for 4 hr with 4 N hydrochloric acid and the contents of amino-acids determined (ref. 13)

other precursor compounds corresponding to the glycine and glucosamine present in the wall must be found. The molecular ratios for the amino acids in other strains of staphylococci or micrococci such as 11, 524 or *lysodeikticus* are not simple and the condensation of a single small peptide could not account for them. If, however, there is more than one mucopeptide in the wall and possibly a multiplicity of uridine peptide precursors, as has been suggested by Ito, Ishimoto and Saito¹¹ then this situation is more easily explained.

The action of lysozyme on a 'staphylococcus' strain 11 has provided some facts which also point towards possible heterogeneity of the wall mucopeptides. This organism has a wall which is qualitatively similar to staphylococci, as can be seen from Table 1 although it is distinguished by a very low glycine content. No glucose could be detected. Its cytochrome composition however is different from other staphylococci and nearer that of *Micrococcus lysodeikticus* (Jackson, private communication).

Fig. 1 shows the lysis of whole organisms of this strain by lysozyme. When the enzyme is allowed to hydrolyse wall preparations, the optical density of the suspension falls to about 28 per cent of the

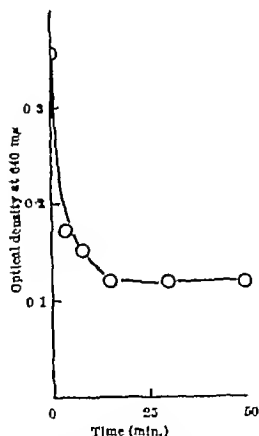


Fig. 1 Lysis of staphylococcus strain 11 by lysozyme. A suspension of organisms grown in broth for 18 hr at 33° with agitation was prepared by centrifuging, washing twice with water and suspending in 0.1 M ammonium acetate buffer pH 6.0. To the suspension warmed to 37° 50 µgm/ml of crystalline (Armour Products Ltd.) lysozyme were added at zero time. The optical density was measured at the times indicated during incubation at 37°.

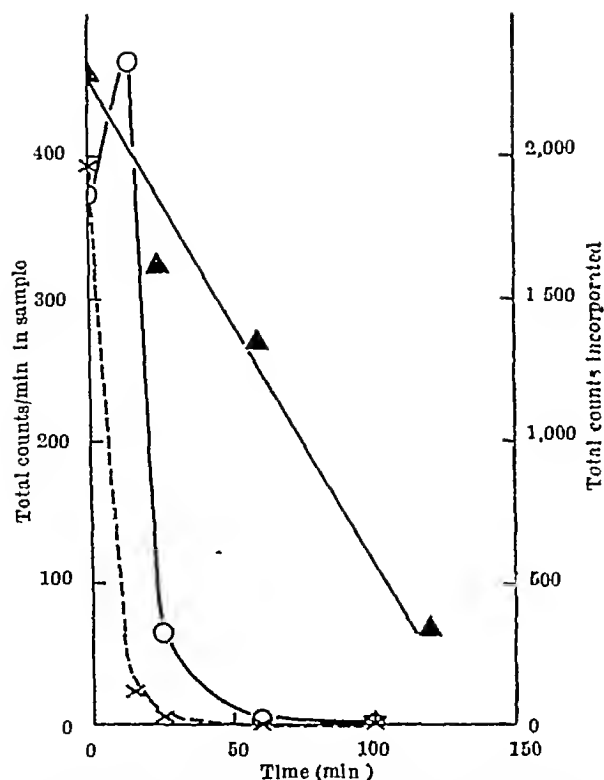


Fig. 2 The sedimentation of whole cells from a broken preparation during centrifugation at 1,000g at 0-4°C. Whole cells of *Staphylococcus aureus* strain 524 were labelled in their cell walls by incubation with labelled glycine (ref. 22) washed and prepared as a thick suspension which was then added to the diluted crush. The crush was prepared from *Staphylococcus aureus* strain 524 by passing a thick suspension of cells in 1M sucrose through the Hughes press working at -30°. The crush was then diluted with either 0.1M sodium-potassium phosphate buffer, pH 7.0, or with further 1M sucrose (▲). At the times indicated the centrifuge was stopped, and samples taken from the supernatant. In order to obtain as representative samples as possible without disturbing the sediment, the pipette was moved slowly down the tube while the sample was drawn into it. The samples were mixed with trichloroacetic acid to give a final concentration of 5 per cent (w/v) and the precipitate washed once with 5 per cent trichloroacetic acid and dried by washing with acetone and ether. The dried precipitates were weighed and assayed for radioactivity at infinite thickness. Total radioactive counts (that is, weight \times specific activity) are recorded. O shows the ability of samples of the supernatants to incorporate radioactive glycine into cell wall material when tested under the conditions given in the legend to Table 3.

and incorporating activity of the cell wall and residual radioactivity due to whole cells remaining in the

supernatant after centrifugation at 0-4°C compared. Two observations from Fig. 2 can be made: (1) that centrifugation at 1,000g in the presence of sucrose can be a very inefficient way of removing whole cells; (2) a difference between the rate of deposition of whole cells and the incorporating activity of the preparations is apparent, thus suggesting that incorporation might be taking place into some particles less dense than the whole cell. This difference, however, can be largely accounted for by the increasing efficiency of the decreasing number of whole cells.

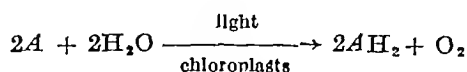
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RELATIONSHIP BETWEEN PHOTOPHOSPHORYLATION AND THE HILL REACTION

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ARISING from the work of Hill¹, it is now well known that isolated chloroplasts illuminated in the presence of a suitable hydrogen acceptor will evolve oxygen



Little doubt now remains that photolysis of water in the Hill reaction with production of reducing power and oxygen represents a partial model of photosynthesis in a cell-free system

Recently, Arnon, Whatley and Allen² have made the important observation that when a phosphate acceptor system (adenosine diphosphate, Mg^{2+} and PO_4^{3-}) is included in the Hill reaction system with coenzyme II or ferricyanide as hydrogen acceptor, oxygen evolution is stoichiometrically related to phosphate esterified into adenosine triphosphate. Moreover, in the ferricyanide reaction the rate of production of oxygen is stimulated two-fold by addition of the phosphate acceptor.

In the present work a similar stimulation of the Hill reaction rate by phosphate acceptors has been

observed with coenzyme II as hydrogen acceptor. The reduction of substrate amounts of pyridine nucleotides by catalytic amounts of chlorophyll has been shown to require a protein factor readily extractable from chloroplasts^{1,4}. A preparation of this factor was obtained from spinach leaves by the method of San Pietro and Lang⁴. Chloroplasts were obtained by grinding spinach leaves in 0.4 M sucrose containing 0.05 M *tris* buffer pH 7.8 and 0.01 M sodium chloride. The fraction sedimenting between 800 and 1,500g was resuspended in the same medium. Reduction of added pyridine nucleotide was followed by observing the increase in optical density at 340 mμ after a period of illumination. The blank cell contained all the reagents except pyridine nucleotide. Fig. 1 shows that the reduction of coenzyme II is stimulated 2.5 fold by the presence of the phosphate acceptor system and that all the components of this system are necessary for appreciable stimulation. In these experiments, contrary to the findings of San Pietro and Lang⁴, coenzyme I was not reduced either in presence or absence of the phosphate acceptor.

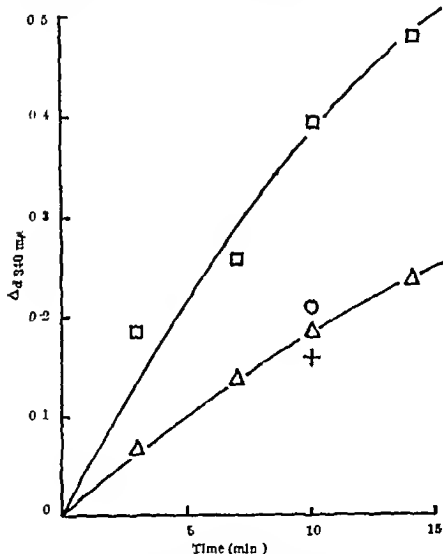


Fig. 1. Effect of phosphate acceptor system on the rate of reduction of coenzyme II by isolated chloroplasts. The reaction mixture contained in a final volume of 2.5 ml. leaf protein 0.25 mg/ml. chloroplasts containing 25 μg/ml. chlorophyll and (except where otherwise indicated) the following in micromoles: *tris* buffer pH 7.4, 80; coenzyme II, 0.5; adenosine diphosphate, 2; magnesium chloride, 10; phosphate buffer pH 7.4, 80. Illumination by 500-watt projector lamp at 1 ft. temp 18°. □ complete system; ○ adenosine diphosphate and magnesium omitted; +, adenosine diphosphate and magnesium omitted; Δ adenosine diphosphate, magnesium and phosphate omitted.

Arnon *et al.*⁵ in their observations on phosphorylation accompanying coenzyme II reduction by illuminated chloroplasts have shown that addition of catalytic amounts of flavin mononucleotide or menadiene abolish both oxygen evolution and the accumulation of reduced coenzyme II and stimulate phosphorylation. A probable mechanism for this effect suggested itself in the course of the present work. All the leaf and chloroplast protein fractions active in mediating coenzyme II reduction were

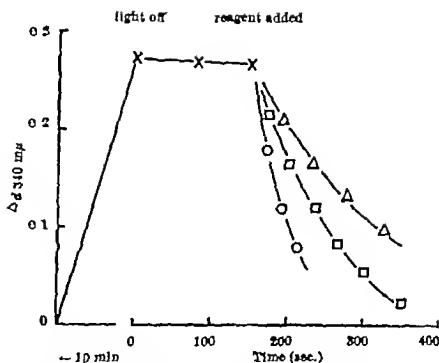


Fig. 2. Recidivation of photochemically reduced coenzyme II by some catalysts of photophosphorylation. Reaction mixture as Fig. 1 (complete system). At the time indicated 0.05 μmole of the following added: Δ flavin mononucleotide; □ pyocyanine; ○ menadiene.

found also to possess a very active coenzyme II diaphorase activity similar to that reported by Arnon and Jagendorf⁶. Diaphorase in the presence of a rapidly autooxidizable hydrogen acceptor should function as a reduced pyridine nucleotide oxidase. Menadiene and flavin mononucleotide are listed by Arnon and Jagendorf as hydrogen acceptors for their coenzyme II diaphorase from chloroplasts. Their effect in reoxidizing reduced coenzyme II produced photochemically by a chloroplast system containing San Pietro and Lang leaf extract is shown in Fig. 2. Here also pyocyanine is shown to have a similar

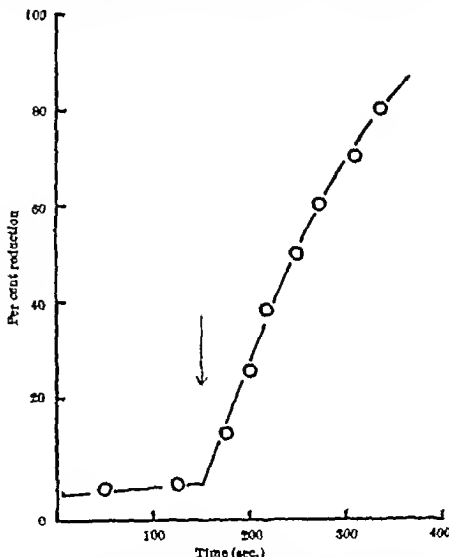


Fig. 3. Catalytic effect of pyocyanine in promoting reduction of methanoglobin by illuminated chloroplasts. Reaction mixture contained chloroplasts equivalent to 35 μg/ml. chlorophyll, whole muscle methanoglobin 0.35 μmole, phosphate buffer pH 7.4, 150 μmoles and water to 5 ml. Pyocyanine (0.05 μmole) added at time indicated by arrow. Illumination by 500-watt projector lamp at 1 ft. temp 18°.

iority of the heterozygote or 'over-dominance'² have not proved entirely acceptable because whenever over-dominance has been investigated using genetic markers, it has not been found generally to occur³. In the absence of a clear-cut unifying hypothesis, present-day concepts of heterosis have become surrounded by highly sophisticated escape clauses involving all the known intricacies of gene action.

Heterosis and its allied expressions are properties of quantitative characters, particularly of such characters as yield, stature, viability and reproductive efficiency. That all expressions of this kind are complex interactions between simpler growth processes is immediately obvious, and this common denominator of quantitative characters is frequently referred to in discussions on heterosis. Nevertheless, the implications inherent in the absence of a direct relationship between gene and complex phenotypic expressions are seldom recognized in interpretation.

In one of the first attempts at explaining hybrid vigour, Keeble and Pellew⁴ suggested that the inheritance of height in peas could be explained on the basis of two complementary loci each possessing one dominant and one recessive allele. Excess height in the hybrid resulted from the complementarity of dominant alleles from opposite parents, one conditioning length of internode and the other thickness of stem. (Although in certain circumstances thickness of stem may contribute to stature in plants, it should be noted that the components mostly directly concerned with height are internode length and internode number. This, however, does not affect the principles revealed by the work.) The genetic interpretation advanced by Keeble and Pellew achieved meaning and simplicity only because of the recognition that stature as a measurable character was not a primary expression of gene function, but resulted from multiplicative interaction on the phenotypic level between components which segregated in a manner suggesting direct genic control. The components of height in this material were not heterotic, and nothing more complicated than dominance was necessary to provide an adequate genetic explanation of the results. This early model of the behaviour of heterotic characters, although widely quoted as a special case, has not been fully explored and understood in later work. Hagberg^{5,6}, although recognizing a similar system in data on *Galeopsis* under the term 'combination heterosis', considered it could be different from 'transgressive heterosis' in which the hybrid is superior in one or more of the components of growth. In this connexion he neglected the most important aspect underlying Keeble and Pellew's interpretation, namely, that height in the pea remained genetically transgressive only so long as the components of height remained unidentified. The complexity of quantitative characters generally is such that the resolution of ultimate cell processes is a matter of utmost difficulty. In these circumstances, therefore, it is more rational to suspect the unitary nature of the component characters than to attribute hypothetical properties to the genetic system when departures from a complementary model are encountered.

Recent evidence from a study of inheritance of yield in the tomato has indicated that systems basically similar to the model governing height in the pea may be of common occurrence. It seemed, therefore, desirable to inquire how far the large body of experimental fact available concerning heterosis and allied

phenomena fits in with a simple genetic system when due weight is given to interactions on the phenotypic level between the components of complex expressions.

Heterosis for Yield in the Tomato

The five characters—number of flowers, date of first flower, average weight of fruit, number of fruit and yield of fruit—were studied in three F_1 hybrids. The parents and their F_1 hybrids were compared using means of thirty replicates set out in randomized blocks.

None of the hybrids exceeded the better parent in any of the characters with the exception of yield per plant. Yield in all three hybrids exceeded the highest yielding parent. Yield when measured as weight is a product of number and weight of fruit, and in two of the hybrids number of fruit equalled the 'mid-parent' while the average weight of fruit was slightly in excess of this value. The third hybrid inherited phenotypic dominance for a high number of fruit from one of its parents but in weight of fruit it was only slightly in excess of the lower parent. Heterosis in the compound character was a product of various levels of expression of the components in the F_1 , ranging from dominance of the better parent to a slight excess over the poorer parent. Heterosis, therefore, is clearly a property of the phenotype, and is conditioned by the nature of the association between the unit characters in the parents. When two parents differ reciprocally for two interacting components, and if the F_1 -levels compensate one another in such a way that their product is greater than in the parent, heterosis is inevitable. Table 1 gives a simple example showing the consequence of mating reciprocally different parents.

Table 1

| | Component A fruit number | Component B fruit weight | Yield |
|-----------------------------|--------------------------------|--------------------------------|-------|
| Parent 1 | 3 | 1 | 3 |
| F_1 (heterosis for yield) | 2 | 2 | 4 |
| Parent 2 | 1 | 3 | 3 |

The genetic system in the above model is one of blending inheritance, and it is difficult and unnecessary to envisage the operation of the remotest form of interaction on the genetic level. The genes or gene products controlling average weight and number of fruit need not and probably do not interact in the sense that an enzyme and a precursor might interact in a synthesis. Complex characters such as yield can be based on units of the genetic system which act completely independently of one another. Interaction occurs on a higher level of organization, among the components of the phenotype. Thus to interpret hybrid vigour in terms only of gene interaction is a basic misconception which has contributed greatly to the present confused state of the subject.

The system described in the tomato has wider application as can be seen from investigations on the inheritance of yield in wheat⁷. Yield of grain and the component characters weight per grain, grain per spikelet, spikelets per ear, ears per plant, were studied in all possible crosses between four varieties. None of the components showed heterosis, and their levels in

F_1 hybrids were on average slightly in excess of the 'mid parent'. Owing to the small number of comparisons possible in a 4×4 diallel cross, one cannot determine with any degree of certainty whether the excess was real. Grain yield in all crosses was heterotic, the average yield of the parents and F_1 families was 31.9 ± 0.76 and 37.7 ± 1.02 respectively. The authors interpreted this behaviour as being the result of multiplicative as distinct from additive gene action, and concluded "it can be said with confidence that gene interaction plays a part in determining the control of this character". It now seems doubtful whether an interpretation based exclusively on genetic considerations was entirely justified.

Detailed examination of the individual wheat crosses shows that all six parental combinations possessed varying patterns of inequality such as was described for the tomato hybrids. Four of the six were reciprocally different for all four components. Since the component levels in the hybrids were close to or slightly in excess of, the 'mid parent', heterosis for grain yield was inevitable. In wheat, as in the tomato, an essentially additive genetic system conditions a multiplicative somatic basis to yield which, when analysed as a simple character leads erroneously to a non additive genetic interpretation.

In a further study on heterosis among 153 hybrids in a diallel cross of 18 inbred lines of the tomato⁴, further aspects of heterosis have been revealed which are relevant to this discussion. First, in certain crosses heterosis has been found for yield components such as number of fruit, and this is interpreted as evidence that the component itself may be a product of sub units. Secondly, heterosis for both yield and its components was expressed only in hybrids between the poorer parents. Hybrids involving the best parents were inferior to the high parent in the crosses. The best varieties possess optimal levels in the yield components whereby maximal yields are achieved. The highest levels of yield in the tomato can be expressed in homozygotes. There is therefore no advantage for an inbreeding species such as the tomato in heterozygosity *per se*. Thirdly, the components, number and weight of fruit, are negatively correlated $r = -0.08$ ($n = 18$) and -0.70 ($n = 153$) in the parents and hybrids respectively. This implies that in the course of the production of a certain finite weight of fruit, a variety producing large numbers will have small fruit and vice versa. The maximal level at which each single component can function separately is far in excess of what can be achieved by their product. The phenotype cannot sustain the production capacity that potentially resides in the multiplicative relationships between maxima at each of the unitary divisions of a complex expression. When the limits for the respective functions are pushed too far by selection, or by inbreeding in outbreeders, a physiological breakdown occurs. This frequently expresses itself as sterility, reduced viability or susceptibility to disease⁷⁻¹¹, and may be the basis of concepts of physiological limits¹².

Heterosis and Inbreeding Depression

Inbreeding is invariably associated with loss of vigour in cross fertilizing species. The commonly accepted explanation for this behaviour is based on the dominance hypothesis and on the segregation of homozygous genotypes. The extent of the average

depression in a randomly breeding population where there is no selection depends only on the relative difference in expression between the segregating dominant and recessive alleles. A genetic system which is strictly additive in expression cannot account for average inbreeding depression because, in the absence of selection, gene frequencies remain unchanged and the mean of the inbred population is therefore unaltered. This appears at first sight to exclude the possibility of commonly occurring systems such as were described for tomato and wheat being concerned in inbreeding depression.

The dominance hypothesis despite the fit to average values of inbreeding, presents to my mind one unattractive feature. Correspondence between experimental evidence and the dominance hypothesis centres around progeny averages and the drop in vigour is related to the frequency of the homozygous recessive which after about five generations of selfing will be approaching the limit of $\frac{1}{4}$ at each locus. The homozygous dominant will also have the same frequency and for n loci the frequency will be $(\frac{1}{4})^n$. The failure in practice to isolate vigorous homozygous dominants has on the dominance hypothesis, been attributed to the size of n and to linkage. A purely mechanistic explanation of this kind is not entirely acceptable for the interpretation of a vital process. Furthermore, in view of the thousands of inbred lines that have by now been studied in maize, it is inconceivable that chance recombinants of near maximal expression would not have appeared if the cause was one merely of permutation. It must also be noted in this connexion that the chance of isolating recombinants will depend not on the potential n , but on that portion which is heterozygous. In crop plants such as maize in which some form of selection for vigour has been practised for centuries, the number of unfixed loci may be fewer than is generally assumed in attempts to make the dominance hypothesis acceptable. It may be prudent therefore, to explore other possible factors of causality.

The negative correlation between the components of complex expressions and the concept of physiological limit may provide the missing factor necessary to explain inbreeding depression in terms of additive genetic factors. Selection experiments already mentioned clearly indicate the undesirable consequences of extremes of selection and of genetic fixation above the optimal level for fitness. In terms of the components of fitness, physiological breakdown means that the tolerance-level of the product of component interaction has been exceeded. Too many components are simultaneously at too high a level. A proportion of the genotypes following inbreeding of heterozygotes should also show loss of fitness similar to that resulting from intense selection. Multiple homozygotes for hypermorphic alleles segregating after inbreeding represent genotypes where all the components are simultaneously at a high level, and might be expected to belong to a class where fitness is severely reduced. They are the equivalent of a highly selected, closed population where sterility, susceptibility to disease or other forms of debilitation are reducing fitness.

The elimination of dominants has been demonstrated by Fisher¹³ in populations of *Paratettix texanus* in which it was estimated that double dominants were eliminated to the extent of not less than 40 per cent in each generation. The mechanism underlying this selective elimination of genotypes is almost certainly physiological and corresponds very closely

to the system postulated here to account for inbreeding depression

If, as seems likely from the above considerations, 'compounds' of dominants or of hypermorphic alleles are to a greater or lesser degree self-eliminating in outbreeders, the dominance hypothesis is not the only explanation for inbreeding depression. The pattern fits additive gene action equally well.

A distinction, therefore, has to be made between gene interaction and the interrelations of the component parts of the phenotype. Phenotypic characters may be multiplicative and may consequently show a mutually dependent relationship while the gene system is strictly additive and its units are strictly independent in function. Heterosis in complex characters has been shown here to occur in hybrids simply as a result of a reciprocal inequality of independent gene action in the parents. Given reciprocal inequality in the levels of component characters in the parents, intermediate levels in hybrids inevitably lead to heterosis in the complex character. It appears, therefore, that many of the difficulties that are encountered in the interpretation of heterosis arise out of the failure to recognize the component parts of complex expressions.

Multiplicative interaction between adjusted levels of component characters may govern the control of the physiological limit, as is indicated by negative correlations between components of yield in the tomato. It is suggested that mal-adjusted, maximal levels of expression in sub characters may be responsible for inbreeding depression in outbreeding species leading to the self-elimination of genotypes homozygous for several dominant or hypermorphic alleles. Inbreeding depression, like heterosis, may therefore be explained simply on the basis of interactions on the somatic level which are controlled by a complementary, essentially additive genotypic system.

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TURNIP YELLOW MOSAIC VIRUS NUCLEOPROTEIN PARTICLES WITH DIFFERING BIOLOGICAL AND PHYSICAL PROPERTIES

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PREVIOUS work¹ has shown that purified preparations of turnip yellow mosaic virus contain two types of particle. One is a nucleoprotein containing 37 per cent of ribonucleic acid within a roughly spherical shell of protein. The other is an apparently identical protein containing no ribonucleic acid. The nucleoprotein is infectious while the protein is not. The ratio of nucleoprotein to protein particles in the preparations is close to 2:1.² The sedimentation patterns obtained in the ultracentrifuge with both these components give no indication of inhomogeneity.^{1,3}

The value of density gradient centrifugation under equilibrium conditions in strong caesium chloride solutions for the fractionation of macromolecules has recently been demonstrated.^{4,5}

We have now found, using sedimentation into dense caesium chloride solutions under non-equilibrium conditions, that the nucleoprotein particles of turnip yellow mosaic virus fall into at least two classes with respect to density and infectivity.

Turnip yellow mosaic virus was isolated from infected Chinese cabbage plants by the ammonium sulphate procedure¹ or by differential centrifugation. Preliminary tests with whole virus preparations showed that incubation with strong caesium chloride solutions for 2 hr. at room temperature, followed by 14 hr. at 4°, had no detectable effect on the infectivity of the virus. To avoid anomalous effects due to crystallization or precipitation of the virus at room temperature in the strong salt solutions employed during sedimentation, all manipulations were carried out at temperatures between 4° and 10° C.

In the sedimentation experiments 1–10 mgm. of a virus preparation in solution in 0.1–0.6 ml. water

was layered over 3.5 ml. of caesium chloride solution (density = 1.39–1.43) in a 'Lusteroid' tube. The samples were then centrifuged for 200–240 min. at 32,000 r.p.m. in the Spinco model L preparative ultracentrifuge using the No. 39S rotor. Under these conditions the virus protein component stays in the boundary between the water layer and the caesium chloride solution. The nucleoprotein sediments through the salt solution and resolves into bands which can be located visually by scattered light (Fig. 1).

The various components were withdrawn by piercing the wall of the tube with the needle of a hypodermic syringe, and dialysed to remove salt. The bands cannot be removed quantitatively by this procedure, but other methods we have tested lead to substantial mixing of closely spaced bands. Estimates of relative amounts of material in various bands were based on the ultra-violet absorption curves of the extracted samples. Such estimates on duplicate pairs of bands varied by as much as 25 per cent.

In preparations of virus made by the ammonium sulphate procedure, two sedimenting bands appear. The faster-sedimenting band (*B*₂) usually contains 1/5–1/20 as much material as the slower band (*B*₁). If these two bands are removed and the material from several tubes combined and run again, each band shows a slight contamination with the other on the second run. A third sedimentation usually gives material with no observable contamination. This result suggests that the bands are not produced by the action of caesium chloride on a uniform population of particles. Both bands give typical virus nucleoprotein spectra, and the nitrogen/phosphorus ratios suggest that both types of particle have the same



Fig. 1. Fractionation of turnip yellow mosaic virus nucleoprotein in a dense caesium chloride solution. Of the two nucleoprotein bands appearing in the photograph the upper (B_1) is infectious while the lower (B_2) is non-infectious. A μ g. of a virus preparation in 0.15 ml. of water was layered over 3.5 ml. of a caesium chloride solution (density = 1.41). The tube was photographed after 220 min. centrifugation at 32,000 r.p.m. in the Spinco No. 385 rotor.

content of ribonucleic acid. Solutions of the B_1 and B_2 components equalized with respect to optical density at 260 m μ were tested for infectivity by inoculation to half-leaves of chinese cabbage. The infectivity of the B_2 component compared with B_1 from once-sedimented bands ranged in different experiments from 25 to 6 per cent.

On three times sedimented bands the B_2 material had only 3 per cent the infectivity of B_1 . Thus the B_2 band is very probably completely non-infectious. However, to test the possibility that B_1 and B_2 were two different strains of the virus of differing infectivity multiplying together in the plant, four single lesion isolates were made from plants infected with virus from each band. The isolates were multiplied in chinese cabbage. No symptom differences were observed. Virus isolated by an initial high speed centrifugation followed by one ammonium sulphate precipitation from each isolate gave a similar band pattern in all cases. The B_2 band was present in about 1/20 the amount of the B_1 band. That virus strains were not involved was confirmed by the production of the B_1 and B_2 bands from a 'necrotic

strain of the virus which is biologically distinct from the type strain.

The B_1 and B_2 bands appear in similar proportions in virus prepared from the same plant material, either by the alcohol-ammonium sulphate procedure, or by differential centrifugation alone. It therefore seems unlikely that either of these bands is an artefact of the procedure used to isolate the virus.

However, in virus material isolated by centrifugation only, a third more slowly moving band (B_3) appears following sedimentation in caesium chloride. This band is not visible in most ammonium sulphate preparations, and can be largely removed from virus prepared by centrifugation by one ammonium sulphate precipitation. The fact that band B_3 sediments into a caesium chloride solution of $D = 1.40$ suggests that it must contain some ribonucleic acid. The ultra violet absorption spectrum and the nitrogen/phosphorus ratio show that the material in the B_3 band contains a lower proportion of ribonucleic acid than the B_1 component and its infectivity is substantially less. However, the B_3 material has not yet been obtained sufficiently free from contamination with B_1 for definitive chemical analysis or infectivity tests.

A detailed study of the serological behaviour of these nucleoprotein components has not yet been made. However, all three give similar virus precipitation end points (based on the optical density of the solution at 260 m μ) when tested with an antiserum prepared against unfractionated turnip yellow mosaic virus.

The experiments described above suggest that these nucleoprotein components are not artefacts of the purification or isolation procedures, although it may be very difficult to prove beyond doubt that they exist as such in the plant. The ability to fractionate a virus nucleoprotein preparation into infectious and non-infectious classes of particle should be useful for more detailed studies on the inactivation of the virus by various agents. The fact that turnip yellow mosaic virus nucleoprotein as usually prepared is not homogeneous may be particularly relevant for structural studies on the virus, for example, for end group assays on the ribonucleic acid, where homogeneity of the starting material is an essential prerequisite.

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NITRATE REDUCTION BY AQUEOUS EXTRACTS OF EXCISED TOMATO ROOTS

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EXCISED tomato roots are normally supplied their nitrogen as nitrate (45 mgm N/l) in a medium of pH 4.5-4.8¹. By substituting ferric ethylenediamine tetracetate for the ferric sulphate of White's medium, active growth in nitrate occurs over

the pH range 4.0-7.3 and in ammonium (4.5 mgm N/l) at pH 6.8 or above². Nitrite (7.0 mgm N/l) at pH 6.0-6.8 and glutamine (4.8 mgm N/l) at pH 6.8 can also function as nitrogen sources for root growth. A preliminary study has now been made of

No such dating tests on the scrolls themselves have hitherto been made. Linen from Cave 1 and palm wood from the settlement ruins have been dated by the radioactive carbon technique and gave median dates of A D 33, with a standard deviation of 200 years for the linen⁹ and of 7 B C and A D 18, each with a standard deviation of 80 years, for the palm wood samples¹⁰. However, the exactness of this dating technique for archaeological purposes is limited and the method can give at best only general confirmation of dates established by other means¹¹.

The fact that many of the scrolls are made from animal skins, the major fibrous component of which is collagen, affords the possibility of an independent method of dating by measuring the shrinkage temperature of the fragments. Unpublished work from this laboratory has shown that the scrolls are parchments, made mainly from the skins of sheep and of goats. Parchment is made from animal skins which have been unhaired and then allowed to dry under tension, usually by stretching on a wooden frame. The resulting material is durable and needs no further chemical treatment, though often, for writing purposes, the surface is made smooth by mechanical means. Thus the making of parchment is quite distinct from that of leather, where the unhaired skin (pelt) is stabilized by treating it chemically with a tanning agent. Skins processed as parchment may last for very long periods provided they are kept dry. Indeed, this is the reason why the Dead Sea scrolls are still in existence. Any degenerative changes occurring in the collagen fibres present in dry parchments are thus likely to be due mainly to the passage of time. Moreover, these changes should be reflected in a lowering of the shrinkage temperature of the collagen fibres. Accordingly, the shrinkage temperatures of a number of scroll fragments were compared with those of other parchment-like materials of known age, in an attempt to establish a correlation between age and shrinkage temperature. The materials studied were

Group A English parchments covering the period 1193–1955 A D. Supplied by the Public Records Office, the Chapter Library of Canterbury Cathedral, Dr M. L. Ryder, Wool Industries Research Association, Leeds, 6, and Mr T. H. Gardner, of Amptill, Beds.

Group B Parchments from the Wady Murabba'at caves, dating from the second Jewish revolt, A D 132–135.

Group C Scroll fragments from Cave 4, Qumran. These and the Murabba'at fragments were supplied by the Department of Antiquities, Hashemite Kingdom of Jordan, and by Mr J. M. Allegro, University of Manchester.

Group D Egyptian Aramaic letter fragments of the fifth century B C, supplied by the Bodleian Library, Oxford.

Group E Egyptian raw hide axe-hafting, c. 1300 B C, supplied by the Department of Egyptian Antiquities, British Museum.

The shrinkage temperatures were determined by the method of Borasky and Nutting¹² as slightly modified by Gill¹³. Small samples of the materials were rehydrated for 1 hr. in distilled water and small fibres teased from them, before mounting (between circular cover slips) on the heating stage of the microscope. Heat was applied at a constant rate (2 deg. C/min.) and, so far as possible, fibres of similar size were used. The shrinkage temperature was taken as being that at which the fibre first began to shrink.

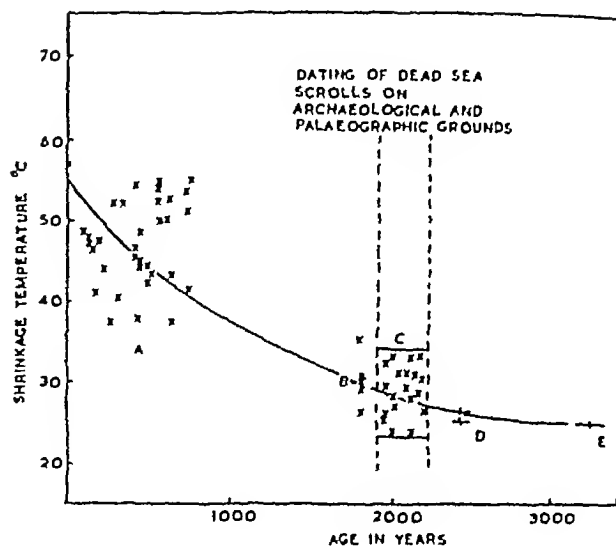


Fig. 1

Usually the mean of three determinations was taken for each material, and the results are shown in Fig. 1.

As regards their shrinkage temperatures, the scroll fragments lie closer to the older samples in groups B, D and E than to the relatively modern parchments (group A), which all show higher values. Hence it is likely that the scroll fragments are indeed old and that they are slightly older than the Murabba'at samples, the age of which is well authenticated. Moreover, it is unlikely that the scroll material dates from medieval times, as Zeitlin⁸ has suggested. The present findings on the date of the scrolls are thus in general agreement with the assessments based on archaeological, palaeographic and radioactive carbon studies. One could be more certain of the usefulness of shrinkage temperature as a guide to age if more parchments older than A D 1200 were available for study, but such samples are very difficult to obtain. It should be emphasized that this method of dating necessarily only gives a general guide to the date at which the scroll materials themselves were processed from animal skins. It throws no direct light on the dates at which the scrolls were copied and deposited in the caves.

We wish to thank the Department of Scientific and Industrial Research for providing a special grant for this work, also those people who have kindly supplied us with the various samples.

¹ de Vaux, R., *Rev. Biblique*, 60, 83 (1953), 61, 296 (1954), 63, 533 (1956).

² Cross, F. M., "The Ancient Library of Qumran and Modern Biblical Studies" (Doubleday and Co., Garden City, New York, 1958); Fritsch, C. T., "The Qumran Community" (Macmillan, New York, 1956); Pfeiffer, C. F., "The Dead Sea Scrolls" (Baker Book House, Grand Rapids, Michigan, 1957).

³ Cross, F. M., "The Ancient Library of Qumran and Modern Biblical Studies", 87 (Doubleday and Co., Garden City, New York, 1958).

⁴ Del Medico, H. E., "The Riddle of the Scrolls", trans. H. Garner (Hurke, London, 1953).

⁵ Suknik, E. L., "The Dead Sea Scrolls of the Hebrew University" (Magnes Press, Hebrew Univ., Jerusalem, 1956).

⁶ Driver, G. R., "The Hebrew Scrolls from the Neighbourhood of Jericho and the Dead Sea" (Friends of Dr. Williams' Library, Fourth Lecture, Oxford Univ. Press, 1951).

⁷ Telcher, J. L., *J. Jewish Studies*, 2, No. 2, 67 (1951).

⁸ Zeitlin, S., *Jewish Quart. Rev.*, N.S., 39 (1948–49) et seq. (passim).

⁹ Sollers, O. R., *Biblical Archaeologist*, 14, 20 (1951).

¹⁰ Zeuner, F. E., "Dating the Past", 344, 4th edn. (Methuen, London, 1958).

¹¹ Vaughan, D. E., *New Scientist*, 3, No. 75, 32 (1958).

¹² Borasky, R., and Nutting, G. C., *J. Amer. Leather Chem. Assoc.*, 44, 830 (1949).

¹³ Gill, A., Ph.D. thesis, Univ. of Leeds (1958).

FORTHCOMING EVENTS

(Meeting marked with an asterisk * is open to the public)

Monday, October 12

INSTITUTION OF ELECTRICAL ENGINEERS (at Savoy Place London, W.2) at 5.30 p.m.—Discussion on "Is the Present Pace of Electrical Progress Good for the Community?"

SOCIETY OF CHEMICAL INDUSTRY SURFACE ACTIVITY GROUP (at 14 Belgrave Square London S.W.1) at 5.30 p.m.—Dr Chas. M. Diarr "The Resolution of Petroleum Emulsion"

UNIVERSITY OF LONDON (in the Anatomy Lecture Theatre, University College, Gower Street, London W.1), at 5.30 p.m.—Prof G. D. O'Malley (University of California Medical School) First of three lectures on "Androgenic Steroids: The Development of a Scientist" (Further lectures on October 14 and 16)

BEES RESEARCH ASSOCIATION (in the Meeting Room of the Zoological Society of London, Bent's Park, London N.W.1) at 6.30 p.m.—Dr F. G. Smith "Bees and Beekeeping in the Tropics" Illustrated by a colour film "Tanganyika Bees" 8 p.m.—Prof G. F. Townsend "The Activity of Royal Jelly Against Leukemia and Aesthetic Tumours"

ROYAL INSTITUTE OF CHEMISTRY London Section (joint meeting with the Ewell County Technical College Faraday Society) at the Ewell County Technical College, Reigate Road, Ewell, Surrey) at 7 p.m.—Dr A. T. James "Gas Phase Chromatography"

Tuesday, October 13

PHYSICAL SOCIETY LOW TEMPERATURE GROUP (at the Royal Institution, Albemarle Street London W.1) at 4 p.m.—Dr H. London "Superfluid Helium" (First Simon Memorial Lecture)

INSTITUTION OF ELECTRICAL ENGINEERS MEASUREMENT AND CONTROL SECTION (at Savoy Place London, W.2) at 5.30 p.m.—Prof A. Tustin "The Relationship of Physical Mechanisms in Psychological Processes" (Chairman's Address)

SOCIETY OF CHEMICAL INDUSTRY FOOD GROUP (joint meeting with the Chemical Engineering Group, at 14 Belgrave Square London S.W.1) at 6.15 p.m.—Mr G. O. Eddie and Mr S. Forbes Pearson Engineering Aspects of Recent Research Projects in the Preservation of Fish

BRITISH ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE IN ASSOCIATION WITH GRAMMATA TV NETWORK (at the Guildhall London E.C.2) at 5.30 p.m.—Sir Edward Appleton F.R.S. First of the Inaugural Series of The Grammatica Lectures on the theme of "Communication in the Modern World"

Wednesday October 14

BRITISH COLLOID UTILIZATION RESEARCH ASSOCIATION (at the Institution of Civil Engineers, Great George Street London S.W.1) at 6.30 p.m.—Sir Eric Rideal F.R.S. Coal—a Colloid and a Chemical" (English Colloid Lecture)

INSTITUTION OF ELECTRICAL ENGINEERS EDUCATION DISCUSSION GROUP (at Savoy Place London W.2) at 6 p.m.—Discussion on "Graduate Training in Industry" opened by Mr W. H. Taylor

INSTITUTION OF MECHANICAL ENGINEERS (at 1 Birdcage Walk Westminster London S.W.1) at 6 p.m.—Mr H. Desmond Carter "The Engineer's Life and Diesel Engines" (Presidential Address)

SOCIETY OF CHEMICAL INDUSTRY CORROSION GROUP (at 14 Belgrave Square London S.W.1) at 6 p.m.—Mr E. H. R. Wright "Preventing Corrosion"

Thursday October 15

SOCIETY OF CHEMICAL INDUSTRY CORROSION GROUP (joint meeting Steel Institute, at 14 Belgrave Square London S.W.1) at 6 p.m.—Discussion of the 6th Report of the B.I.S.R.A. Committee

Mining and Metallurgy (at the Geological Bureau House Piccadilly London W.1) at 6 p.m.—Papers

SOCIETY OF LONDON (at Burlington House Piccadilly London W.1) at 6 p.m.—Dr C. R. Metcalfe "A Botanical Visit to the Tropics" Dr Norman K. H. Robson "Tropical Zoonoses"

INSTITUTION OF ELECTRICAL ENGINEERS UTILIZATION SECTION (at Savoy Place London W.2) at 5.30 p.m.—Mr T. E. Houghton "The Design of the Electrical Engineer and the Heavy Chemical Industry" (Chairman's Address)

ASTROPHYSICAL SOCIETY (at the Royal Institution, 21, Bedford Square, London W.1) at 6 p.m.—Sir Lawrence Bragg "The Nature of Light" (Golden Jubilee Lecture)

SOCIETY OF CHEMICAL INDUSTRY ROAD AND BUILDING MATERIALS GROUP (at 14 Belgrave Square London S.W.1) at 6 p.m.—Dr E. D. Hughes and Mr N. Wright "An Investigation of the Weathering of Tar in Open Textured Surfaces" Dr J. R. Dewhurst "An Investigation of the Settling of Road Tar in Surface Draining"

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE (at Mansel House 20 Portland Place London W.1) at 7.30 p.m.—Sir William MacArthur, F.R.C.S., D.S.O.: "The Identification of some Pesticides of the Past" (Presidential Address)

APPOINTMENTS VACANT

APPOINTMENTS are invited for the following appointments on or before the dates mentioned

SCIENTIFIC ASSISTANT (with a biological degree the ability to write correct English and preferably some knowledge of foreign languages) for work which includes the abstracting and reviewing of biological literature—The Director Commonwealth Bureau of Plant Breeding and Genetics, School of Agriculture, Cambridge (October 15)

SCIENTIFIC OFFICER (male with a first or second-class honours degree in physics or chemistry and preferably some experience of polymers or biological systems, or ionizing radiation) at the Royal Military College of Science, Shrivenham, Wiltshire for a two or three years programme of fundamental research (of an academic character and intended for publication) on effects of high energy radiation on polymers in air—Scientific Officer, Commonwealth Bureau of Plant Breeding and Genetics (Scientific) with a qualification in physics or chemistry at G.O.R. "A level or alternatively some laboratory experience) for work on the same programme—Technical and Scientific Registrar (K) Ministry of Labour and National Service 26 King Street London S.W.1 quoting A.410/MA (October 15)

UNION CASO FELLOW (graduate in medicine) in Urology in the Department of Urology at the University of Sydney and in the Department of Urology at the Royal Prince Alfred Hospital—The Professor of Surgery The University Sydney, Australia (October 23)

LECTURER OR ASSISTANT LECTURER IN THE DEPARTMENT OF EDUCATION—The Registrar The University, Leeds 2 (October 24)

UNIVERSITY TUTOR OR ASSISTANT LECTURER IN MICROBIOLOGY—The Secretary The Queen's University Belfast (October 30)

LECTURER OR ASSISTANT LECTURER IN PURE MATHEMATICS—The Registrar The University Leeds 2 (October 31)

LECTURER (with an honours degree of a British university and appropriate teaching experience) in Philosophy at the University of Hong Kong—The Secretary Association of Universities of the British Commonwealth 30 Gordon Square London W.C.1 (Hong Kong November 6)

LECTURER (preferably with qualifications in stratigraphical and structural geology) in Geology at the University of Sydney Australia—The Secretary Association of Universities of the British Commonwealth 30 Gordon Square London W.C.1 (Australia November 7)

SCIENTIFIC OFFICER (with a good honours degree and preferably with postgraduate experience and an interest in soil ecology) in the Entomology Department—The Secretary Rothamsted Experimental Station, Harpenden, Herts (November 14)

SENIOR DEMONSTRATOR (with experience in physical chemistry) and a **LABORATORY TECHNICIAN** (with experience in physical chemistry) in the Department of Chemistry University of Queensland Australia—The Secretary Association of Universities of the British Commonwealth 30 Gordon Square London W.C.1 (November 14)

LECTURER IN PATHOLOGY—The Secretary The University Edinburgh (November 16)

LECTURER (preferably with special qualifications in biometry or biochemistry and physiology or mycology and plant pathology) in Botany at the University of Tasmania—The Secretary Association of Universities of the British Commonwealth 30 Gordon Square London W.C.1 (Australia November 30)

MYCOLOGIST (with a good honours degree in botany with mycology as a special subject and a knowledge of the more fundamental aspects of animal and human mycology), at the Commonwealth Mycological Institute, The Secretary Commonwealth Agricultural Bureaux, Farnham House, Farnham, Royal Wicks (November 30)

SENIOR RESEARCH FELLOW (with a postgraduate degree or research experience in the biochemistry or immunology of parasitic infections) in Immunology—The Registrar University of Queensland St. Lucia Brisbane Queensland Australia (December 1)

MYCOLOGIST (with a good honours degree in zoology with at least two years postgraduate experience or training in agricultural entomology) in the Department of Agriculture, Nyamaland to control crop pests—The Department of Recruitment Colonial Office London S.W.1 quoting BOD 63/4/1016

REPORTS AND OTHER PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

Iron and Steel Institute, Thirty Report of the Corrosion Committee Compiled by Dr J. O. Hudson (Spon. Catalogue No. 66) Pp. x+217 (London: Iron and Steel Institute, 1958) 65s

Anti Locust Bulletin No. 36 Reproduction in the Red Locust (*Nomadacris septemfasciata* Serville) in the Laboratory By Dr. H. J. Morris, Pp. 11-46. (London: Anti Locust Research Centre 1959) 7s. 6d.

Relationships Between Water and Soil By T. J. Marshall (Technical Communication No. 60 of the Commonwealth Bureau of Soils, Harpenden). Pp. vi+101 (Farnham Royal Commonwealth Agricultural Bureaux 1959) 20s

Department of Scientific and Industrial Research Torry Research Station, Torry Technical Paper No. 1 The Temperature of British Fish during Distribution in Summer By Dr. G. H. O. Burgess, R. M. Cockburn, Dr. G. L. Cutting and W. B. Robb Pp. iv+53 (Edinburgh: H.M.S. Stationery Office 1959) 3s. 6d.

British Empire Cancer Campaign, Thirty-sixth Annual Report covering the year 1958. Part 1: The Campaign's Statement of Accounts. Pp. 11-43. Part 2: The Scientific Report of the Researches undertaken by the Central Organisation and its Autonomous Councils in the United Kingdom, and by some of its Affiliated Organisations Overseas. Pp. iv+11-636. (London: British Empire Cancer Campaign 1959) 7s.

Lister Institute of Preventive Medicine Report of the Governing Body, 1955 Pp. 24. (London: Lister Institute of Preventive Medicine 1959) 7s.

- The Journal of Mechanical Engineering Science*, Vol 1, No 1 (June 1959) Pp ii+91 Published quarterly Annual subscription rates (4 issues) Members 30s Non-members 60s Single copies Members 10s Non-members 20s (London Institution of Mechanical Engineers, 1959) [77]
- Greenwich Observations in Astronomy, Magnetism and Meteorology made at the Royal Observatory Greenwich, the Royal Greenwich Observatory, Herstmonceux, and the Royal Greenwich Observatory, Abinger, in the year 1950, under the direction of Sir Harold Spencer Jones Pp xxx+322 (13 plates) (London H.M. Stationery Office, 1959) 100s net [77]
- Colonial Development Corporation Annual Report and Statement of Accounts for year to 31 12 58 Pp v+69 (London H.M. Stationery Office, 1959) 4s 6d net [107]
- University of Reading National Institute for Research in Dairying Report 1958 Pp 154 (Shinfield National Institute for Research in Dairying, 1959) [107]
- Thirty-ninth Annual Report of the Board of the Institute of Physics Pp 18 (London Institute of Physics, 1959) [107]
- Digest of Soviet Technology* No 2 (May, 1959) Edited by Dr M. M. Barash and Dr P. L. B. Oxley (Express Information on recent Technological Developments in the Soviet Union and Eastern Europe) Pp 49 Annual subscription rate (12 issues) £6 6s 0d (post free) (Kirkham, Preston Engineering Information Services, 1959) [107]

Other Countries

- University of California Publications in Geological Sciences Vol 32, No 6 Geology of the La Venta Badlands, Colombia, South America. By Robert W. Fields. Pp 405-444+plates 37-40 (Berkeley and Los Angeles University of California Press, London Cambridge University Press, 1959) 1 dollar [77]
- Army Map Service, Washington Technical Report No 24 Statistical and Harmonic Analysis of Gravity (Project No MQ-011, March, 1959) Pp iv+142. (Washington, D.C. Army Map Service, 0500 Brooks Lane, 1959) [77]
- Museum of Applied Science of Victoria Report of Activities for the year ended 30th June 1958 Pp 27 (Melbourne Museum of Applied Science of Victoria, 1959) [77]
- Bulletin of the American Museum of Natural History Vol 117, Article 4 Organism Communities and Bottom Facies, Great Bahama Bank. By Norman D. Newell, John Imbrie, Edward G. Purdy, and David L. Thurber Pp 177-228+plates 58-69 (New York American Museum of Natural History 1959) 1.75 dollars [77]
- California Academy of Sciences Proceedings Vol 29, No 13 (May 29, 1959) From Pipefish to Seahorse—a Study of Phylogenetic Relationships By Earl S. Herald Pp 465-473 Vol 29, No 14 (May 29, 1959) A Review of the Snakes of the Genus *Pseudorabdion* with remarks on the status of the Genera *Agrophis* and *Tuphiophis* (Serpentes Colubridae) By Alan E. Leviton and Walter C. Brown Pp 475-508 Vol 29, No 15 (May 29, 1959) Behavior and Reactions of the Pacific Sardine, *Sardinops caerulea* (Girard), Under the Influence of White and Colored Lights and Darkness By Anatole S. Loukaskin and Norman Grant Pp 509-548 Annual Report for the year ending June 30, 1958 with a condensed Report for the years since 1954 Pp 48 (San Francisco California Academy of Sciences, 1959) [77]
- Canada Department of Northern Affairs and National Resources National Museum of Canada Bulletin No 154 (Biological Series No 53) Mammals of the Islands in the Gulf of St. Lawrence By A. W. Cameron Pp iii+165 2 dollars Bulletin No 156 (Biological Series No 55) Plants of the Clay Belt of Northern Ontario and Quebec By W. K. W. Baldwin Pp vi+324 (17 plates) 2 dollars Bulletin No 158 (Biological Series No 56) The Marine Algae of the Labrador Peninsula and Northwest Newfoundland—(Ecology and Distribution) By Robert T. Wilce Pp iv+103 (11 plates) 1.50 dollars Bulletin No 159 (Biological Series No 57) The Mammals of Banff National Park, Alberta By A. W. F. Banfield Pp v+53 1 dollar (Ottawa Queen's Printer, 1953) [77]
- Ghana Annual Report of the Forestry Department for the Calendar year 1957 Pp iv+43 (Accra Government Printer London Crown Agents for Oversea Governments and Administrations, 1959) 5s [77]
- Smithsonian Institution Bureau of American Ethnology Bulletin No 171 The North Alaskan Eskimo—a Study in Ecology and Society By Robert F. Spencer Pp vi+400+9 plates (Washington, D.C. Government Printing Office, 1959) 2.50 dollars [77]
- Republik Indonesia Kementerian Perhubungan Lembaga Meteorologi dan Geofisik Verhandelingen No 53 (1) Further Remarks on Pyrheliometric Measurements and Measurement of the Brightness of the Sky in Indonesia By J. J. M. Reesneek and Soetrisno Hadji (2) Nightly Decrease of Relative Humidity at the Summit of Mt. Tangkuban Prahur, Compared with Results of Radiosonde Observations at Djakarta By J. J. M. Reesneek and Kho Sin Tjoen Pp 24 Verhandelingen No 54 (1, Δ) Curves for Bodily Seismic Waves of any Focal Depth. By A. R. Ritsema Pp 10 Earthquakes in Indonesia 1956 Pp ii+20 (Djakarta Kementerian Perhubungan Lembaga Meteorologi dan Geofisik, 1957 and 1958) [77]
- Publikationer fra det Danske Meteorologiske Institut, Charlottenlund. Isforholdene i de Arktiske Have 1950 (The State of the Ice in the Arctic Seas 1950) Prepared by Cmdr M. V. L. Lorck, R. D. N. T. (Appendix to the Nautical-Meteorological Annual 1950) Pp 34+5 maps (Charlottenlund Danske Meteorologiske Institut, 1959) [77]
- Indian Council of Medical Research The Nutrition Research Laboratories, Coonoor, S. India Annual Report for 1957-58 Pp iii+60 (Coonoor Indian Council of Medical Research, 1958) [77]
- Indian Council of Agricultural Research Misc Bulletin No 82 Bovine Stars of India All India Cattle Show 1955 Pp iv+20 Rs 2.87, 4s Bulletin No 81 The Fungi of Delhi By B. L. Chona, G. Lall, and N. O. Kakria Pp iii+43 Rs 3.60, 5s 6d (Delhi Manager of Publications, 1957 and 1958) [77]
- The Carlsberg Foundation's Oceanographical Expedition Round the World 1928-30 and previous "Dana" Expeditions "Dana" Report No 48 Etude des Larves Leptocephales du Groupe *Leptocephalus lanceolatus* Strömman et Identification à la Famille des Serriomuridae Par Marie-Louise Banchot Pp 148+2 planches 40 Danish kr [77]
- "Dana" Report No 50 Descriptions of *Fulthynnus* and *Auzus* Larvae from the Pacific and Atlantic Oceans and Adjacent Seas By Walter M. Matsumoto Pp 34 10 Danish Kr (Copenhagen Andr. Fred. Hest & Son, 1959) [77]
- 1° Simposium Internazionale sul Lisozioma di Fleming, Milano, 3, 4, 5, Aprile 1959 Riassunti delle Relazioni e Comunicazioni Pp 160+xxiv (Milano Segretaria 1° Simposium Intern sul Lisozioma di Fleming, Via Modica 6, 1959) [77]
- Bulletin of the American Museum of Natural History Vol 117, Article 6 Studies on Social Groupings in Fishes By C. M. Breder, Jr Pp 393-482+plates 70-80 (New York American Museum of Natural History, 1959) 1.50 dollars [77]
- Skrifter fra Danmarks Fiskeri-og Havundersogelser Nr 19 Fiskeriundersogelser I 1958 ved Danmark, Faerøerne og Grønland Ved E. Bertelsen og Paul M. Hansen Pp 40 (København C. A. Reitzel, 1959) 3 Swedish kr [77]
- Metropolitan Life Insurance Company Statistical Bulletin, Vol 40 (May 1959) Marriages Decrease Again Health in Hawaii Recent Trends in Infant Mortality Injuries on the Job Pp 12 (New York Metropolitan Life Insurance Company, 1959) [77]
- The South African Institute for Medical Research, Johannesburg Annual Report for the year ended 31st December 1958 Pp 122 (Johannesburg South African Institute for Medical Research, 1959) [77]
- Insitnt pour l'Encouragement de la Recherche Scientifique dans l'Industrie et l'Agriculture, Bruxelles Rapport Annuel, Exercice 1958 Pp 233 (Bruxelles Institut pour l'Encouragement de la Recherche Scientifique dans l'Industrie et l'Agriculture, 1959) [77]
- Institut National pour l'Etude Agronomique du Congo Belge Bureau Climatologique—Communication No 17 Etude Statistique des Chutes de Crée au Congo Belge et au Ruanda-Urundi Par Dr. Franz Bultot Pp 43 (Bruxelles Institut National pour l'Etude Agronomique du Congo Belge, 1959) [77]
- Berichte des Deutschen Wetterdienstes, Nr 53 (Band 7) Die Strömung an Windschützstreifen Von Heinz Kaiser Pp 36 mit 25 Abbildungen und 2 Tabellen im Text (Offenbach a. M. Deutschen Wetterdienstes, 1959) [77]
- United States Department of the Interior Geological Survey Bulletin 1028-I Geology of the Delarof and Westernmost Andreof Islands Aleutian Islands, Alaska By George D. Fraser and H. Frank Barnett Pp v+211-248+plates 27-32 Bulletin 1045-E Core Logs from Seares Lake, Bernardino County, California By David V. Haines Pp iii+317+plates 5-10 2 dollars Bulletin 1052-II Dielectric Constant and Electrical Resistivity of Natural-State Cores. By G. V. Keller and P. H. Lilestro Pp iv+257-285 20 cents Bulletin 1073 Quaternary Geology of the Smoke Creek—Medicine Lake—Grenora Area, Montana and North Dakota By Irving J. Wilkind Pp v+80+plates 1-10 1.75 dollars (Washington, D.C. Government Printing Office, 1959) [77]
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- United States Department of the Interior Geological Survey Professional Paper 302-B Vegetation of the Arctic Slope of Alaska By Lloyd A. Spetzman (Exploration of Naval Petroleum Reserve No 4 and Adjacent Areas, Northern Alaska 1944-53—Regional Studies) Pp iii+19-58+plates 7-12 55 cents Professional Paper 305-I Core Test, Sentinel Hill Area, and Test Well, Fish Creek Area, Alaska By Florence M. Robinson and Florence R. Collins (Exploration of Naval Petroleum Reserve No 4, and Adjacent Areas, Northern Alaska, 1944-53 Part 5 Subsurface Geology and Engineering Data) Pp iii+485-521+plates 31-34 1 dollar Professional Paper 327 Geology and Mineral Resources of Paraguay—a Reconnaissance By Edwin B. Eckel With sections on Igneous and Metamorphic Rocks by Charles Milton and Edwin B. Eckel Soils by Pedro T. Sulsona Pp v+110+plates 1-3 (Washington, D.C. Government Printing Office, 1959) [77]
- Smithsonian Miscellaneous Collections Vol 137 (Whole Volume) Studies in Invertebrate Morphology (Published in Honor of Dr Robert Evans Snodgrass on the Occasion of his Eighty-fourth Birthday, July 5, 1959) Pp v+416+49 plates (Publication 4350) (Washington, D.C. Smithsonian Institution, 1959) [77]

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LETTERS TO THE EDITORS

COSMOLOGY

The Steady-State Universe and the Deduction of Continual Creation of Matter

DURING his recent visit to Australia, Prof H Bondi has re-affirmed the notion of continuous creation which he and T. Gold apparently deduced in 1948¹ from their perfect cosmological principle. This notion is also presented explicitly as a deduction in his book on Cosmology² as is evident from the following quotation from Section 12.3 (p. 143):

The next deduction to be made from the perfect cosmological principle has formed the most controversial point of the theory. The expansion of the universe which can be inferred either from thermodynamics or from astronomical observations, would seem to lead to a thinning out of material. By the perfect cosmological principle the average density of matter must not undergo a secular change. There is only one way in which a constant density can be compatible with a motion of expansion and that is by the continual creation of matter.

On p. 144 he explains that 'the creation here discussed is the formation of matter not out of radiation but out of nothing'.

In the present communication it is desired to point out that the notion of continual creation from nothing is not a true deduction from the perfect cosmological principle, and that a scientific hypothesis can be advanced which explains the known facts within the frame of this principle.

First it should be noticed that Bondi and Gold implicitly assume that their steady-state universe must be describable in a four-dimensional space-time frame. On such an assumption the notion of creation seems to follow logically if it is also assumed that the energy density in space of all infra-red radiation may be neglected (This last assumption does not appear to have been adequately discussed and may well be wrong if we include the energy residing in cosmic low-frequency electromagnetic waves.) But if we exclude this assumption the following argument leads to another hypothesis.

Since the apparent continual escape of matter from the visible universe requires a continual supply of matter from somewhere, it is not unusual to suppose that this 'somewhere' exists outside our four-dimensional space-time. This hypothesis is equivalent to the hypothesis that the space-time universe U_4 is really a hyper-surface in a five-dimensional universe U_5 . In this postulating the existence of a fifth dimension to overcome a difficulty in the current framework of cosmology, we are merely following the well-established practice of postulating new entities (such as atoms, electrons, the quantum of action etc.) to explain other phenomena which are not explicable in the current framework of science.

The notion of a universe U_5 is however by no means new, whether considered as a physical universe

or as a convenient mathematical fiction. For example, it has been used by Kluza³, Klein⁴, de Broglie⁵, Einstein⁶ and others⁷ for the purpose of unifying the gravitational and electro-magnetic fields and the wave equation of quantum theory. It is also mathematically convenient for expressing de Sitter's metric.

Thus we see that the perfect cosmological principle suggests a U_5 universe. Moreover the hypothesis of a fifth dimension (so obtained) is fruitful since it serves not only to account for the steady-state universe of Bondi and Gold but also to unify three other great branches of physics. On the other hand the notion of continual creation of matter does not appear to have led to any verifiable consequences of comparable importance.

There is one assertion about our U_5 which can be made immediately, namely, the laws of conservation of momentum and energy must apply in U_5 rather than in U_4 . In addition there may be a law of conservation of electric charge in U_5 .

The problem of formulating a metric for U_5 which is consistent with the perfect cosmological principle is under consideration. But meanwhile it seems desirable to direct attention without delay to the fact that a steady-state universe is possible without the 'formation of matter' out of nothing.

The knowledge of this fact will undoubtedly cause relief in the minds of many persons who would otherwise be unable to accept the steady-state theory. For the old dictum *ex nihilo nihil fit* seems to be one of the few things about which philosophers, scientists and the common man agree. The contrary notion appears mainly in works which we label as fairy tales or 'phantasies' or in conjuring for entertainment.

There are many weighty reasons why a steady-state theory of the visible universe is more acceptable than its present rivals, so it is fortunate that it no longer need be associated with the primitive belief in creation. It may however be pointed out that even for an evolving (non-stationary) visible universe our U_5 can help to prevent the heat-death which current thermodynamics appears to suggest by supplying an 'outside' source of order.

In conclusion, I should like to acknowledge with thanks the benefits received from private discussions on these matters which I have had with Prof H. Bondi, Dr J. Moval and Mr D. Mustard.

V. A. BAILEY

University of Sydney

It is not easy to see at first sight how Prof Bailey's suggestion assists the reconciliation of the notion of continual creation and of ordinary ideas of conservation as these are concerned with empirical evidence of conservation in four dimensions and not in five. However the value of his idea becomes clearer owing to his reference to the electromagnetic significance of five-dimensional systems. It may therefore be appropriate to mention here that Dr R. A. Lyttleton and I, in a forthcoming paper in *Proceedings of the Royal*

Society, have investigated the connexion between a possible electric phenomenon and continual creation

H BONDI

King's College, London

¹ Bondi, H., and Gold, T., *Mon Not Roy Astro Soc*, 108, 252 (1948)

² Bondi, H., *Cosmology* (Cambridge University Press, 1952)

³ Kaluza, T., *Sitz Preuss Akad*, 966 (1921)

⁴ Klein, O., *Z Phys*, 37, 805 (1926)

⁵ De Broglie, J., *de Phys et le Radium*, 8, 65 (1927)

⁶ Einstein, A., *Sitz Preuss Akad*, 23 and 26 (1927)

⁷ See the footnotes 2 and 3 to page 191 in Whitaker's *History of the Theories of Aether and Electricity, 1900-1926* (T. Nelson and Sons, Ltd., 1953), and Bergmann's *Introduction to the Theory of Relativity*, Part 3 (Prentice Hall, Inc., 1946)

RADIOPHYSICS AND GEOPHYSICS

Effect of Atomic Tests on Radio Noise

Two high-altitude atomic explosions which were set off over Johnston Island in the Pacific in August 1958 appear to have had a rather pronounced effect on the radio noise as recorded at Kekaha, Hawaii. This recording station, located on the south-west coast of the Island of Kauai, is about 700 miles north-west of Johnston Island, and is a part of a world-wide chain of noise-recording stations supervised by the U.S. National Bureau of Standards.

power received for a period before and after the first explosion. The usual diurnal pattern is evident during the three days prior to the blast, with the highest noise-levels recorded at night and a rapid decrease in level between 0400 and 0800 local time. In the hour following the blast, however, the noise decreased by as much as 32 db (at some frequencies) at a time of day when it would normally be rising or holding steady. Recovery apparently occurred in a matter of hours at 13 kc/s and 5 Mc/s, but from 51 kc/s to 2.5 Mc/s a changed pattern was evident for several days with levels at night much below normal. A sudden drop in the received noise-level was also noted following the second explosion on August 12, again the noise-levels at night in the frequency range of 51 kc/s-2.5 Mc/s continued below normal for several days, and the usual pattern of noise was considerably disturbed until about September 1.

Because of the very low incidence of thunderstorms in Hawaii, most of the radio noise received is believed to be propagated from storms at a considerable distance. Changes in propagation conditions are reflected more clearly on the Kekaha noise records than at stations situated on large land masses, where

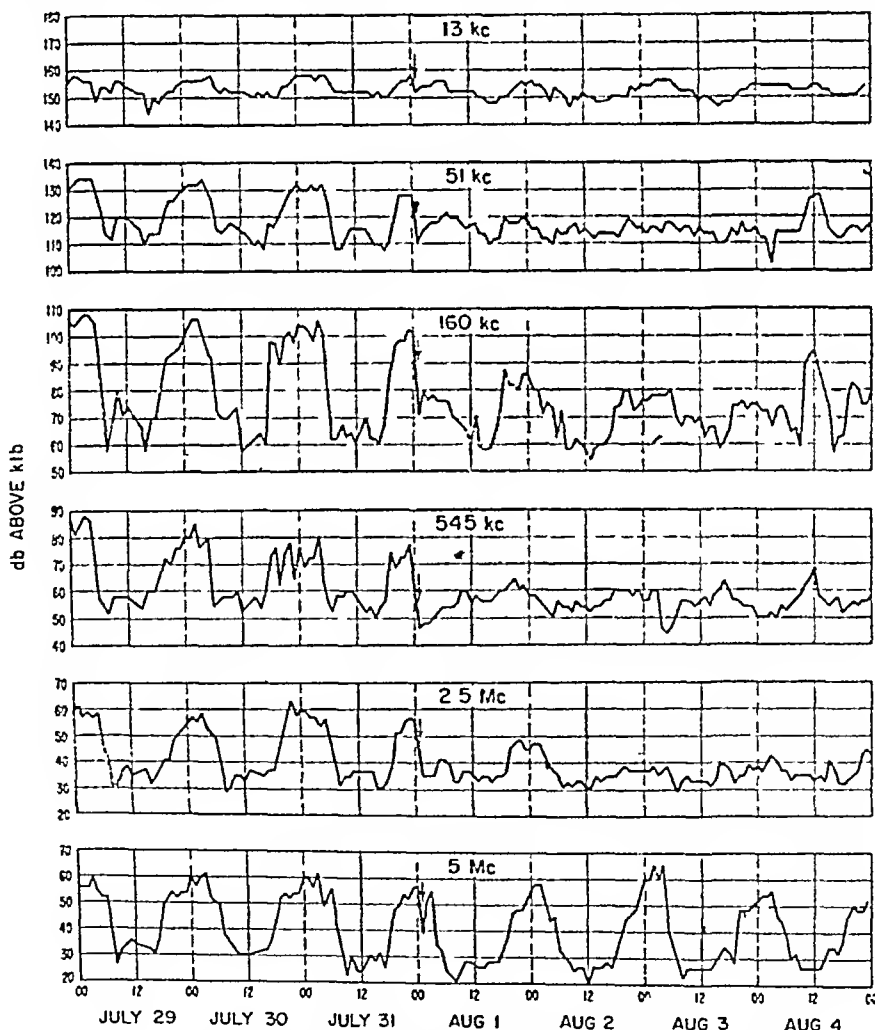


Fig 1 Radio noise power recorded at Kekaha, Hawaii, July 29-August 4, 1958 (Time of explosion indicated by arrows)

The two bomb bursts occurred shortly after midnight on August 1 and August 12 at elevations variously reported by the Press as from 25 to 100 miles. Fig 1 shows the atmospheric radio-noise

local and short-distance storm effects tend to mask changes in propagation.

Since an omnidirectional antenna is used at the Kekaha recording station, it would seem that the

influence of the explosions may have been rather widespread, as has been suggested previously¹. The length of time over which there was an apparent increase in the night-time absorption of noise suggests the possibility that high altitude nuclear explosions may have a rather persistent effect on radio communications at certain frequencies.

A more complete account of this noise anomaly is being prepared and will be published in the near future in the *Journal of Research of the National Bureau of Standards*, Section D.

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¹ Ohyanagi T, Coroniti B C. and Pierce E T *Nature* 183 1476 (1959)

The Aurora, the Radiation Belt and the Solar Wind: A Unifying Hypothesis

RECENT high time resolution spectroscopic studies of the aurora¹ at College Alaska, have revealed a rather consistent pattern in the spatial distribution of the hydrogen emission lines. It was observed that during the first phase of a typical polar auroral display the intensity peak of the hydrogen emission would shift in a continuous fashion from the northern horizon to the southern horizon in 1.3 hr. During nights of moderate auroral activity the intensity peak would remain near the southern horizon and then recede back to the north at the conclusion of the display, some time after midnight. Nights of strong auroral activity were characterized by the hydrogen emission features either disappearing below the local southern horizon or being present in the entire portion of the magnetic meridian monitored by the spectrograph. The shift in zenith distance is interpreted as reflecting a change in the geomagnetic co-latitude of the incoming protons as described below. The solid line in Fig. 1 represents typical data obtained in a six-day period.

In the same study it was established that certain auroral spectra can be characterized entirely by proton excitation while others are best explained by electron excitation, the latter accounting for the greater part of the auroral luminosity. The proton associated spectra were observed during the first phase of an aurora, sometimes this occurred when the aurora was still too faint to be easily visible with the naked eye. The electron induced aurora is associated with the break up and post break up phase of a typical display. Details of the investigation are presented in another publication¹.

The latitude drift of the hydrogen emission can be explained in a semi quantitative way by examining the effect of incoming solar particle streams (the

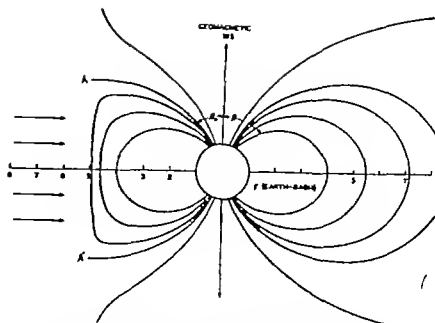


Fig. 2 The distortion of the geomagnetic field on the day-side of the earth due to an approaching solar particle stream

'solar wind' of Biermann² and Parker³) on the trapped Van Allen radiation⁴. The work of Chapman and Ferraro⁵ showed that the magnetic effects of a particle stream could be represented to a first approximation by that of an image dipole situated as far behind the face of the stream front as the Earth-dipole is in front, and that the resultant configuration of the Earth's magnetic field would be as shown in Fig. 2. The field is seen to be compressed on the day side of the Earth, but remains almost unaffected on the night side.

If we accept this picture it seems reasonable to assume that the Van Allen radiation belt on the day side of the Earth must be terminated close to the stream front and we shall assume further that this termination is represented approximately by the field line which meets the stream front orthogonally (at A and A') and meets the Earth at geomagnetic co-latitude β . Field lines which meet the Earth to the south of this point are compressed dipole lines while those to the north are violently disturbed by the particle stream.

The trapped particles have a slow longitudinal drift motion in the direction $\pm (H \times \nabla H)$ due to the inhomogeneity of the magnetic field and since their motion is governed by the constancy of their magnetic moment they tend to remain in a region of constant field strength as they drift around the Earth. Inspection of Fig. 2 shows that on the comparatively undisturbed night-side of the Earth the trapped particles will be under the influence of field lines which intersect the Earth in a more southerly region of geomagnetic co-latitude β . Thus as the Earth rotates under this pattern which is fixed with respect to the Sun, the region which is connected magnetically to the outer part of the Van Allen belt will move south during the evening and north again during the morning.

The extent of this latitude drift is shown in Fig. 3, which has been constructed on the assumptions that the solar particle stream consists of protons travelling towards the Earth at 1,000 km/sec, and that the stream front is brought to rest at the point where the kinetic energy density of the stream is equal to

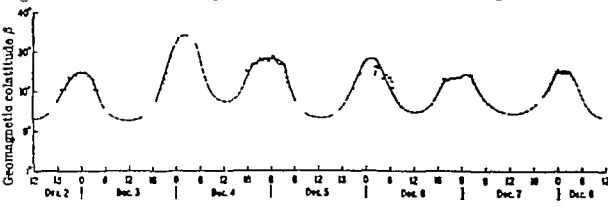


Fig. 1 Variation of the geomagnetic co-latitude with time for a six-day period

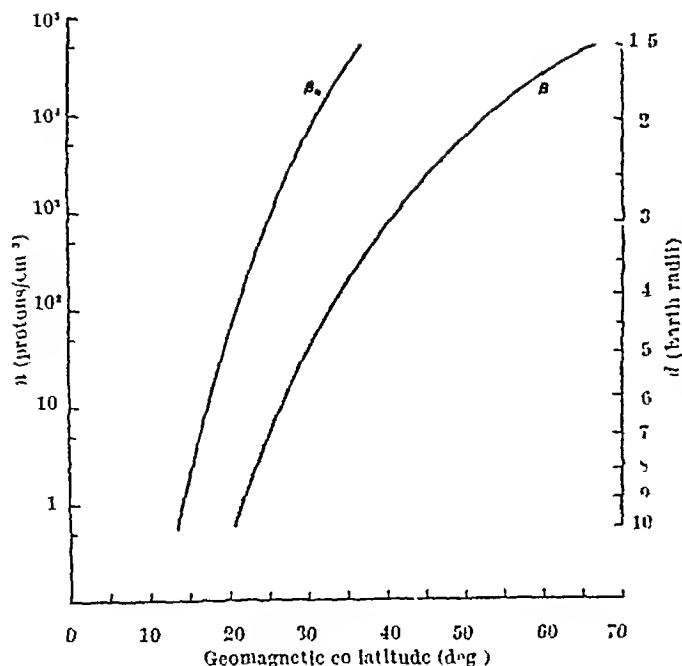


Fig. 3 Geomagnetic co latitude of points on the Earth's surface connected magnetically to the outer edge of the Van Allen belt on the side towards the solar wind (β_0) and away from the solar wind (β). The right-hand scale shows the stationary position of the stream front and the left-hand scale gives the corresponding solar wind density, assuming the particles to be protons travelling with a velocity of 1,000 km/sec

the increased magnetic energy density of the field. The extent of the drift can be seen to correspond roughly to the observed latitude drift of the hydrogen emission shown in Fig. 1 if moderate particle stream densities are assumed.

This correspondence leads us to suggest that the Van Allen belt contains protons which are removed by some process not yet fully understood, and which then penetrate the atmosphere and give rise to visible emissions. On this view the particles responsible for the initial stages of the aurora are not directly of solar origin, though they may be remnants of previous particle streams which have become trapped in the geomagnetic field. The Van Allen belt merely acts as a reservoir which is induced to spill over by the increase of the solar wind 'strength' on the sunward side of the Earth.

These ideas will be discussed more fully in a future publication⁶ where more detailed consideration will be made of the underlying assumptions and of the processes which are operative.

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Colour Photography of the Aurora

STORMER¹ refers to the difficulty of photographing the aurora in colour, and states that satisfactory results have not been obtained except for arcs and more quiet forms. However, with a colour film now available commercially, it has been found that the aurora australis can be photographed with exposure times comparable to those used in monochrome photography.

A test series of colour photographs has been taken at Scott Base, in Antarctica, during May and June of this year. Super Anscochrome daylight film (speed rating 100 ASA) has been used in an all-sky camera² with an $F/1.4$ lens, and exposure times of up to 2 min. Using a standard Super Anscochrome developing kit, the speed of the film has been increased to approximately 200 ASA by increasing the time of the first development 75 per cent over the recommended time. This has led to little noticeable change in the colour balance of the film.

With exposure times of 1 min., stars of the second magnitude are plainly visible on the film. A 2-min. exposure enables the Milky Way to be seen on the film. This corresponds to the visual limit of auroral observation and is confirmed by comparisons with visual observations. An aurora just detected by a visual observer is recorded on the colour film with a 2-min. exposure. Auroras of this intensity are below the human colour vision threshold, and thus appear colourless. (Observers frequently record these auroras as faintly greenish-white.) Because of the integrating properties of the colour film, the colour latent in these colourless displays is recorded on the film. Thus aurora observed recently at Scott Base have frequently appeared white by direct observation, and red, purple, blue and white on the colour film. Spectrograms taken at the same time have shown relative spectral intensities which, it is estimated, would correspond to the colours observed with the colour film.

These observations are part of the research programme at Scott Base and are being made in conjunction with the observational programme of the Dominion Physical Laboratory Auroral Station, Invercargill, New Zealand.

The loan of the all-sky camera from the Air Force Cambridge Research Center, Bedford, Massachusetts, is gratefully acknowledged.

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¹ Stormer, C., *The Polar Aurora* 141 (Oxford 1955)
² Elvey, C. T., and Stoffregen, W. *IGA Instruction Manual*, Part 2 133 (London 1957)

Possible Reversals of the Earth's Magnetic Field in the Jurassic Period

IN a recent study of the natural remanent magnetization of the Upper Lias Sands of the West of England, seventeen samples collected from two sites were found to have reverse directions of magnetization. Samples a little higher and lower in the succession were found to be normally magnetized. Numerical details of the results and reasons for considering the rocks in question to possess a stable magnetization will be given separately.

¹ Rees, M. H., Romick, G. J., and Belon, A. *Plan and Space Sci* (in the press)

² Biermann, L., *Z. Astrophys.* 29, 274 (1951), *Z. Naturforsch.* 7a, 127 (1952), *Observatory* 77, 109 (1957)

³ Parker, E. N., 'Physics of Fluids' 1, 171 (1958)

⁴ Van Allen, J. A., and Frank, L. A., *Nature*, 183, 430 (1959)

⁵ Chapman, S. and Ferraro, V. C. A., *Terr. Mag. and Atmos. Elec.* 36, 77, 171 (1931), 37, 147, 421 (1932)

⁶ Reid, G. C. and Rees, M. H., *Plan and Space Sci* (in the press)

The results are especially interesting as the sands which are exposed in various localities extending from the Dorset coast to the Cotswold Hills are all lithologically similar, and Boswell directed attention to the remarkable constancy of their mineral content and fine grade. In view of this and the fact that the sands were sampled in fourteen sites it would be surprising if a physical or chemical mechanism were responsible for the reversed direction of natural remanent magnetization at just two sites, and it is suggested that there may have been a reversal of the Earth's magnetic field during the time the sands were being deposited.

By a careful study of ammonite species Buckman^{2,3} showed that the sands get progressively younger towards the south although they are lithologically similar. The Upper Lias has consequently been divided into 13 sub-zones which are given by Arkell⁴.

Using this sub-zonation scheme and the recent geological time scale of Maviné *et al.*⁵, it is possible to obtain an upper limit for the duration of the period of reversal. The reversely magnetized Cotswold Sands were collected from sub-zones 6 and/or 7 and rocks immediately below (sub-zones 4-5) were found to be normally magnetized and the Midford Sands (sub-zones 8-9) which are exposed about thirty miles to the south are also normally magnetized. If we assume a linear division of the time scale, we find that the Upper Lias was deposited in less than 4×10^6 years and therefore each sub-zone corresponds to approximately 3×10^5 years. A rough estimate for the period of reversal is therefore 6×10^5 years. This is a maximum estimate as the sampling was restricted to two sites and these may not, of course, have extended over two sub-zones or even one sub-zone.

It is concluded that there may have been a reversal of the Earth's magnetic field in the Lower Jurassic period which lasted for a period of less than 6×10^5 years. It is possible from Nafrin's results⁶ that there was another reversal a few million years later. Evidence of reversals in the Jurassic period has also been obtained from igneous rocks and baked sediments in South Africa by Graham and Hales⁷ and from volcanic rocks of South America by Creer⁸.

It happens that the estimate for the time of reversal compares favourably with Hospers's estimates for the reversals in the Tertiary period. In an extensive study of the Tertiary Icelandic lava flows, Hospers⁹ came to the conclusion that the average length of time over which the Earth's magnetic polarity remains unchanged is $2.5-5 \times 10^5$ years. The agreement may or may not be significant.

The results are of value in considering theories of the detailed origin of the Earth's magnetic field. Recently, both Rikitake¹⁰ and Allen¹¹ have demon-

strated that reversals are theoretically possible for two coupled disk dynamos and Allen has shown that oscillations of the main field with reversals at intervals of hundreds of thousands of years would be quite conceivable.

I wish to thank the Royal Dutch Shell Oil Company for a Studentship supporting the research which was carried out at the Department of Geodesy and Geophysics, University of Cambridge.

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- ¹ Boswell P. G. H. *Geol. Mag.* 41, 246 (1924)
² Buckman S. S. *Quart. J. Geol. Soc.* 45, 410 (1889)
³ Buckman S. S. *Quart. J. Geol. Soc.* 65, 80 (1910)
⁴ Arkell W. *Jurassic System in Great Britain* (Oxford University Press 1933)
⁵ Maviné K. J., Lambert, R. St. J. and York D. *Nature* 183, 212 (1959)
⁶ Nafrin A. F. M. *J. Geol. Mag.* *Suppl. Adv. in Physics* 6, 162 (1953)
⁷ Graham, K. W. T. and Hales, A. L. *Ibid.* 6, 149 (1953)
⁸ Creer, H. M. *Ann. Geophys.* 14, 3-33 (1958)
⁹ Hospers, J. *Journal of Volcanology and Petrology* 1957, 11-12 (1954)
¹⁰ Rikitake, T. *Proc. Camb. Phil. Soc.* 54, 80 (1958)
¹¹ Allen, D. W. *Nature* 182, 469 (1958)

Radiation Balance at Scott Base

SINCE March 1, 1957 a net exchange radiometer of the Ger and Dunkle type manufactured by Beckman and Whitley has been in continuous operation at Scott Base (77°51'S, 160°48'E.) on Ross Island. The radiometer measures the difference between the total incoming and outgoing long and short wave radiation through a horizontal surface 6 ft. above the ground. The site of the radiometer is such that the surface beneath the instrument is not snow at all times because bare rock is exposed in the summer. However the radiation properties of the surface as a whole are probably typical of many areas in McMurdo Sound and other partially snow-free areas of the Antarctic and the results are of particular interest for this reason.

Table 1 summarizes the first two years measurements.

For the year March 1, 1957-February 28, 1958 the net radiation gain was 17,000 cal/cm². During the following year the gain was 18,800 cal/cm². This is considerably different from substantial net yearly losses recorded over a permanent snow cover in the Antarctic.^{2,3} Most of the positive balance at Scott Base is due to very high absorption by the rock surface in December and January when the snow cover was partially or wholly absent.

Table 1 RADIATION, CLOUD AND TEMPERATURE AT SCOTT BASE

| March 1 1957-February 28 1958 | | | | | March 1 1958-February 28 1959 | | | | |
|-------------------------------|----------------------|-------|-------|--|-------------------------------|----------------------|-------|-------|--|
| Q | T | C | Temp | | Q | T | C | Temp | |
| cal cm ⁻² | cal cm ⁻² | Oktas | °C | | cal cm ⁻² | cal cm ⁻² | Oktas | °C | |
| M | -60 | 4000 | -10.8 | | -50.0 | 6.2 | | -20.4 | |
| A | -1700 | 350 | -25.6 | | -2150 | 380 | 5.0 | -24.0 | |
| M | -2510 | 0 | -27.1 | | -2900 | 0 | 4.0 | -24.8 | |
| J | -2040 | 0 | -26.0 | | -2010 | 0 | 5.8 | -23.6 | |
| J | -2260 | 0 | -29.3 | | -1370 | 0 | 3.4 | -34.8 | |
| A | -2340 | 60 | -27.7 | | -2710 | 70 | 4.0 | -25.6 | |
| K | -1000 | 200 | -23.7 | | -2120 | 6.0 | 4.0 | -24.8 | |
| N | +60 | 3300 | -8.1 | | +650 | 104.0 | 4.8 | -2.3 | |
| N | +2050 | 1800 | -9.4 | | +1000 | 18400 | 4.0 | -10.7 | |
| 1) | +1120 | 2450 | -4.8 | | +1220 | — | — | -6.7 | |
| J | +1200 | 2200 | -4.2 | | +1400 | 2380 | — | -4.4 | |
| J | +1700 | 1000 | -8.0 | | +6720 | — | — | -11.5 | |
| Total | +1700 | 9100 | | | +18800 | (81700) | | | |

Q net flux of long and short wave radiation. T total hemispheric short wave radiation. C mean total cloud amount. $\epsilon = 0.8$. Temp. mean monthly screen temperature.

During the winter months, March–October inclusive, less than $\frac{1}{2}$ per cent of the area within a radius of 20 ft of the radiometer was snow free. Towards the end of November further isolated rocks began to appear through the surface of the snow, by the end of December, 1957, 95 per cent of the ground was clear of snow, and by the end of December 1958, 40 per cent of the ground was clear. By mid-January in both 1958 and 1959 all snow had vanished, and the surface remained clear except for some very short periods following light precipitation. In February heavier snowfalls in the first week in 1958 and somewhat later in 1959 caused a return to the winter condition.

The rock is scoriaceous basaltic debris, black in colour and consisting of pieces 18-in in diameter down to very small particles. The snow was not always perfectly clean, being at times discoloured by small particles of dust blown from the surroundings.

In November, December and January 1959 an Eppley pyranometer was mounted in an inverted position at the radiometer site, to measure the reflected short-wave radiation. Together with measurements of the hemispheric short-wave radiation, this enabled the albedo of the surface to be calculated. The mean albedos were November 71 per cent, December 67 per cent, 1–15 January 32 per cent, 16–31 January 14 per cent. No figures are yet available for February, but it is readily seen that the differences between the observed albedos and a figure of 80–85 per cent appropriate to a clean snow surface, taken in conjunction with the hemispheric short-wave radiation, are of the right order to account for the positive balance.

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- ¹ Rusin, N. P., *Information Bull., Soviet Antarctic Expedition*, 2, 25 (1958)
² Liljequist, G. H., *Norwegian-British-Swedish Antarctic Expedition 1949–52. Scientific Results*, 2, pt 1, Norsk Polarinstitutt, Oslo (1956)
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PHYSICS

Titanium as a Gettering Material

DURING recent development work, it was found to be necessary to operate a cathode ray tube at a pressure materially lower than 10^{-6} mm mercury. For this purpose, conventional barium getters were found to be inadequate, and an investigation of other materials was carried out.

The use of an ion pump was first investigated. This type of pump consists essentially of an electron-emitting tungsten source, an accelerating grid, and a negatively charged coating of titanium which could trap and absorb positively charged particles. The titanium was evaporated from an electrically heated heavy tungsten filament. The gauge used to measure the pressure was of the cold cathode, Penning type.

When a sealed-off ion pump was attached to an ion gauge, the successful operation of the ion pump was confirmed. However, it was soon found that a comparable pumping action could be achieved merely by the use of a wall coating of titanium with no ion-forming complications.

The superior gettering power was readily demonstrated by constructing tubes with the appropriate

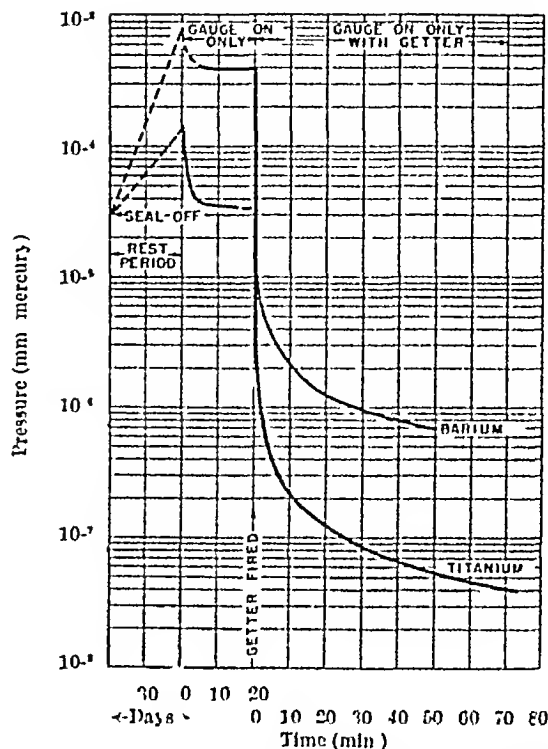


Fig. 1 Time-pressure comparison of titanium and barium getters

getter material flashed on the wall, and connected to an ion gauge, the whole constructed in 'Pyrex'.

This system was outgassed at 350°C for 1 hr and sealed off at a pressure of 5×10^{-5} mm mercury. When the tube containing a barium getter was fired, the pressure fell to 6×10^{-7} mm, while the tube containing titanium recorded a pressure of 2×10^{-8} mm, probably limited by the range of the gauge.

Similar systems were then constructed in 'Pyrex' which contained in addition to the getter a conventional cathode ray tube electron gun. This gun was activated on the pump before sealing off. When it was sealed off and operated at a normal temperature, a tube with the barium getter gave an ultimate pressure of 1×10^{-6} mm mercury while a tube employing the titanium getter still registered 2×10^{-8} mm, as measured by a cold cathode gauge.

While the results of these simple experiments make it abundantly clear that the ultimate pressure obtainable with titanium is at least forty times lower than that obtained with barium, it is important to note that the gauge was in continuous operation during these measurements.

It has been well demonstrated by Alpert¹ and Bloomer and Haine² that the conventional hot filament ion gauge exhibits remarkable pumping properties, moreover, we have found that the cold cathode type of gauge exhibits a comparable pumping action.

Thus the use of a conventional ion gauge for the measurement of pressure is an embarrassing feature in the attempt to measure the absolute efficiency of getter materials, though there is no reason to doubt the measurements of relative efficiency which have been quoted.

For the purposes of comparison, similar experiments were performed using the hot-filament ionization gauge of the Alpert design, type WL5966, manufactured by Westinghouse Electric Corporation.

Two 7052 glass envelopes were fabricated, which enclosed an electron gun, a phosphor and an ion

gauge. The barium getter used was of the type Komet 01018. The titanium getter consisted of a loop of tantalum 0.030 in diameter around which was wound a fine titanium ribbon 0.002 in \times 0.020 in.

The two tubes were given identical treatment, being sealed on the same pump system. This system employed an oil diffusion pump, conventional baffling, but no coolant.

The tubes were heated briefly to 325° C and allowed to cool. The filaments of the gauge were outgassed, but the filaments of the oxide cathodes were heated only enough to drive off moisture but insufficiently to reduce the cathode coating. Finally, the getters were outgassed. The tubes were then sealed off at a pressure of 3×10^{-6} mm mercury and allowed to stand for 30 days, at which time measurements were begun.

The pressures were recorded and the getters fired the ion gauges being operated continuously (Fig. 1). Again, it is seen that the final pressure is an order lower in the case of the titanium gettered tube.

The filaments of the electron gun were next heated. Marked superiority of the titanium showed except when a very large amount of gas was liberated by strongly overrunning the cathode filament. In this case, the pressures obtained were similar. On disconnecting the filament supply, a much lower pressure was again recorded in the case of the titanium getter.

Two points concerning the use of titanium have come to light during this work. To a greater extent than in the case of barium oil vapour is apparently anathema to the absorbing powers of titanium, and oil should therefore be trapped well away from the getter.

As with other getters, it is desirable to fire the titanium as quickly as possible in order to obtain a porous layer.

It is concluded that the use of titanium as a flash getter offers the possibility of significantly lower residual pressures in most sealed-off vacuum devices.

Acknowledgment is due to the facilities and help offered by J. H. Owen Harries (in the early part of this work), and by Westinghouse Electric Corporation where the getters have been designed for production tubes and operational results obtained.

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* Alport D. J. *App. Phys.* 24, 860 (1953).

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METALLURGY

Crack Behaviour at a Weld Structure Discontinuity

It is of both theoretical and practical interest to consider how a growing crack will behave at the structural discontinuity presented by a weld pass interface. Recently we were concerned with how a crater crack in a 5356 aluminium alloy (5 per cent magnesium type) would behave when mechanically forced to grow to the weld pass interface in a multipass weld. We have found, basically, that cracks in a multipass weld have certain significant properties which pertain to the performance and especially the structure of the weld metal.



Fig. 1. Photograph of a Multipass Oxweld 67 seam weld in 5356 aluminum, the crater crack originally present having been opened by plastic deformation. The dark-etching weld metal is of a rather coarse dendritic nature. Note how the two large cracks have been stopped at the weld discontinuity. There are many fine cracks present in the above sample which are not evident at this magnification ($\times 35$).



Fig. 2. The same weld specimen as in Fig. 1 ($\times 65$). Note the left side a crack which did not encounter the other weld passes.



Fig. 3. The junction region between weld passes shown in Figs. 1 and 2 ($\times 500$). Note the coarse dendritic structure of the upper (cracked) pass, the fine structure of the bottom pass.

In an Oxweld 67 filler metal of a weld, one made by the Linde sigma arc process in $\frac{1}{8}$ in thick aluminium alloy 5356, we noted metallographically that a major crack propagating in one weld pass stopped completely at the junction with another weld pass the metal of which had a finer dendritic array. These effects are shown in Figs 1, 2 and 3.

Essentially, this means that the growing crack is reluctant to jump across the array of grain boundaries produced by the weld interface discontinuity. While this point was theoretically implied at the April 12-14 National Academy of Science—National Science Foundation Conference on "Fracture" in Swampscott, Massachusetts, this experimental finding is presented not only because it demonstrates so clearly the subject crack behaviour but also because it is a new finding of major moment to the welding designs of many engineering structures¹. It would appear that a multipass weld in this 5356 alloy has—other things being equal—a greater crack resistance reserve in comparison with that of a single-pass weld in the same alloy. We also have since this finding, confirmed a similar behaviour in copper embrittled 5356 multipass welds—the cracks stop at the weld structure discontinuity when one pass of a two-pass butt weld is deliberately contaminated with copper to induce cracking therein.

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¹ Cottrell, A. H. "Theoretical Aspects of Fracture", 1-12, Preprint Volume, Conference on Fracture April 12-14, 1959, U.S. National Academy of Sciences—National Research Council.

CRYSTALLOGRAPHY

Effects of Heating on X-Ray Diffraction by Carbons

A NUMBER of X-ray studies have been carried out on the diffuse bands of the diffraction patterns of carbons. The major objectives were the determination of the crystal size, the expansion of layer spacings and the atomic distribution functions of carbons of different origins and carbons subjected to heat or chemical treatment. Measurements of the thermal expansion coefficient of graphite were made by Nelson and Riley¹ and others, and more recently of graphitized carbons by Walker². However, it appears that systematic studies on the effects of thermal expansion upon the more diffuse bands of amorphous carbons have not yet been made. I report here some results obtained along such lines.

A 9-cm Debye Scherrer camera of the type for multiple exposure film, fitted with a furnace for heating the specimen, was used. The monochromatization was achieved with Ross filters of iron and manganese which isolate the cobalt $K\alpha$ line. The diffraction patterns of carbons at 18° C and at 800° C through iron and manganese filters were recorded together on the same film. The patterns of the high-temperature specimens were photographed first. The resulting intensity distribution curves of the (002) band were selected and arranged in the order of the breadth and the shift of the peaks and are shown in Fig 1, where the curves have been reduced to true intensities, corrected for polarization. All the peaks for 18° C (full lines) and 800° C (broken lines) are drawn at different levels. As can be seen from

Fig 1, in each case a nearly equal shift to the low angle side occurred at 800° C. Each pair of curves crosses at about $2\sin\theta/\lambda = 3.6$ and also at the next (100) maximum to the right, where the relative intensities were the same and no peak shifts were observed as would be expected from the turbostratic structure of carbons.

The eleven samples of the curves A to K were as follows: (A) non caking, low-rank Ube coal carbonized *in vacuo* at 900° C, (B) low ash filter-paper carbonized as above, (C) cane sugar carbonized as above, (D) carbon-black from petroleum, (E) sample (B) heated at 1,800° C for 30 min, (F) polyvinyl chloride carbonized *in vacuo* at 900° C, (G) caking bituminous Moke coal carbonized as above, (H) sample (A) heated at 1,800° C for 30 min, (I) sample (C) heated as above, (J) Ormine anthracite, (K) sample (F) heated

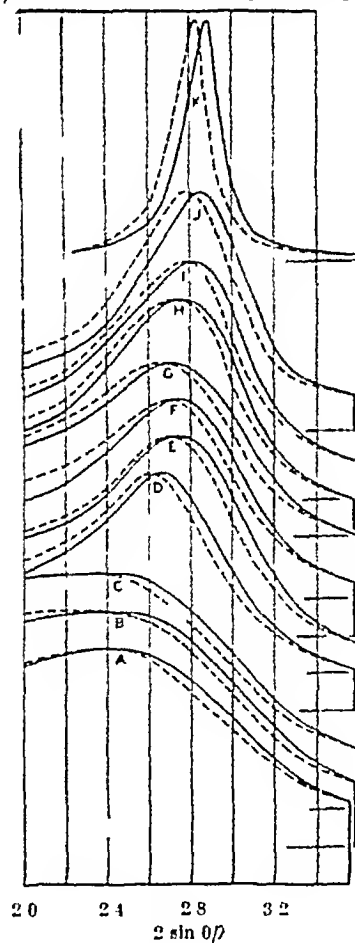


Fig 1

at 1,800° C for 30 min, similar curves of other samples having rather sharp maxima have been omitted.

The specimen rods were coated with small amounts of powdered Ceylon graphite so that the sharp (002) line of the graphite was superimposed on the diffuse band, although in Fig 1 it has been eliminated. The comparison lines helped to determine the position of the peaks and the true temperature of the specimen, since accurate thermal expansion coefficients for the graphite are known. Under close examination a possible slight decrease of the thermal peak shift with increase of the band-width breadth was observed, but the rather intense background made this uncertain. Franklin³ supposed that the polyvinylidene chloride char prepared at 1,000° C consisted of paired layers of graphite and unorganized carbon, and she obtained by calculation an intensity distribution curve close to the observed (002) band. Assuming the pairs of layers

have the same thermal expansion coefficient as the bulk graphite, by using her formula a shift of the band as large as the graphite was calculated. The shift could be found on the right-hand slope of the curves in Fig. 1, however in the present results the shifts were smaller by about 20 per cent than those of the graphite. Another result of heating appearing in Fig. 1 is the enhancement of the roentgen amorphous scattering on the low angle side, which was largest with the polyvinyl chloride char and least with the cane sugar char. This was confirmed by three series of experiments.

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CHEMISTRY

A Sensitive Chemical Dosimeter for Ionizing Radiation

A NUMBER of chemical systems have been employed for the measurement of the quantity of ionizing radiation. Among the most sensitive dosimeters are those employing dyes.¹ One system utilizes the destruction of a dye^{2,3} and another the production of a coloured dye by transformation of the leuco form.⁴ These systems are not particularly sensitive and, for a 1 mm. thick sample would require the order of 10^3 – 10^4 roentgens to give a perceptible effect. During the course of our studies on the photochemistry of thiazine dyes in rigid media⁵ we noticed that leuco forms of these dyes produced photochemically gave a red species with ultra violet light irradiation and a blue colour (normal form of the dye) with ionizing radiation. This latter effect is extremely sensitive and we have pursued the matter further with the view of developing a sensitive dosimeter for ionizing radiation.

One system which is sensitive to as little as 0.5 r of X rays from a molybdenum target is made as follows: an aqueous solution containing 3.2 per cent polyvinyl alcohol, 0.04 per cent methylene blue, 7.0 per cent lead nitrate, 17 per cent ethylene diamine tetracetic acid and 8.5 per cent glycerol was dried on a glass slide to give clear blue films. The film is protected from the atmosphere by covering with a transparent pressure-sensitive tape. The film is illuminated with light from a 500 watt tungsten lamp until decolorized and allowed to stand. In order to remove trace amounts of oxygen, any restored colour is further eliminated with repeated illuminations. The film 1 mm thick shows a blue image of the X ray beam at dosages in the one roentgen range, the optical density of which is proportional to the dosage.

At room temperature the irradiated film exhibits a colouration which reaches full intensity about 5–10 min after irradiation. On the other hand, an irradiated film which is stored at -10°C will not show any colouration but will do so when warmed to room temperature. These results indicate that the oxidizing radicals formed in the plastic matrix slowly diffuse to the leuco dye molecules. The observed sensitivity is

equivalent to a G value (molecules converted per 100 eV absorbed) of the order of 10^4 in contrast to a G value of about unity for other dye systems. It is apparent that the medium is participating in some chain process.

Despite the high sensitivity of our system it still is only one hundredth that of an X ray film (for example, Ilford, red seal, safety base). Nevertheless our system is well adapted to measure dosages by a single observation of colour, especially those in the region of greatest personal danger. Our system is obviously more convenient than liquid dosimeters and is far more sensitive.

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Some Stoichiometric Gas Hydrates

TWO communications recently appeared on the problem of the non-stoichiometric gas hydrates and the validity of the heat content changes derived from P T saturation curves.¹

There is no question of the validity of the use of the Clapeyron equation

$$\Delta H = (dP/dT)T\Delta V$$

in the determination of ΔH at points along the gas hydrate three phase equilibrium lines, provided that it is recognized that these saturation ΔH values must be suitably corrected² before they are used for determination of hydrate stoichiometry. Furthermore this equation defines ΔH at a fixed point, say at fixed temperature T , for which the three phase hydrate system is then invariant and for which the hydrate M n H_2O , whether stoichiometric or non-stoichiometric, will have a fixed composition. The ΔH thus derived for molar transfer of hydrate-former will involve n moles of water characteristic of temperature T . The effect of any dn/dT should appear in higher derivatives of ΔH with T .

In this connexion experimental work at present in progress (to be published) on two halogenated methanes has definitely shown that (1) The chemical stoichiometry derived by thermodynamic methods is equal to the ideal crystallographic value for these M $17\text{H}_2\text{O}$ hydrates. (2) The hydrate heat capacity changes are those for $dn/dT = 0$.

Similarly when a complete thermodynamic treatment, allowing for phase volume changes, gas impurities, gas solubility and water saturation, is applied to data for methane hydrate³ a formula CH_4 5.81 H_2O is found at 0°C , whereas when only the gas compressibility correction was made the formula CH_4 7.18 H_2O was obtained.⁴ The importance of making all corrections to the Clapeyron ΔH cannot be overstressed particularly when hydrate saturation pressures greater than one atmosphere are involved, for example, for argon and methane hydrates.

It appears therefore that some doubt still exists as to whether the simple gas hydrates, formed in two-component systems, do in fact present large deviations from the ideal stoichiometry or exhibit significant changes of n along the saturation lines, except perhaps in the special case when the hydrate-former volume is near the upper limiting size for its lattice cavities, as for example ethane, methyl bromide and bromine in lattice structure I

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Supercooling of Water Droplets

As part of a research programme designed to study the kinetics of nucleation in solutions of electrolytes, I have made some observations on the supercooling of water droplets in the form of water in oil emulsions stabilized by a number of W/O emulsifying agents

The procedure adopted was to disperse the water in 'Nujol' oil containing about 5 per cent of the emulsifying agent. In this way particles which catalyse the nucleation of the water can be isolated in individual droplets, thus reducing their effect to negligible proportions. This method has been previously used in the study of the solidification of molten metals¹. The emulsions which resulted contained a distribution of particle sizes with a sharp maximum in the region 2–4 μ . The solidification of the water was followed dilatometrically and indicated by a rapid increase in the volume of the emulsion at some well-defined temperature. The rate of cooling in the experiments was ~ 0.15 deg./min.

Table 1

| Emulsifier | Nucleation temperature (deg. K) | Supercooling (deg. C) | σ_{homo} (ergs cm ⁻²) | θ | K_s |
|-----------------------|---------------------------------|-----------------------|---|----------|-------|
| Lanolin | 257.5 | 15.5 | 16.5 | 84 | 480 |
| Sorbitan monolaurate | 261.0 | 12.0 | 14.0 | 68 | 635 |
| Sorbitan trioleate | 259.5 | 13.5 | 15.1 | 74 | 590 |
| Sorbitan sesquioleate | 260.0 | 13.0 | 14.7 | 72 | 585 |
| Soymul A B | 259.5 | 13.5 | 15.1 | 74 | 590 |

In these experiments much smaller degrees of supercooling were observed than previously reported by other workers². This I attribute to the formation of ice crystals on the inside surface of the droplets and catalysed by this surface. Since it is reasonable to suppose that molecules of emulsifying agent adsorbed on the droplet surface should not show any long-range order or 'crystallinity', this catalytic effect cannot be attributed to epitaxial growth on the droplet surface as is the case with the seeding of ice crystals by silver iodide. There is not sufficient evidence to say why the ice forms at the surface (heterogeneous nucleation) instead of in the bulk of the droplet (homogeneous nucleation), but the electrical charges which reside at the surface of the droplet and are presumably responsible to some extent for the stability of the emulsion, may also play some part in the catalytic activity of the surface.

From the nucleation theories of Volmer and by assuming that the nucleus forms as a spherical cap on the inside of the droplet, I have estimated values for the angle of contact θ , between the critical ice nucleus and the surface of the droplet and also the number of molecules K_s , in this critical nucleus (Table 1). Values for the interfacial energies σ_{homo} are interpolated from the results of Jacobi³.

My thanks are due to Dr P. Sherman of the Gestetner Co., London, for information concerning the emulsifying agents.

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BIOCHEMISTRY

Extraction of the Total Protein from Wheat Flour in the Form of Soluble Derivatives

SWAN¹ has recently developed a method for solubilizing keratins which depends on the fission of cystine disulphide bonds by reaction with cupric and sulphite ions, with the formation of S-sulpho cysteine residues. The protein when modified in this way becomes water-soluble, with amino-acid residues other than cysteine and cystine unchanged. Swan's method has been applied by Peckers, Dixon, Maybury and Neurath² to trypsinogen and chymotrypsinogen, and in these cases also the resulting S-sulpho derivatives were water-soluble.

We have found that when Swan's method is applied to white flour (approximately 70 per cent extraction) the protein is readily dissolved. Most of the starch remains as an insoluble residue which may be separated by centrifugation from the clear solution containing the protein derivatives, less than 3 per cent of the carbohydrate is solubilized with the protein, and this includes pentosan material. Table 1 giving the nitro-

Table 1

| | Wheat | Manitoba | Svenno | Bersee | Hybrid 43 |
|--------------------------------|-------|----------|--------|--------|-----------|
| Nitrogen in flour (per cent) | | 2.31 | 2.47 | 2.11 | 1.03 |
| Nitrogen in residue (per cent) | | 0.03 | 0.03 | 0.06 | 0.01 |

10 gm. defatted flour extracted at room temperature for 1–2 hr. with 125 ml. of reagent essentially similar to that described by Swan. The mixture centrifuged and the insoluble residue washed and centrifuged successively with 0.1 M ammonia, water, 1 per cent acetic acid, water.

gen content of the insoluble residue, shows, for flours derived from different wheats, that the extraction of protein is virtually complete.

The solution containing the protein may be freed from copper after removal of excess reagents by dialysis against 0.1 M ammonia by dialysis against ethylenediaminetetraacetate in 0.1 M ammonia or against 0.1 M hydrochloric acid. The solubility of the protein derivatives is extremely sensitive to pH. The solutions are clear at pH 7.5–8.0 but, in the presence of McIlwaine's buffer, precipitation occurs at pH 7.0 and increases to a maximum at about pH 4.0.

The proteins in gluten, freshly washed out from flour, are also solubilized by the Swan process—when the material is left in contact with the reagent overnight at room temperature. Some of the carbohydrate contained in the gluten complex is also dissolved.

Work is proceeding on the separation of the soluble carbohydrate from the soluble protein derivatives and on a comparison of these derivatives from wheats of different types.

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Interaction of Anti-Staling Agents with Starch

FOLLOWING an observation that sucrose stearate, a compound claimed to have anti-staling activity, precipitated starch from solution (to be published), the study was extended to other substances known to have anti-staling properties.

As most known anti-staling agents have surface active properties, two surfactants were included in the programme—a sulphonated hydrocarbon (anionic) and cetyl trimethyl ammonium iodide (cationic). For purposes of comparison, *n*-butanol and thymol (amphiphilic) were also included.

The following compounds claimed to have anti-staling activity, were tested: sucrose monostearate, sucrose distearate, polyoxyethylene monostearate, glyceryl monostearate (commercial), glyceryl monostearate (pure, Myverol 18 00) and stearyl tartrate.

Solutions of the test agents were added to solutions of wheat starch to give final concentrations starch 0.5 per cent, sodium chloride 0.05 per cent, test agent 0.005–0.075 per cent (except in the case of stearyl tartrate where the maximum concentration was 0.03 per cent due to its low solubility). The amount of precipitate was determined turbidimetrically.

Butanol, thymol and the two ionic surfactants had virtually no precipitating effect in this concentration range. Among the anti-staling agents only stearyl tartrate showed little precipitating power. The most effective precipitants were sucrose monostearate, glyceryl monostearate (pure) and polyoxyethylene monostearate. Glyceryl monostearate (commercial) was slightly less effective and sucrose distearate much less effective.

These results show that five out of six substances with anti-staling activity give a precipitate with starch. Whether or not this reaction is a prerequisite for all anti-staling agents is not certain, but in any event this reaction must change the characteristics of flour products.

Ofelt *et al.*¹ reported that glyceryl monostearate decreased the crumb firmness of bread (an anti-staling characteristic) and that glyceryl distearate had no such effect, nor did it act synergistically with the monostearate. Our results show that glyceryl monostearate (pure) is a more effective precipitant for starch than the commercial material, but only slightly so. However the commercial glyceryl monostearate employed contained about 33 per cent monostearate with the remainder largely distearate. If there were a

strict parallel between the baking and precipitation tests, it would be expected that there would be a greater difference between the two samples of glyceryl monostearate in the precipitation tests. Ofelt *et al.*² also found that the crumb softening effect decreased in the order polyoxyethylene monostearate, glyceryl monostearate, sucrose monostearate but the precipitation tests showed little difference between the three compounds. In addition, Axford and his colleagues³ have found no direct correlation between the amount of precipitate which we have observed with starch and the effectiveness of an anti-staling agent in bread. Thus one is led to the conclusion that complex formation between known anti-staling agents and starch must occur in flour products and that it may well explain the action of these agents as bread improvers, if this is so, then the effectiveness of such an agent in bread must be determined not only by the amount of complex formed but also by the properties of that complex, such as its permeability to moisture.

We are grateful to the Sugar Research Foundation for financing this investigation and to Dr D. W. C. Axford, of the British Baking Industries Research Association for helpful discussion.

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A New Inhibitor of Serotonin Metabolism

It has been postulated that a change in amino concentrations in the brain is causally related to the activity of a drug in the central nervous system. In 1940, Mann and Quastel¹ suggested that the central stimulant activity of 'Benzadrine' was related to its ability to inhibit the oxidation of tyramine by amine oxidase. Follows and Bornheim² observed an excellent correlation between the increased motor activity in the rat and the inhibition of amine oxidase by a series of aryl 2-aminopropane derivatives. Recently, Tedeschi *et al.*³ observed that SKF No. 385 2 phenylcyclopropylamine in the rabbit, demonstrated an activity suggestive of *in vivo* monoamine oxidase inhibition. Since this compound was not a hydrazine, it was decided to study its effect on amino oxidase activity.

In vitro amino oxidase activity was determined^{4, 5} by measuring the rate of disappearance of serotonin incubated with rat brain homogenates. Adult male rats were killed by exsanguination, the brains were rapidly removed, weighed and homogenized in 2 volumes of distilled water. 1 ml of brain homogenate was added to 300 μ g of serotonin in phosphate buffer and the mixture incubated for 60 min at 37°C. Optimal substrate concentration was determined to be 300 μ g/ml, and serotonin disappearance was found to be linear between 15 and 60 min. A 15 min preincubation of the drug with the rat brain homogenate, prior to the addition of substrate, was utilized to obtain maximal inhibition. Serotonin

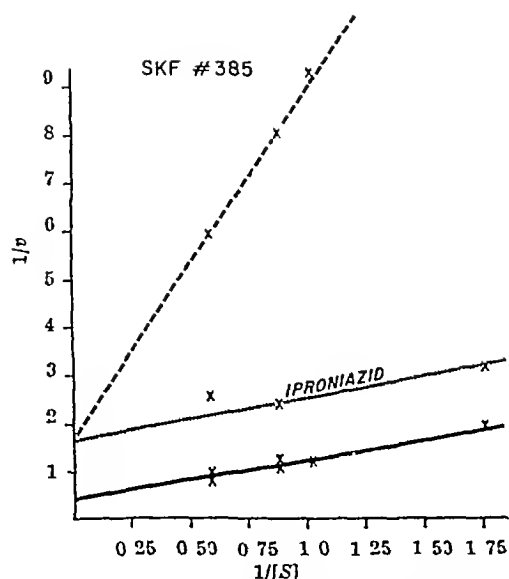


Fig. 1 Lineweaver-Burk (ref. 7) plot of the effect of SKF No 385 and 'Iproniazid' on the rate of disappearance of serotonin incubated with rat brain homogenate

was isolated and determined colorimetrically by the method of Udenfriend *et al.*⁶

The effectiveness of SKF No 385, 2-phenylcyclopropylamine, 'Doxedrine', 2-phenyl isopropylamine, and 'Iproniazid', 1-isonicotinyl-2-isopropylhydrazine, on the disappearance of serotonin was determined over a wide range of drug concentration.

A sigmoid-shaped curve was obtained by plotting per cent inhibition against drug concentration, serotonin disappearance being inhibited 50 per cent by SKF No 385 at $2.8 \times 10^{-6} M$, by 'Doxedrine' at $7 \times 10^{-5} M$ and by 'Iproniazid' at $7 \times 10^{-4} M$. Substrate concentration was then varied and a Lineweaver and Burk⁷ plot of the results suggested that SKF No 385 was a non-competitive inhibitor (Fig. 1).

To determine their *in vivo* inhibitory activity these compounds were administered to the rat and the serotonin content of whole brain was determined spectrofluorometrically by the method of Bogdanski *et al.*⁸

'Iproniazid', administered intraperitoneally at doses of 25–100 mgm/kgm, increased the rat brain serotonin content 30 and 60 per cent, respectively, above control animals. However, administered orally for comparison with SKF No 385-A, 'Iproniazid' was found to have little effect on brain serotonin content (Table 1). SKF No 385-A was active orally at doses of 2.5 mgm/kgm, 65 per cent increase, but the maximal response obtained at 10 mgm/kgm (Table 1) was unchanged at doses up to 60 mgm/kgm. 'Doxedrine', *in vivo*, had no effect on the level of serotonin in whole brain. Therefore, it would

Table 1 EFFECT ON RAT BRAIN SEROTONIN OF 'IPRONIAZID' AND SKF No 385-A, ADMINISTERED ORALLY

| Time (min.) | Serotonin, $\mu\text{gm/gm}$ of brain | |
|-------------|---------------------------------------|-------------------------|
| | 'Iproniazid' 400 mgm/kgm | SKF No 385-A 10 mgm/kgm |
| 0 | 0.53 (6)* | 0.48 (10) |
| 30 | 0.51 (2) | 0.70 (4) |
| 60 | — | 0.74 (3) |
| 120 | 0.56 (2) | 0.80 (4) |
| 180 | 0.66 (6) | 1.08 (10) |
| 240 | 0.86 (2) | 0.86 (4) |
| 300 | 0.65 (2) | — |

* The figures in brackets are the number of animals killed to obtain the average serotonin content recorded

appear that, in agreement with Vogt⁹, the excitatory reactions following the administration of 'Doxedrine' are not due to an accumulation of serotonin in the brain.

The results obtained with 'Iproniazid' are in agreement with Zeller and Barsky¹⁰, Schayer¹¹ and Sjoerdsma *et al.*⁴, who have reported on the *in vitro* and *in vivo* inhibition of monoamine oxidase by 'Iproniazid'. However, the far greater inhibitory activity of SKF No 385, a non-hydrazine compound, both *in vitro* and *in vivo*, opens a whole new area of search for pharmacologically active stimulant drugs.

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Infra-Red Spectra of Carbohydrate Sulphate Esters

IN recent years considerable interest has been expressed in the use of infra-red spectroscopy in studies on the location of the ester sulphate group in the isomeric chondroitin sulphuric acids, A, B and C. Although Orr's¹ original assignment of bands in the 700–1,000 cm^{-1} region of spectra of sulphated mucopolysaccharides has been criticized², his views have recently received further support from the work of Mathews³, and Meyer and co authors⁴.

Accumulated evidence from studies of the infra-red spectra of chondroitin sulphate isomers indicates that apart from a band of strong intensity at 1,240 cm^{-1} which is associated with the S–O stretching vibration, displacement of bands in the 800–850 cm^{-1} region, attributed to vibrational modes involving stretching in the C–O–S system can be associated with the spatial distribution of sulphate groups on the hexosamine moieties. Observations^{1–4} of the presence of the characteristic band at 820 cm^{-1} in chondroitin sulphate C, and at 850 cm^{-1} in chondroitin sulphates A and B, and the disappearance of these bands following chemical desulphation⁵, have been repeated in the Cardiff laboratories. Moreover, persistence of the 850 cm^{-1} band in the spectrum of N-acetylchondrosin sulphate isolated from chondroitin sulphate A after enzymic hydrolysis⁶ has also been noted.

The development of methods for the definitive synthesis of hexose and hexosamine monosulphate esters⁷ has now provided another approach to this problem. Sulphation of glucose, galactose, and N-acetylglucosamine to yield the corresponding monosaccharide-6-O-sulphate esters is accompanied by the appearance in the infra-red of new bands at 1,240 cm^{-1} and 820 cm^{-1} . Preparations of N-acetylgalactosamine monosulphate⁷, the structure of which

has still not been established with certainty, also exhibit these characteristic absorption frequencies. On the basis of these observations the association of the 820 cm^{-1} band with the 6-O sulphate position in the monosulphate esters of glucose, galactose and N-acetylglucosamine may be postulated. By analogy, the location of the sulphate group on position 6 of N-acetylgalactosamine monosulphate for which some preliminary evidence has already been obtained⁷, may also be proposed. Evidence supporting these views may be derived from the fact that chondroitin sulphate in which the sulphate group has been assigned to position 6 of the galactose moiety⁸, also exhibits the 820 cm^{-1} band. Consequently, the proposed correlation between the 820 cm^{-1} band of chondroitin sulphate C, and substitution of the 6 (equatorial) position of galactosamine residues in this polymer is well supported.

The establishment of the sulphate group on the 4 (axial) position of galactosamine in chondroitin sulphate B by methylation studies⁹, supports the assignment of the 850 cm^{-1} band to sulphation of position 4 of the hexosamine moiety of this compound, and by analogy, of chondroitin sulphate A. Additional evidence in favour of these postulates is obtained from the appearance of the 850 cm^{-1} band in spectra of *Chondrus ocellatus* mucilage polysaccharide (gift from Prof. T. Mori), and carrageenin (gift from Dr. F. A. Rose), in which the sulphate group has been established as being on position 4 of galactose by methylation studies¹⁰.

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Interference by Azide with Diazotization Procedures used in Biological Assay Systems

When sodium azide ($5 \times 10^{-3} M$) was added as an inhibitor of nitro reductase activity of a *Nocardia* sp. using p-dinitrobenzene as substrate we were unable to detect the formation of p-nitroaniline by means of a diazotization assay¹ although the appearance of a yellow colour indicated its formation. However, after extracting the reaction mixture with ether it was possible to show electrophoretically the presence of p-nitroaniline in the ether extract and that sodium azide at the above concentration has no inhibitory effect on the nitro reductase system.

We later studied the effect of sodium azide on the p-nitroaniline assay system using known concentrations of arylamine compounds. To a series of 15 ml centrifuge tubes containing 10 μgm . of either p-aminobenzoic acid or p-nitroaniline, plus various concentrations of sodium azide in a total volume of 2 ml. of distilled water were added at room temperature 0.5 ml. N-hydrochloric acid and 0.25 ml. aqueous sodium nitrite (0.1 per cent w/v). After 5 min. 0.25 ml. ammonium sulphamate (0.5 per cent w/v) was added and thoroughly mixed. Three minutes later 0.25 ml. of N-(1-naphthyl)-ethylenediamine hydrochloride (0.1 per cent w/v) was added. After 30 min. at room temperature the optical density of the solution was estimated at 540 m μ using the Beckman model DU spectrophotometer. The results (Table 1) demonstrate a marked inhibitory effect of sodium azide on the diazotization reaction.

Table 1. EFFECT OF SODIUM AZIDE ON DIAZOTIZATION REACTIONS

| Concentration of sodium azide added (M) | Colour formation with p-nitroaniline | | | |
|---|--------------------------------------|-----------------------|--------------------------------|-----------------------|
| | Optical density at 540 m μ | Inhibition (per cent) | Optical density at 540 m μ | Inhibition (per cent) |
| None | 1.080 | — | 1.700 | — |
| 1×10^{-4} | 1.080 | — | 1.170 | 2 |
| 5×10^{-4} | 0.824 | 20 | 0.804 | 53 |
| 1×10^{-3} | 0.402 | 61 | 0.372 | 69 |
| 5×10^{-3} | 0.082 | 92 | 0.010 | 100 |
| 1×10^{-2} | 0.010 | 100 | 0.010 | 100 |

Sodium azide has been reported by many workers to inhibit the activities of several enzyme systems (nitrate and nitrite reductases, nitroethane oxidase, organic nitrate reductase and nitroaryl reductases, among others) in which the diazotization reaction was used to determine the extent of the reaction. In the light of the findings reported here it might be of interest to re-investigate the effect of sodium azide on these enzyme systems.

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Immunochemical Studies of Polypeptidyl Proteins and Synthetic Polypeptides

The polymerization of N-carboxyamine acid anhydrides¹ has made available synthetic polypeptides of high molecular weights which consist of a single polypeptide chain containing one type of amino acid residue copolymers of two or more different amino acids or multichain polypeptides. The molecular weights and some chemical and physical properties are similar to those of proteins.

It is also possible to link chemically synthetic polypeptides to protein molecules by initiating polymerization of N-carboxyamine-acid anhydrides with proteins² yielding modified or polypeptidyl proteins which are chemically very similar to the native protein. Because the antigenic character of proteins may be associated with their polypeptide structure, we have studied the immunological properties of polypeptidyl proteins and synthetic polypeptides.^{3, 4}

Preparations of bovine serum albumin modified by the addition of peptides of glutamic acid, lysine, leucine, or phenylalanine⁵ were strongly antigenic in

rabbits. Precipitin reactions were obtained between antisera to each polypeptidyl bovine albumin and a similarly modified rabbit serum albumin or unmodified bovine albumin, indicating the presence of antibodies specific for each of the added peptides and for the carrier protein. The antisera to the poly-leucyl and polyphenylalanyl bovine albumins were able to precipitate the homologous antigen after absorption with a similarly modified rabbit serum albumin and the unmodified bovine serum albumin, suggesting that a third type of antibody had been formed which required the added peptide and a part of the carrier protein.

Similarly modified rabbit albumins² were also antigenic in rabbits. Their antisera gave precipitin reactions with the correspondingly modified bovine albumins. Absorption experiments showed some antibodies were formed to the poly-leucyl and polyphenylalanyl rabbit albumins which were specific for the modification and others which required the added polypeptide and a part of the carrier protein.

Antisera to the polypeptidyl proteins cross reacted with several purified protein preparations with which antiserum to the unmodified bovine albumin did not. The modification of the bovine albumin with the various polypeptides reduced the amount of antibody precipitated by the polypeptidyl albumin from an antiserum against unmodified albumin.

Twenty-five different synthetic polypeptide preparations, not linked to a carrier protein, were tested for antigenicity in rabbits. Linear polypeptides studied were a series of acidic polyglutamic acids of molecular weights of about 1,200–80,000, two basic polylysine preparations, poly-leucine and polyphenylalanine—neutral polypeptides insoluble in water, polyproline—neutral and water-soluble, and several copolypeptides of two different amino acids. A complex multichain polypeptide of glutamyl, leucyl, glycyl, and lysyl residues was also studied.

Only one of the polyglutamic acids and the multichain polypeptide were sufficiently antigenic to cause the formation of antibody titres high enough to give definite zones of precipitation in agar diffusion tests and to measure by quantitative precipitin methods. The antibodies formed did not precipitate with the homologous synthetic polypeptide, but cross-reacted with related polypeptidyl albumins and certain purified protein preparations. Antisera against a few other synthetic polypeptides gave weak, questionable precipitin tests. The antisera to the polyglutamic acid and multi-chain polypeptide produced weak anaphylactic reactions in guinea pigs challenged with the homologous or a similar synthetic polypeptide and moderate to fatal anaphylactic shock in guinea pigs challenged with polyglutamyl bovine albumin or unmodified bovine albumin.

The synthetic polypeptides did not inhibit precipitin or anaphylactic reactions between their antisera and cross-reacting proteins or between antisera to similarly modified proteins and their homologous antigens. The reaction between modified rabbit proteins and antibodies to modified proteins were more easily inhibited by high salt concentrations than precipitins of unmodified proteins. A few polyglutamic acid preparations, which gave no precipitate with their antisera in physiological saline, gave specific precipitates when the ionic strength was lowered to 0.05, suggesting that ions react with the highly polar polypeptide to prevent precipitin formation. The high charge of the soluble synthetic polypeptides may hinder the formation of a stable combination between the polar antigen and antibody as compared to

proteins and so block precipitation or inhibition reactions and reduces antigenicity.

We conclude that a few of the synthetic polypeptides studied incited antibody formation in rabbits. The polypeptides coupled to bovine or rabbit albumin⁴ were all antigenic. The precipitin reaction of highly polar, synthetic, soluble polypeptides and their antisera was weak and more sensitive to ionic strength than reactions of protein antigens. Antisera to some synthetic polypeptides cross-reacted with certain purified proteins. The structural requirements for the antigenicity of synthetic polypeptides, like that of proteins, is not yet understood. Continued study of the immunochemical properties of the model synthetic polypeptides and polypeptidyl proteins, may contribute to our understanding of the structural basis for antigenicity and of antibody-protein reactions.

Further details will be published elsewhere.

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Occurrence and Quantitative Determination of 2-Dimethylaminoethanol in Animal Tissue Extracts

RECENTLY the function of 2-dimethylaminoethanol (Deanol) in the biosynthesis of choline and its role as a possible precursor of cerebral acetylcholine¹ has intensified interest in this substance. Levine and Chargaff² could not find it in phospholipides. Artom and Crowder³ claimed the occasional occurrence of traces of it in rat liver. Recently Wolf and Nye⁴ reported that they were able to isolate it from a mutant strain (47904) of *Neurospora crassa*, which accumulates this substance. In a preliminary paper, Venkataraman and Greenberg⁵ showed on the basis of chromatographic evidence, that incubation of a rat liver extract with aminoethanol and formaldehyde yielded methylated intermediates of choline. To clarify the question of the natural occurrence of 2-dimethylaminoethanol in animal tissue a method was developed for the isolation, characterization and quantitative determination of small amounts of this substance in the presence of other amines.

For the separation of bound and unbound amines the tissue was homogenized in 80 per cent ethanol, adjusted to a pH of 2–3 with concentrated hydrochloric acid and centrifuged. This extraction was repeated 3–4 times. The ethanolic extract contained the unbound amines, whereas the bound amines remained in the precipitate. In order to obtain the volatile components of unbound amines, the supernate was concentrated *in vacuo* (water bath tempera-

ture 40–50° C), saturated with barium hydroxide and subjected to a fractional steam distillation *in vacuo* (15–25 mm mercury) under nitrogen. Four different fractions (F 1–4) were collected in 1 *N* hydrochloric acid at increasing water bath temperatures (F1 14–10° C 90 min, F2 19–36° C 10–15 min, F3 30–56° C 60–75 min, F4 55–60° C 60–75 min). The excess hydrochloric acid was removed under reduced pressure. To liberate the bound amines, the residue from the steam distillation and the ethanol insoluble precipitate were refluxed for 6 hr in a saturated barium hydroxide solution. This hydrolyzate was subjected to an extraction with 80 per cent ethanol at pH 2, or to a preliminary steam distillation *in vacuo* under nitrogen and the volatile amines collected in 1 *N* hydrochloric acid. The crude amine mixture was then fractionated by the procedure described for the unbound amines (fractions FH 1–4). The fractional steam distillation served to separate amines like ammonia and methylamine, which occur in relatively large quantities, from the other tissue amines. The main amount of 2-dimethylaminoethanol appeared in fractions F 3 and FH 3 whereas most of the ammonia and methylamine came off in F 1 and FH 1 and 2.

The separation of the small amounts of 2-dimethylaminoethanol found in tissues from the amines and aminoalcohols, which are usually present in much larger quantities, is rather difficult. Paper-electrophoresis and paper-chromatography are not entirely satisfactory since these amines have similar migration properties in these systems. These methods are useful for the further characterization of the amines after recovery from the separation by gas phase-chromatography. The electrophoresis was carried out on Whatman paper No 1 (57 × 15 cm, buffer content 130–150 per cent) in 1/10 *M* citric acid buffer pH 3.8 at 1000 volts (12 m-amp) for 90 min. The ascending chromatogram was developed overnight on Whatman paper No 1 (18 × 38) impregnated with the citric acid buffer. The solvent mixture butanol:ethanol:water:acetic acid = 8:4:3:1 was used. The detection of the amines on paper is limited by the sensitivity of the dye reaction. Under the best experimental conditions 15–20 µgm of 2-dimethylaminoethanol could be detected with potassium bismuth iodide. The optimal results were obtained by gas phase chromatography. For the separation of the individual components of the amino mixtures by this technique the amine hydrochlorides were converted to the free amine form by treatment with 1 per cent methanolic sodium hydroxide and this solution was injected into the following gas phase-chromatography system: the support, 'Chromosorb' (Johns Manville, mesh size 30–60) pretreated with 5 per cent methanolic sodium hydroxide was mixed with the stationary phase 'Carbowax 20 M', 24–28 weight per cent dissolved in methanol:acetone (3:1). This mixture was stirred until dry and packed in a 5 ft column which was put in a Wilkens aerograph instrument. Helium, 96 ml/min was used as carrier gas, and the temperature was kept at about 125° C.

Fig 1 shows the clear resolution of a test mixture containing 1-dimethylamino 2-propanol, 2-dimethylaminoethanol, 2-diethylaminoethanol, 2-methylaminoethanol, 2-aminoethanol and phenylethylamine.

The quantity of 2-dimethylaminoethanol was determined from the peak area on the gas-chromatogram (peak height × half width) as suggested by Cremer⁶. From known amounts of pure 2-dimethylaminoethanol solutions a standard curve was drawn and used in the quantitative estimation of this substance in natural

sources. The error of the quantitative estimation ranged from 1–2 per cent (with quantities above 20 µgm) to 10 per cent (with quantities less than 20 µgm). The smallest amount of 2-dimethylaminoethanol detectable (with the thermoconductivity cell filament current 250 m-amp and a 1 mV Bristol recorder full sensitivity) was 0.1–0.5 µgm.

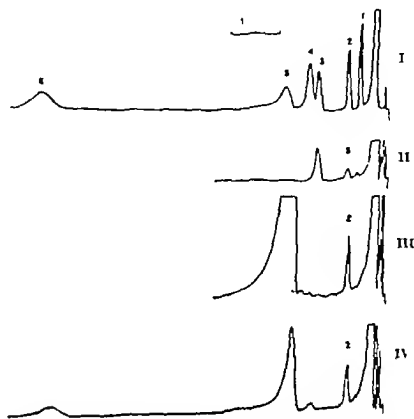


Fig. 1 Gas-chromatogram of test mixture and tissue extracts. I test mixture, II P774 human brain, III P3 pig brain, IV P4 salmon roe. Peak 1, 1-dimethylamino-2-propanol, peak 2, 2-dimethylaminoethanol, peak 3, 2-diethylaminoethanol, peak 4, 2-methylaminoethanol, peak 5, 2-aminoethanol, peak 6, phenylethylamine.

The procedure for the quantitative isolation of 2-dimethylaminoethanol was checked for accuracy as follows to 13.6 gm salmon roe 1 mgm of 1,2-¹⁴C labelled 2-dimethylaminoethanol was added. After completion of the isolation for bound and unbound 2-dimethylaminoethanol an aliquot of the amine extract equivalent to 1 µgm of added 2-dimethylaminoethanol was injected into the gas-chromatograph, the collected peak contained 90 per cent of the expected radioactivity.

Tissue extracts from about 1 kgm of human brain, pig brain and salmon roe were prepared, and the amounts of 2-dimethylaminoethanol determined in the manner described (see peak 2 in Fig. 1). In the case of salmon roe, which is relatively rich in 2-dimethylaminoethanol the peak corresponding to this substance was collected at the outlet of the gas chromatograph and further characterized by paper-electrophoresis (migration value 0.04 where glycine has a migration value of 0 and methylamine a migration value of 1.0) and paper chromatography (*R_F* value 0.27). It was shown that the peak has the same migration properties and the same dye reaction in both systems as pure 2-dimethylaminoethanol.

The quantities of 2-dimethylaminoethanol found in these tissues were as follows: in salmon roe 260 µgm/kgm unbound and 1662 µgm/kgm bound; in human brain 5.1 µgm/kgm unbound and 76.4 µgm/kgm bound; and in pig brain 173 µgm/kgm unbound and 73.5 µgm/kgm bound.

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Tropolone Biosynthesis: the Enzymatic Decarboxylation of Stipitonic and Puberulonic Acids

ISOTOPE tracer studies have established an important role for acetate and formate in the biosynthesis of stipitonic acid (6-hydroxytropolone-4-carboxylic acid) by *Penicillium stipitatum* and it is probable¹ that the C₇ tropolone ring is not formed by ring expansion from known C₆ structures as proposed by Seshadri². Seshadri also suggested 6-hydroxytropolone-3,4-dicarboxylic acid as the immediate precursor of stipitonic acid. This possibility seemed likely since other *Penicillium* species yielded the compounds puberulic and puberulonic acids³ which are now known to be 6,7-dihydroxytropolone-4-carboxylic acid and the anhydride of 6,7-dihydroxytropolone-3,4-dicarboxylic acid, respectively⁴. Recently Segal⁵ isolated from *P. stipitatum* cultures an anhydride, stipitonic acid, originally believed to be the 6-hydroxytropolone-3,4-dicarboxylic acid proposed by Seshadri, but now established as the 4,5 isomer⁶. Although puberulonic acid is usually written as indicated above, it seems reasonable to suppose that any adjacent pair of the four oxygen functions may form the tropolone function and it may equally be regarded as 3,4-dihydroxytropolone-5,6-dicarboxylic acid, or analogous to stipitonic acid, as 3,7-dihydroxytropolone-4,5-dicarboxylic acid.

In the light of these structural considerations it seemed possible that the final stage of the Seshadri hypothesis might be correct in principle, but that the precursors of the tropolone monocarboxylic acids were the 4,5- rather than the 3,4-dicarboxylic acids. We have therefore investigated the enzymatic decarboxylation of both stipitonic and puberulonic acids.

The enzyme preparations were obtained from *P. stipitatum* NRRL 2104 cultures grown in 1-litre Erlenmeyer flasks on 200 ml of Czapek-Dox medium supplemented with 0.1 per cent yeast extract and 0.3 per cent corn steep liquor. On the eighth or ninth day after inoculation the mycelial pad was ground with glass beads and 0.1 M phosphate buffer, pH 5.8, (about 7 ml per culture) essentially as described for *cis*-aconitic acid decarboxylase by Bentley and Thiessen⁷. The paste obtained by this treatment was centrifuged with an additional portion of the buffer at 1860 g for 25 min to remove the powdered glass and cell debris. The cloudy supernatant was further centri-

fuged at 24,500 g for 30 min and the resultant supernatant filtered through a rapid paper. The preparation was used as such or could be dialysed for a short time against cold, distilled water without loss of activity. A typical preparation was a pale yellow opalescent solution at about pH 6 and contained 5.0–5.5 mgm/ml of protein.

The decarboxylase activity was measured manometrically by observing the evolution of carbon dioxide at 37° with stipitonic acid as substrate. The stipitonic acid solution (8–10 μmoles/0.4 ml), prepared by dissolving the anhydride in 0.1 M phosphate buffer, pH 7.5, with warming, was added from the side arm after equilibration. The preparations showed a small and variable oxygen uptake in the absence of substrate and all experiments were corrected for this. The decarboxylase was active over a broad pH range with a maximum at about pH 6.6. However, assays were usually run at a slightly lower flask pH (about 6.0–6.2) so that evolution of carbon dioxide could be followed manometrically with appropriate corrections for retention of carbon dioxide. Under these conditions a linear production of carbon dioxide was obtained for 90 min, corresponding to about 1.4 μl carbon dioxide/min/ml enzyme preparation.

A stoichiometric relationship between stipitonic acid removed, and carbon dioxide and stipitonic acid formed was established in the following manner. On incubation of 1 ml of enzyme solution with 8.5 μmoles of stipitonic acid, 6.25 μmoles of carbon dioxide were produced after 102 min. The flask contents were heated in a boiling water bath for 5 min and a protein-free filtrate prepared. The stipitonic acid remaining was found to be 2.2 μmoles. (The stipitonic acid used as substrate in these experiments was extracted from *P. stipitatum* cultures by a method developed in this laboratory. The determination of stipitonic acid was carried out by a spectrophotofluorometric method. Details of these procedures will be published separately.) Stipitonic acid formed was determined to be 6.3 μmoles by measuring the optical density of an aliquot at 275 mμ at pH 7 and correcting for that due to the stipitonic acid remaining as previously determined. All values were corrected by use of a blank treated identically but containing no stipitonic acid as substrate. With a boiled enzyme preparation and stipitonic acid, no carbon dioxide was produced and the stipitonic acid added was recovered.

Magnesium, zinc and manganese divalent ions added as the chlorides at a concentration of 10⁻⁴ M and cysteine, 10⁻³ M, were without effect on the decarboxylase activity while mercuric chloride, 10⁻⁵ M and 10⁻⁴ M, caused 25 per cent and 55 per cent inhibition, respectively.

The enzyme preparations, as well as decarboxylating stipitonic acid, showed considerable decarboxylating activity towards a crude mixture of puberulic and puberulonic acids. Since there was no decarboxylation of pure puberulic acid, this must be presumed to represent a decarboxylation of the puberulonic component. Puberulic and puberulonic acids are not normal metabolites of *P. stipitatum* and it is not yet known whether the two decarboxylation activities are associated with the same enzyme. Work to purify the crude enzyme preparation and to characterize it further is now in progress.

It seems most likely that the pairs stipitonic acid—stipitonic acid and puberulonic acid—puberulonic acid are related biochemically through the action of

the tropolone dicarboxylic acid decarboxylase described here. Unless fixation of carbon dioxide is involved in formation of the carboxyl groups and the previous isotope data do not support this possibility, it is clear that the precursors of stipitatonic and puberulonic acids must at least be C_6 compounds.

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Action of Ribonuclease on Nerve Axoplasm as Demonstrated by Silver Staining

It was observed that crystalline ribonuclease selectively prevented demonstration of nerve axoplasm by a simple silver method reported elsewhere.¹ The tissue was treated with 0.01 per cent crystalline ribonuclease in distilled water at 60°C for 1 hour. Ribonuclease was also observed to prevent axon staining as well as to alter the staining capacity of the Nissl substance and nucleoli of the spinal cord when the Bodian and toluidine blue methods were used.

Two lots of crystalline ribonuclease were used. The results were similar in the two instances. Both lots of enzyme had given negative reactions to standard tests for proteolytic activity. In addition, the enzyme was treated with ammonium sulphate heated at 100°C after the procedure suggested by Swift,² without change in the results obtained.

A series of inhibitors of the activity of ribonuclease was utilized. Sodium chloride, magnesium chloride, copper sulphate, phenylisocyanate and periodate, in concentrations published as inhibiting agents for ribonuclease, allowed silver staining of the axoplasm to occur. Control sections treated at 60°C for an hour with ribonuclease alone showed no staining.

Extraction of formalin fixed nerve tissue with 10 per cent perchloric acid for periods up to 24 hours did not change the stain. Extraction of Bouin fixed material with trichloroacetic acid at 90°C for 30–60 minutes did remove the staining capacity of axoplasm.

The nature of the substance that permits silver staining of nerve tissue is not known. The action of ribonuclease points towards a nucleoprotein basis for staining. Purine and pyrimidine bases may bind silver as seen in the methods for urates. Silver purine com-

pounds are used in the isolation and analysis of nucleic acid. The relation of formalin fixation to ribonuclease activity and other related problems are under investigation.

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ANIMAL PHYSIOLOGY

Active Transport of Uric Acid Through the Human Erythrocyte Membrane

Active Transport of Uric Acid Through the Human Erythrocyte Membrane

In connexion with determinations of the uric acid pool in man by means of labelled uric acid, it has been repeatedly observed that it takes several hours before the injected uric acid reaches equilibrium in the total volume of distribution. This indicates that the cell membranes have a limited permeability to uric acid. It is known^{1,2} that uric acid is able to penetrate the erythrocyte membrane of man. The ratio between uric acid/l. of red blood cells and uric acid/l. of plasma³ is 0.55. The extra- and intracellular concentrations of uric acid in the water phase are nearly the same when correction is made for the Gibbs-Donnan effect.

We have now been able to demonstrate, that a part of the transport of uric acid into human erythrocytes is inhibited by hypoxanthine. These results, together with results from experiments employing variations in temperature, indicate that the system responsible for the transport of uric acid through the human erythrocyte membrane has two components. Furthermore, experiments carried out at different pH values, suggest that the uric acid crosses the erythrocyte membrane in its undissociated form.

Fresh heparinized blood was washed three times with isotonic phosphate buffer (0.11 M), pH 7.0 (unless otherwise indicated). The buffer contained 1 gm. of glucose per litre, and the same uric acid concentration as the original plasma to avoid fluctuations in the intracellular concentration of uric acid. After washing the red blood cells were suspended in the buffer with or without addition of hypoxanthine, to give a final hematocrit of 50–60 per cent. After 15 min. equilibration at 22°C (unless otherwise stated) and shaking 1 µc. of uric acid $8\text{-}^{14}\text{C}$ ($2\text{-}4\text{ }\mu\text{M}$) was added at zero time. The flasks contained a total volume of 24 ml. each. At different time intervals, samples were taken, and the cells removed by centrifugation in the cold at 9,000g. The supernatant was measured for radioactivity, and from the decline in specific activity with time, the velocity of uric acid exchange was calculated.

Fig. 1 shows uric acid exchange as a function of hypoxanthine concentration. It can be seen that by increasing hypoxanthine concentrations the uric

acid exchange decreases until 20 per cent of the control value is reached. From this point, increase in hypoxanthine concentration will give no additional inhibition. At hypoxanthine concentrations giving maximal inhibition, there is still a considerable exchange, thus indicating two mechanisms for uric acid transport: one sensitive to hypoxanthine, and another which accounts for the remaining transport at maximal hypoxanthine inhibition.

In order to obtain a further description of the two components of the transport system, we have investigated uric acid exchange under variations in pH and in temperature.

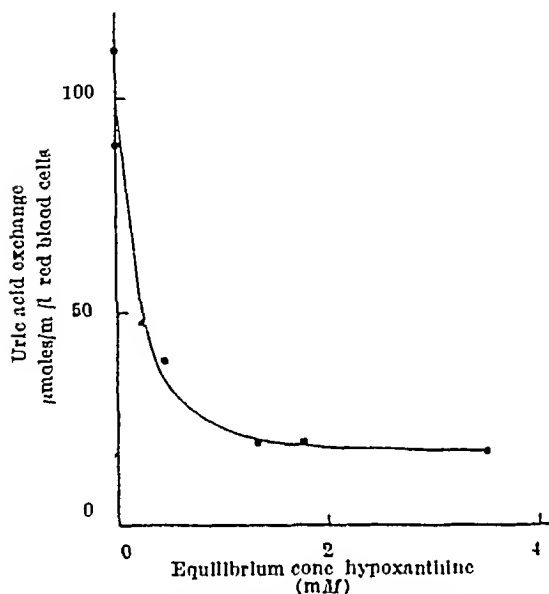


Fig. 1. Inhibitor action of hypoxanthine on uric acid exchange in human red blood cells.

Table 1. URIC ACID EXCHANGE IN HUMAN BLOOD RED CELLS SUSPENDED IN ISOTONIC PHOSPHATE BUFFER AT DIFFERENT pH VALUES

| pH | Calculated half-time for supernatant radioactivity (min) | Uric acid exchange (μM/hr/l red blood cells) | Undissociated uric acid (μM/l) (supernatant) |
|------|--|--|--|
| 7.15 | 13.9 | 273 | 3.33 |
| 7.58 | 32.5 | 116 | 1.55 |

Uric acid concentration 187 μM/l of supernatant. Temperature 22° C. Hematocrit 60 per cent.

Table 2. INFLUENCE OF TEMPERATURE ON URIC ACID EXCHANGE IN HUMAN RED BLOOD CELLS

| Temperature (°C) | Calculated half-time for supernatant radioactivity (min) | Uric acid exchange (μM/hr/l red blood cells) |
|------------------|--|--|
| 37.0 | 8.9 | 485 |
| 16.5 | 52.1 | 82 |

Uric acid concentration 216 μM/l of supernatant, pH 7.0. Hematocrit 60 per cent.

From Table 1 it may be seen that uric acid transport was accelerated with decreasing pH. This increase in velocity could be accounted for by the increasing concentration of undissociated uric acid, indicating that undissociated uric acid may be the only form of uric acid able to be transported through the human erythrocyte membrane.

Results from experiments in which different temperatures were maintained are seen in Table 2, which shows that uric acid exchange increases from 82 μM/hr/l red blood cells at 16.5° C to 485 μM/hr/l red blood cells at 37° C, showing that the velocity of uric acid exchange increased 2.8 times when temperature is increased 10° C. The corresponding value of simple diffusion in the same temperature interval is

0.035. This suggests that at least a part of the uric acid transport into the erythrocytes was undertaken by an active, probably enzymatic system.

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Effect of Pempidine on the *in vitro* Synthesis of Acetylcholine

CORNE and Edge¹, working in these laboratories, found that large doses of pempidine (1.2266 g pentamethylpiperidine), a new ganglion-blocking agent used in the oral treatment of hypertension, caused some reduction in the output of acetylcholine from the perfused superior cervical ganglion of the cat during preganglionic stimulation. The reduction in output was insufficient to account for the complete block in transmission observed, nevertheless an investigation into the possible interference of pempidine with the *in vitro* synthesis of acetylcholine seemed worth while. It has already been shown that the inhibitory effect of pempidine on the breakdown of acetylcholine by acetylcholinesterase is of a low order and the drug cannot be classed as an active cholinesterase inhibitor such as physostigmine¹.

The experimental method adopted for studies on the synthesis of acetylcholine was similar to that used by Hebb² and is based on work by Korkes *et al.*³ An extract of choline acetylase was prepared by suspending an acetone-powder of rabbit brain in cysteine saline solution (3 mgm cysteine/ml of 0.9 per cent sodium chloride) in a concentration of 40 mgm/ml. This was stored in a frozen state in suitable aliquots and centrifuged at 2800 r.p.m. immediately before use. 0.1 ml samples of the extract were incubated at 37° C in a system containing 15–20 units of coenzyme A, 0.08 ml of reaction mixture (containing equal parts of 4 per cent choline chloride and 30 per cent potassium chloride), 0.08 ml of 1.2 per cent crystalline magnesium chloride, 0.14 ml of 1 per cent acetyl phosphate*, 0.12 ml of 3 per cent L-cysteine solution, 0.1 ml of 0.25 per cent phosphotransacetylase* contained in 0.02 M potassium bicarbonate, 0.1 ml of 0.1 per cent physostigmine and water to give a final volume of 1.0 ml. Pempidine and for comparison mecamlamine (3-methylaminosocamphane) were added to individual incubates to give final concentrations of 6.4×10^{-2} to 10^{-5} M and 6.0×10^{-2} to 10^{-5} M, respectively. The above constituents were incubated for 15 min before the addition of the choline acetylase extract to allow acetyl-coenzyme A to form. One hour after the addition of the extract the reaction was stopped by boiling and the acetylcholine content of the acidified and diluted incubates was assayed on a frog rectus abdominis preparation⁴.

At concentrations up to 6.4×10^{-3} M or 6.0×10^{-5} M neither pempidine nor mecamlamine, respectively, had any effect on the enzyme system which produced acetylcholine at a rate of 2.0–2.4 mgm/gm of acetone powder/hr. The method of assay could not be applied when higher concentrations were used.

because the drug inhibited the acetylcholine induced contractions of the rectus abdominus muscle. This effect of direct action on the rectus muscle was in agreement with the findings of Corne and Edge¹ and of Stone *et al*².

Gardiner's³ experiments with a 'hemicholinium' compound (Scheuler's⁴ compound No 3, a hemiacetal containing a choline-like moiety) at a concentration of 10^{-4} M led him to believe that the compound does not inhibit choline acetylase as was first thought but acts on the system which transports choline into the cell and through the mitochondrial membrane. Preliminary work in this laboratory with whole homogenates and intact mitochondrial fractions prepared in the way described by Hebb⁵ indicates that the same phenomenon is not true of pemphidine and mecamlamine at concentrations of 10^{-4} M.

I am indebted to Dr H J Barber and Dr R Wien for encouragement during this work.

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* Samples obtained from the Worthington Biochemical Corporation
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PLANT PHYSIOLOGY

A Kinin in Apple Fruitlets

Two challenging questions in developmental biology are the causes of the induction of cell division, and of the cessation of cell division. In plant tissues cell division may be aroused in response to treatment with diffusible substances collectively referred to as kinins¹. One might enquire whether the meristems are self-perpetuating, through an ability to produce or accumulate such a kinin^{2,3}. In asking this question our aim has been twofold: to learn whether the activation of the meristem is under the control of a diffusible substance, and to attempt to isolate and identify such a substance with the view of providing a means of chemically and possibly commercially, controlling meristematic activity.

The known growth substances occur in minute concentrations in growing tissues. Since primary meristems are small, it would be impractical to try to obtain enough material of this kind to permit possible isolation and identification of an unknown kinin. As a more readily available source of bulk material the apple 'fruitlet' was chosen. In the fleshy receptacle the phases of cell division and cell enlargement are separate in time, up to three weeks after pollination growth is due to increase in cell number, after which cell division ceases and growth is due to cell enlargement^{4,5}.

Apples (*Pyrus malus*, variety Granny Smith) were harvested on October 31, 1958, approximately 14 days after pollination. They were 5-8 mm in diameter and averaged 0.2 gm in weight. The apples were pressure cooked for 2 min at 18 lb/sq in, macerated in water, filtered and the filtrate evaporated to dryness *in vacuo* below 40°C. The residue was taken up in basal medium⁶.

Activities of the crude extract and of subsequent fractions were assayed by examining their ability to induce cell division in blocks of tobacco stem pith in the presence of 10^{-4} M indole-3-acetic acid.

Under these conditions, crude apple extract at concentrations equivalent to 3, 10 or 30 gm fresh tissue/100 ml medium induced cell proliferation (Fig 1). In the presence of indole-3-acetic acid alone there was no cell division, but only cell enlargement. The response to 10 gm/100 ml apple extract was earlier and greater than those due to optimal concentrations of kinetin (10^{-6} M) or coconut milk (6 per cent).

It appears that, as with kinetin, coconut milk and immature maize endosperm the apple extract requires the presence of auxin in order to act. When indole-3-acetic acid is omitted and the native auxin present is removed from the extract by shaking with ether at pH 3 no cell division is induced. Adding indole-3-acetic acid (10^{-6} M) restores the activity.

The kinin activity is not an artefact of autoclaving. This has been shown by making the original extraction in 70 per cent aqueous ethanol concentrating to dryness *in vacuo* below room temperature under sterile conditions, taking up the residue in sterile basal medium containing 10^{-6} M indole-3-acetic acid and dispensing this solution into sterile assay vessels. Activity obtained was comparable with that of extracts made and sterilized by autoclaving.

Dissection of a quantity of fruitlets before making extracts revealed that the kinin activity resided mainly in the fleshy receptacle and to a much lesser extent, per fruitlet, in the ovules.

Disks of cortical tissue excised from receptacles of apple fruit no longer undergoing cell division have recently been stimulated to grow by resuming cell division under the influence of coconut milk kinin and an auxin⁷. We have repeated this work and it has proved possible to replace coconut milk with the

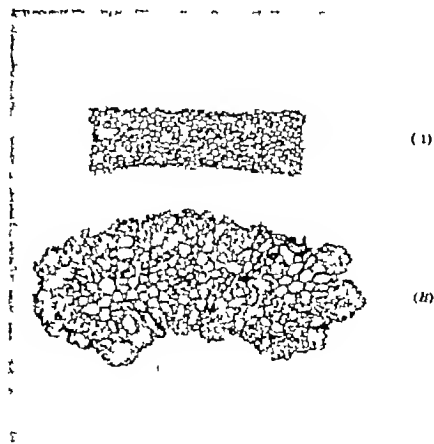


Fig. 1. Transsections of blocks of tobacco stem pith incubated for 14 days (25°C) on: (A) basal medium; (B) basal medium containing apple extract equivalent to 0.3 gm fresh weight/ml plus 10^{-6} M indole-3-acetic acid. Stained with ruthenium red.

kind of the apple fruitlet. Thus we may postulate that this kind is responsible for the cell division occurring in the receptacle of the fruitlet.

Water extracts from larger apples (6-7 cm diameter, 17 weeks after pollination) were tested at concentrations equivalent to 3, 10 and 30 gm fresh tissue/100 ml medium, and little if any activity was detected. Higher concentrations were toxic, so comparison with extracts from fruitlets on a per cell basis awaits purification of the extracts.

Work on the purification of the extract is proceeding.

The apples used were kindly provided by Dr P Geier, of the Division of Entomology, Canberra

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Effects of Auxin and Gibberellic Acid on Growth of *Ulothrix*

THE profound biological effects produced by indoleacetic acid and gibberellic acid, when applied to higher plants, have led many investigators to study their activity on algae. In general, the results of such experiments have not been striking. An excellent review of the literature concerning the effect of auxins on algae is to be found in the studies of Thimann and Beth¹. These workers demonstrated a two-fold increase in stalk elongation of *Acetabularia* in the presence of $5 \times 10^{-5} M$ indoleacetic acid. Further, they were able to show that cap formation was enhanced both in the intact as well as enucleated cells, a conclusive demonstration that indoleacetic acid acts directly on the cytoplasm.

We have discovered that a freshwater green alga, *Ulothrix subtilissima* Rabenh, No 462, obtained from the Culture Collection of Algae, Department of Botany, University of Indiana, shows a dramatic growth response in the presence of either indoleacetic acid or gibberellic acid. An inoculum of cells, 0.7-1.0 mgm air-dried weight, was transferred aseptically to 10 ml of a sterilized modified Bristol's solution² in a 25-ml culture tube. Indoleacetic acid and gibberellic acid (75 per cent pure) were obtained from Nutritional Biochemicals Corporation, and were added to the tubes in a small volume of distilled water to the concentration desired. The use of ethanol to dissolve the indoleacetic acid or gibberellic acid was avoided because of its known growth promoting effect on *Chlorella*^{3,4}. The tubes were placed in inclined racks in front of the light source in order to provide optimal surface area for illumination. Three light sources were tested: (1) a single daylight fluorescent light emitting 25 foot candles at the surface of the alga, (2) a single incandescent bulb emitting 100 foot candles, and (3) normal sunlight from a southern exposure with care taken that sunlight did

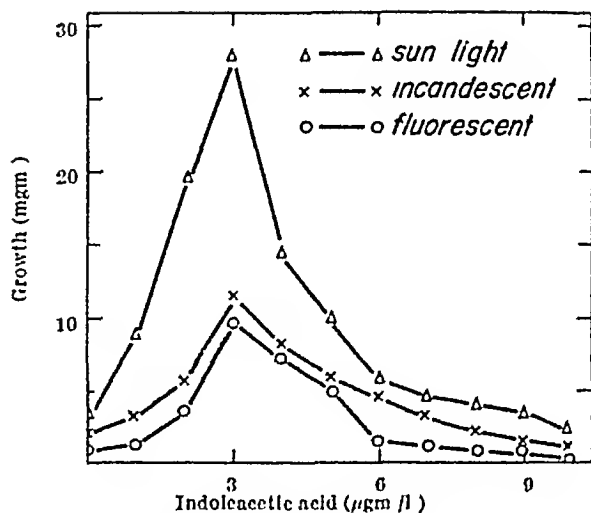


Fig 1 The increase in growth of *Ulothrix* expressed as net increase in air-dried weight as a function of indoleacetic acid concentration at three different intensities of illumination

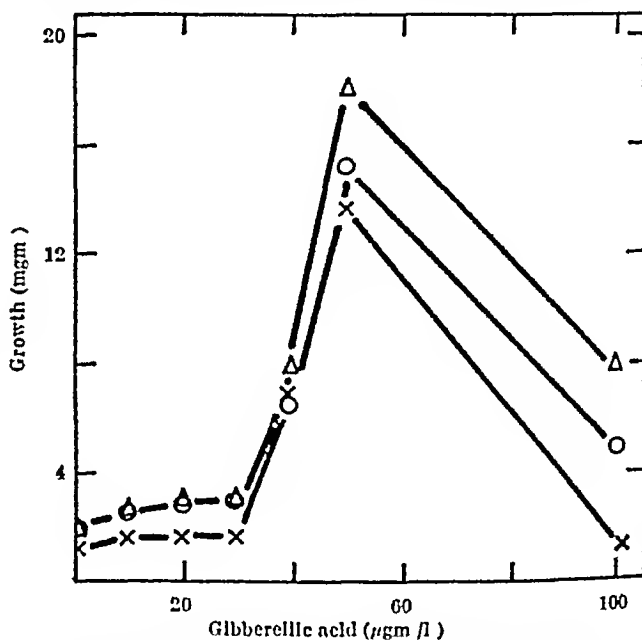


Fig 2 The increase in growth of *Ulothrix* as a function of gibberellic acid concentration at three intensities of illumination. Symbols on graph are the same as in Fig 1

not fall directly on to the tubes. The artificial light was administered continuously, the sunlight was subject to normal diurnal variation with a maximum intensity of 700 foot candles. After 15 days the contents of each tube were passed through a tared membrane filter, rinsed with distilled water, air dried and weighed. Net increase in air-dried weight is reported. Each point on the graphs represents an average of two experiments.

The increase in growth of *Ulothrix* as a function of indoleacetic acid concentration is shown in Fig 1. Under the three light conditions tested it can be seen that the optimal growth is obtained at 3 μgm/l of indoleacetic acid. Higher concentrations of indoleacetic acid produced a characteristic inhibition of growth⁵. The thirteen-fold increase in air-dried weight under sunlight is to be noted. It appears that light intensity is a limiting factor for the cultures grown under artificial light.

The effect of gibberellic acid in growth is seen in Fig 2. Although the growth at optimal gibberellic acid concentration is less than that observed for

indoleacetic acid, it is nevertheless, a seven fold increase when compared with the controls. It should be remembered that the gibberellic acid used is only 75 per cent pure. Intensity and quality of light seem to have little effect on the gibberellic acid response. Similar effects, of less magnitude, have been reported by Provostoli using *Utrix*⁶.

Microscopic examination of cells grown with indoleacetic acid and gibberellic revealed no appreciable change in either size or shape. However there was an increased number of zoospores present. These findings support the concept that the growth substances accelerate cell division rather than cell elongation. Further investigations are in progress to elucidate the mechanisms by which indoleacetic acid and gibberellic acid stimulate the growth of *Utrix*.

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Influence of Kinetin, β -Indoleacetic Acid and Gibberellic Acid on Nuclease Activity of Bean (*Phaseolus vulgaris*) Hypocotyls

RECENTLY Skoog, Miller and co-workers¹ have drawn attention to the role of growth substances in nucleic acid synthesis connected with mitosis and cytokinesis. Silberberger and Skoog² reported that treatment of tobacco pith with indoleacetic acid in sterile culture caused an increase in ribo- and deoxyribonucleic acids. Studies of the cytological effects of auxins and kinins in tobacco callus and stem tissue cultured *in vitro*³ have shown that a delicate balance between indoleacetic acid and kinins may determine all types of growth from cell enlargement to organ formation. The biochemical nature of this interaction, especially its role in nucleic acid metabolism, remains to be determined. This communication deals with the influence of kinetin, indoleacetic acid and gibberellic acid on the activity of deoxyribonuclease and ribonuclease—enzymes concerned in nucleic acid metabolism.

Extracts of hypocotyls from 8–10 days old plants of dwarf bean (*Phaseolus vulgaris* var. Canadian Wonder) grown in the glass house in sand without added nutrients were used to determine enzyme activity. 2 gm. of fresh hypocotyls were ground with buffer solution (5 ml.) in a porcelain mortar and the extract squeezed out by hand through strong cotton cloth. The suspension was centrifuged at 1,500 g for 5 min., the green deposit removed and the clear supernatant fluid used as enzyme solution. Enzyme activities were measured by the methods described by Holden and Pirio⁴. 1 ml. of enzyme solution was used for deoxyribonuclease activity and 0.3 ml. for ribonuclease activity. The mixtures of enzyme solutions and substrates were incubated in 37° C with or without solutions of kinetin, indoleacetic acid or gibberellic acid in a range of concentrations.

The results of typical experiments on kinetin and indoleacetic acid are shown in Tables 1 and 2, where

Table 1 THE INFLUENCE OF KINETIN AND INDOLACETIC ACID ON RIBONUCLEASE ACTIVITY IN UNITS PER GM. FRESH TISSUE OF BEAN HYPOCOTYL

| Concentration of indoleacetic acid ($\mu\text{g./ml.}$) | Concentration of kinetin ($\mu\text{g./ml.}$) | | | | | | | | | |
|---|---|------------------|------------------|------|------|------|-----------------|-----------------|-----------------|-----------------|
| | 0 | 10 ⁻³ | 10 ⁻² | 0.1 | 1 | 10 | 10 ² | 10 ³ | 10 ⁴ | 10 ⁵ |
| 0 | 4.6 | 5.4 | 7.8 | 9.3 | 9.3 | 9.5 | 7.4 | 4.0 | 3.8 | — |
| 10 ⁻³ | 6.5 | — | — | — | — | — | — | — | — | — |
| 10 ⁻² | 6.7 | — | — | — | — | — | — | — | — | — |
| 0.1 | 6.8 | 6.6 | 6.8 | 9.2 | 9.0 | 8.0 | 6.0 | 3.6 | 4.0 | — |
| 1 | 6.4 | — | — | 9.5 | 9.8 | 9.2 | — | — | — | — |
| 10 | 6.6 | 6.8 | 8.0 | 12.3 | 12.3 | 12.5 | 6.5 | 5.8 | 4.4 | — |
| 10 ² | 5.3 | 7.0 | 8.0 | 8.2 | 8.2 | 9.0 | 7.0 | 4.2 | 4.0 | — |
| 10 ³ | 4.4 | 6.4 | 8.2 | 9.6 | 8.8 | 7.3 | 6.5 | 5.0 | 3.8 | — |
| 10 ⁴ | 4.4 | — | — | — | — | — | — | — | — | — |

Table 2 INFLUENCE OF KINETIN AND INDOLACETIC ACID ON DEOXYRIBONUCLEASE ACTIVITY IN UNITS PER GM. FRESH TISSUE OF BEAN HYPOCOTYL

| Concentration of indoleacetic acid ($\mu\text{g./ml.}$) | Concentration of kinetin ($\mu\text{g./ml.}$) | | | | | |
|---|---|------------------|------------------|-----------------|-----------------|-----------------|
| | 0 | 10 ⁻³ | 10 ⁻² | 10 ² | 10 ³ | 10 ⁴ |
| 0 | 0.75 | 0.80 | 1.80 | 2.00 | 1.40 | — |
| 10 | 0.80 | 0.76 | 2.80 | 3.20 | 2.70 | — |
| 10 ² | 0.73 | — | — | — | — | — |
| 10 ³ | 0.70 | 0.75 | 1.60 | 2.50 | 2.00 | — |
| 10 ⁴ | 0.74 | 0.69 | 1.75 | 2.70 | 2.20 | — |

the enzyme activity is expressed in the units defined by Holden and Pirio⁴. There were strong interactions between kinetin and indoleacetic acid in their effects on the activities of both ribonuclease and deoxyribonuclease. Kinetin increased the activities of both enzymes when given alone and still more in presence of indoleacetic acid. The latter alone had no effect, but in presence of kinetin increased the enzyme activities. The maximum effect on ribonuclease occurred with concentrations of 0.1 to 10 $\mu\text{g./ml.}$ of kinetin and 10 $\mu\text{g./ml.}$ of indoleacetic acid which nearly doubled the activity of the control. The maximum effect on deoxyribonuclease occurred with concentrations of 10² $\mu\text{g./ml.}$ of kinetin and 10 $\mu\text{g./ml.}$ of indoleacetic acid, which trebled the activity. Thus kinetin was effective in much lower concentration on ribonuclease than on deoxyribonuclease. Other combinations of kinetin and indoleacetic acid supply had smaller effects, and the highest concentrations tested depressed ribonuclease activity.

Gibberellic acid did not stimulate the activities of deoxyribonuclease and ribonuclease and at very high concentrations (10⁵ $\mu\text{g./ml.}$) slightly depressed both enzymes.

The interaction between kinetin and indoleacetic acid may be the biochemical basis of cytological effects noted by Daa, Patau and Skoog⁵, who found that some deoxyribonucleic acid was formed and some mitoses induced by kinetin without added indoleacetic acid. Conversely, a few cell divisions were induced by indoleacetic acid without added kinetin, whereas no cell division or mitosis was found when neither indoleacetic acid nor kinetin was added⁵. These slight effects were attributed by Skoog and Miller¹ to the small endogenous quantities of these substances. The bean extracts used in my experiments could be expected to contain small amounts of growth substances, but the results show that both kinetin and indoleacetic acid are required for optimal activities of deoxyribonuclease and ribonuclease.

The present results indicate that further biochemical studies of the role of growth substances as stimulants of nucleic acid metabolism would be profitable.

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BIOLOGY

Failure of Corpuscles of Stannius from Winter Flounder (*Pseudopleuronectes americanus*) to Synthesize Adrenocorticosteroids in vitro

THE corpuscles of Stannius, supposedly endocrine glands, are peculiar to teleostean fishes. Their function is uncertain¹, but Rasquin² has suggested that they are concerned in osmoregulation. Unequivocal evidence that the interrenal tissue of teleosts is the homologue of the adrenal cortex^{3,4} strongly suggests that a role other than production of corticosteroids be attributed to the corpuscles of Stannius. In order to supply direct evidence to support this assumption, procedures used in studies on interrenal tissue of *Fundulus heteroclitus*⁴ were applied to corpuscles of Stannius collected from *Pseudo-pleuronectes americanus*. Sixty-one fish, caught in Niantic Bay and Long Island Sound, Conn., in December 1958 yielded 95 corpuscles of Stannius weighing 104.7 mgm. This tissue and 162 mgm of mesonephric kidney which served as control tissue, were separately incubated with tritiated progesterone in a manner previously described⁴.

Each medium was extracted twice with 1/2 vol methylene chloride and the extract washed once with 1/10 vol 0.05 N sodium hydroxide, twice with 1/10 vol water, dried with N sodium sulphate, evaporated *in vacuo* and the dried residue applied to a paper chromatogram. Chromatographic separation followed in the toluene/propylene glycol system. The three areas corresponding to cortisol, cortisone, and corticosterone were eluted and rechromatographed in Bush C system. Four areas closely approximating the positions of cortisol, cortisone, aldosterone, and corticosterone, run in parallel, were eluted together with a paper blank from an area between the origin and cortisol. An aliquot from each eluate was taken for estimation of radioactivity. All areas, even from the controls, contained a small amount of the above background radioactivity. In order to determine whether or not the radioactivity could be accounted for by non-specific impurities, the remaining eluates from the various areas were dried down and applied to paper and chromatographed in the E₂B system⁵. Elution of the areas corresponding to cortisol, cortisone, corticosterone and aldosterone followed, and aliquots were again taken for estimation of radioactivity. Radioactivity in each area was equal to or lower than background radiation. It is concluded from this that the small amount of radioactivity from the previous chromatographic run was accounted for by non-specific impurities, and that within the limitations of the techniques employed the corpuscles of Stannius are not concerned with the production of adrenocorticosteroids.

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Rediscovery of *Bathynella chappuisi* Delachaux in Britain

IN 1927 Lowndes discovered *Bathynella chappuisi* Delachaux in the Bath Oolite quarries at Corsham in Wiltshire¹. Since 1932 this genus has not been reported from Britain although it and related genera have been recorded from the Continent² and Japan³. In February of this year, however, a single specimen of *Bathynella chappuisi* Delachaux was collected in some mud and sand taken from a spring-fed cattle trough in a pasture in Wytham Park, Berkshire (Dr I. Gordon of the British Museum has tentatively confirmed this identification). Further collections, some made at night, have failed to produce any more specimens although the common subterranean amphipod *Niphargus aquilex* Schüdtle has turned up regularly.

Chappuis (in ref. 4) suggested that *Bathynella* occurred only by accident in wells, springs and streams and that the animals had been washed into these habitats from their normal ones, which he has shown to be in the interstitial spaces of the permanent water table. This seems to be the most likely explanation for the occurrence of this animal in a spring at Wytham, where it could have been washed out of the hill. The spring is one of a number situated between the 300- to 400-foot contours along the eastern edge of Wytham Hill. These springs rise between the Coral Rag and Wheatley Limestones above, and the Oxford Clay below. Between these is a thin edge of Lower Calcareous grit sand, the remains of a thicker layer still present in the middle of the hill, that is slowly being washed away from under the Coral Rag cap⁵. The fine sand below a cap of Coral Rag may provide a suitable interstitial habitat for *B. chappuisi* and the continuous trickle of water from the soil above, down through the Coral Rag and out at the springs, may supply enough detritus to sustain a subterranean fauna. It seems unlikely that the animals are living in the pasture soil around the spring as it is very muddy and well trampled by cattle, but only by digging into the Calcareous Grit sand could it be confirmed that there is a permanent aquatic interstitial fauna.

This new record of *Bathynella* is of interest because it is the only known site of living members of the Syncoarida in Britain, the original habitat having now almost certainly been destroyed

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Floral Initiation and Its Relationship to Growth-Stage in Red Clover (*Trifolium pratense* L.)

THE vegetative apex of red clover (*Trifolium pratense*, L.) is hemispherical, cutting off leaf initials by almost vertical divisions on alternate sides and producing internodes by basal elongation. At the beginning of floral initiation the apex enlarges and the florets then begin to appear as swellings near the base on the side proximal to the penultimate leaf. Each floret initial rapidly cuts off a bract initial which enlarges to cover the developing floret. The bract becomes hairy and if it is removed at this stage the developing ovary is exposed as a conical projection about 0.2 mm in length, ringed at the base by cells which eventually develop to form the calyx, corolla and nectaries. The pentamerous symmetry of the

genus is apparent even at this early stage.

The production and extension of stem internodes as well as the formation of leaves appears to be principally regulated by temperature and light intensity. This is instanced by the ability of Aberystwyth S 123 extra late flowering red clover to produce a large number of extended internodes when grown under non inductive day length conditions but in high light intensity and high temperature regimes.

Under favourable day length conditions, floral initiation occurs after the production of a protracted internode number of internodes, the apex enlarging to form a terminal head initial. No exposure to low temperature or short day appears to be necessary in this species. The day length requirement for flowering varies widely, being about 12 hr for early flowering types and in the region of 16 hr for late flowering varieties. It can therefore, be seen that the exact stage at which the apex ceases to be vegetative depends largely upon the variety in question and is the product of the interaction between genotype, temperature and photoperiodic conditions.

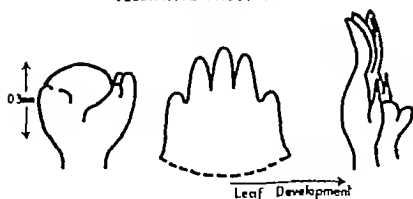
Under field conditions at Aberystwyth English broad red clover which produces 6-7 extended internodes before heading forms a terminal head initial when 1-2 are externally visible usually in mid April. Aberystwyth S 123, a late flowering type producing 14-18 elongated internodes, shows no apparent change-over until 0-7 are externally visible, normally near the end of May.

In conclusion it is suggested that length of day rather than growth stage is the main factor determining the point at which floral structures are initiated.

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VEGETATIVE SHOOT APEX



REPRODUCTIVE SHOOT APEX



EARLY DEVELOPMENT OF SINGLE FLORET



A Lesion of the Follicle and of the Fibre of Wool and its Possible Relation with an Excess of iron in the Forage

It HAS been observed that sheep which graze in certain regions of the Iberian Peninsula for example along the Iberian Cordillera and especially in the Maella zone¹, to which this work refers, lose their wool progressively (Fig 1). Histological analysis shows that the follicular bundles separated by loose, very thin and elastic connective tissue, assume at the beginning a slightly polygonal arrangement. As the alteration advances they assume first a roundish shape and later an elongated one until the follicles become completely independent (Fig 2).

The degeneration of the follicles (Fig 3) is closely associated with this process of modification of the follicular bundles. The secondary follicles are lost because of (a) their projection towards the surface and lack of activity of the bulb in producing a Malpighian epithelial small duct, (b) follicular necrosis and atresia, while Henle and Huxley laminae become horny, and an empty space is formed in the follicle which becomes filled with remains of elastic connective tissue. The degenerative process can lead to an almost complete loss of these follicles. The primary follicles persist even when they have degenerated, as they are lost with difficulty. Their degeneration which begins after that of the secondary follicles takes the following course: (a) separ-

ation and isolation of the follicle, which becomes surrounded by connective tissue, (b) keratinization of Henle and Huxley laminae in their lower part, (c) degeneration of the papilla of the bulb so that an atypical, completely void medulla is formed. The follicles producing this type of fibre (which replaces the wool fibre) remain thus enclosed in the derm. The epidermis decreases considerably in thickness and shows deep microscopic incisions because of the degeneration of the hair. The volume of the sebaceous glands is considerably reduced.

The fact that animals born at Maella, taken immediately to other zones, grow normal fleeces during their whole life and, on the other hand, that sheep taken to Maella from other regions develop the alterations described above, indicate that this

Table 1 ANALYSIS OF SOILS AND FORAGE FROM THE MAELLA REGION

| | Soil | Forage |
|------------|--------------|---------------|
| Sulphur | 18 per cent | 0.20 per cent |
| Iron | 9,891 p.p.m. | 1,026 p.p.m. |
| Molybdenum | 0.95 p.p.m. | 0.37 p.p.m. |
| Copper | 21.16 p.p.m. | 31 p.p.m. |

Average of 24 samples of soil and 60 of forage

process is not due to genetic factors. Moreover, the flocks are kept on a régime of almost permanent grazing, and the soils at Maella have a skeletal and semi-desert character, with about 55 per cent calcium carbonate. The forage is provided by the association *Rosmarinus-Ericum*, typical of the Mediterranean



Fig. 1 (a) Lamb six months old, (b) sheep 4 years old

region. The most frequent plant species are *Rosmarinus officinalis*, *Fumaria thymifolia*, *Brachypodium ramosum*, *Ononis tridentata*, *Thymus vulgaris* and *Cistus clusi*.

These circumstances have led us to consider a possible influence of nutritive factors. G. Gonzalez and J. Garcia¹ reviewed recently the food constituents which have been shown to influence the growth of wool. Of these we selected sulphur, copper, molybdenum and selenium for investigation.

Four groups of three lambs each were dosed by mouth during 14 months with 10 mgm selenium (as sodium selenite), group A, 30 mgm molybdenum (as ammonium molybdate), group B, 10 mgm selenium + 8 gm potassium sulphate, group C, and 30 mgm molybdenum + 10 mgm copper (as copper sulphate), group D, a fifth group was kept as control. After the first seven months the molybdenum of the groups B and D was raised from 30 to 90 mgm daily. It was found that 30 mgm of molybdenum daily as ammonium molybdate do not produce any alteration in the weight and characteristics of the fleece and wool fibre, 90 mgm molybdenum daily provokes a slight diminution of the absolute and relative resistance, and of the extensibility of the wool fibre. Also, this amount of molybdenum produces a loss of crimp in some of the animals, but not in all of this group. The addition of 10 mgm copper, as copper sulphate, to the 90 mgm molybdate counteract these effects. In the selenium groups A and C, the results showed no variation in the weight of the fleece, in the absolute and relative length, or in the crimp and mechanical properties of the wool fibre compared with the controls⁴.

On the other hand, the composition of the soil and of the vegetation, shown in Table 1, indicates an outstanding fact, namely, the abnormally high iron content. In contrast with normal values for sulphur, molybdenum, manganese and copper, the average values obtained for iron were 1,026 p.p.m. in soils and 9,891 p.p.m. in the forage, the ranges being



Fig. 2. (a) Follicular arrangement in perfect polygonal shape, typical of crossed sheep, (b) Isolation of wool hairs. Appearance of skin folds, A.



Fig. 3. (a) Degeneration starting at the base of the wool follicle, A. (b) Premature keratinization of the cuticle of the sheath and of the cuticle of the fibre, with loss of the medullary structure of the fibre.

32-2 000 and 4 400-20 000, respectively. High values were obtained even after the plants analysed had been washed to eliminate soil particles.

The histo-chemical analysis of livers of sheep from Maella during the degenerative process showed by means of a Perls reaction, that there is a large quantity of iron in the sweat glands as well as in the outcrops of the sheath and fibre and in the epithelial scales, this is drawn up by the growing fibres and comes out at the surface.

The possible effects on sheep of ingesting abnormally large quantities of iron, on the general metabolism and the formation of the wool fibre, are under investigation and the results will be published elsewhere.

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In North America I have seen few distribution maps indicating the prevalence of the disease but it is generally considered to be high in south western Quebec the southern part of Ontario and in central Nova Scotia. In all these areas there are abundant limestones in places dolomitic and some granitic rocks.

One other point appears worthy of note: higher than normal quantities of lead are known to occur in these rocks referred to above as occurring in areas where the prevalence of multiple sclerosis is high. The Eocambrian sediments of Norway and Sweden, some granites in Telemark, Norway, the Old Red Sandstones of northern Scotland and many of the limestones of southern Quebec, Ontario and central Nova Scotia are all known to contain significant although not necessarily commercial amounts of lead. Similar rocks in the north-eastern United States and southern Manitoba may likewise be assumed to carry lead. It should also be noted the anomalous amounts of lead may on occasion be accompanied by anomalous amounts of some other elements such as silver, barium, magnesium, and fluorine.

These observations are founded on the published work and personal communications of many workers in the fields of medicine and geology. Acknowledgement will be made to these authors in a paper now being prepared for publication.

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PATHOLOGY

Geology and Multiple Sclerosis

Most areas where there is a high prevalence of multiple sclerosis coincide in a highly suggestive fashion with areas where glaciation has played an important part in providing parent material for soils. However, the converse is certainly not true: all glacial soils cannot be correlated with areas where the prevalence of multiple sclerosis is high. Maps showing the distribution of multiple sclerosis cases in Northern Ireland, south-eastern Ontario, Sweden, and Denmark are alike in one respect—they all bear a remarkable resemblance to maps illustrating the distribution of boulders or geochemical anomalies in any map prepared for the purpose of searching in a glaciated area for buried artefacts.

A consideration of some epidemiological maps reveals the following facts. In Scandinavia and northern Scotland where on the whole the prevalence of multiple sclerosis is high there are at least five islands where it is significantly low, namely, (1) Gäddede province north of Gäddede, Sweden, (2) Södermanland province, Sweden, (3) large sections of Halland, Göteborg and Bohus Provinces, Sweden, (4) the Norwegian coastal provinces of Rogaland, Hordaland, Sogn og Fjordane and Møre og Romsdal, (5) the Outer Hebrides of Scotland. With the solitary exception of Rogaland and southern Hordaland all the above areas are substantially underlain by old gneisses, which in a general map of Scandinavia are mapped as being similar. Conversely, if we note areas where prevalence is high we find an entirely different set of geological formations, namely, in Norway and Sweden either Eocambrian sediments or granitic rocks and in northern Scotland by Old Red Sandstones and granitic rocks.

An Experimental Enterococcal Pylonephritis in Mice

In the course of studying the animal pathology of various bacterial species obtained from human infections, we noted that certain strains of enterococci localized and persisted in the kidneys of mice subsequent to intravenous challenge. Moreover this enterococcal pyelonephritis could be induced with regularity in mice simply by intravenous injection and did not require kidney traumatization as described by Braudo et al.¹ for the initiation of enterococcal kidney disease in rats. Since enterococci, particularly *Streptococcus faecalis*, are frequently associated with urinary tract infections in man,^{2,3} we felt that it would be pertinent to conduct further experiments on the murine disease. This communication presents our initial observations on certain bacteriological aspects of experimental enterococcal pyelonephritis. Additional results, including the histopathological characteristics of this mouse infection will be reported elsewhere.

The strain of *Str. faecalis*, designated 'MGH 2' which was employed in our studies was submitted by Dr. B. A. Waisbroo of the Milwaukee County General Hospital, Wisconsin, shortly after its isolation from the urine of a patient. This organism was maintained on ordinary blood agar and apparently did not require passage through mice to sustain its virulence. The growth from a 6-8 hr. culture in trypticase soy broth at 37° C. was diluted with an equal volume of saline and 0.2 ml. was injected into the dorsal tail vein of each mouse. Male albino CF-1 mice 4-5 weeks old and weighing approximately 16 gm. were used in the

hopeless to resume the search for tumour specific antigens were it not for two circumstances. The first of these is the work of Zilber^{1,2} and others in the U.S.S.R. who by means of anaphylactic reactions in the guinea pig have provided strong evidence for the existence of tumour-specific antigens. The second is the phenomenon of immunological suppression, including acquired tolerance for homologous transplants³ and suppression of specific antibody response⁴ by the introduction of tissues or simple antigens into embryonic or early post-natal mammals. The present experiments were based on the assumption that if one could suppress antibody formation against normal tissues as suggested by the work of Feldman and Yaffee⁵, it might be possible to produce antibodies directed exclusively against the specific antigens of tumours—providing such antigens exist. Our results thus far encourage the conclusion that the immunologically suppressed animal provides the long sought means of producing antisera capable of discriminating between tumours and normal tissues.

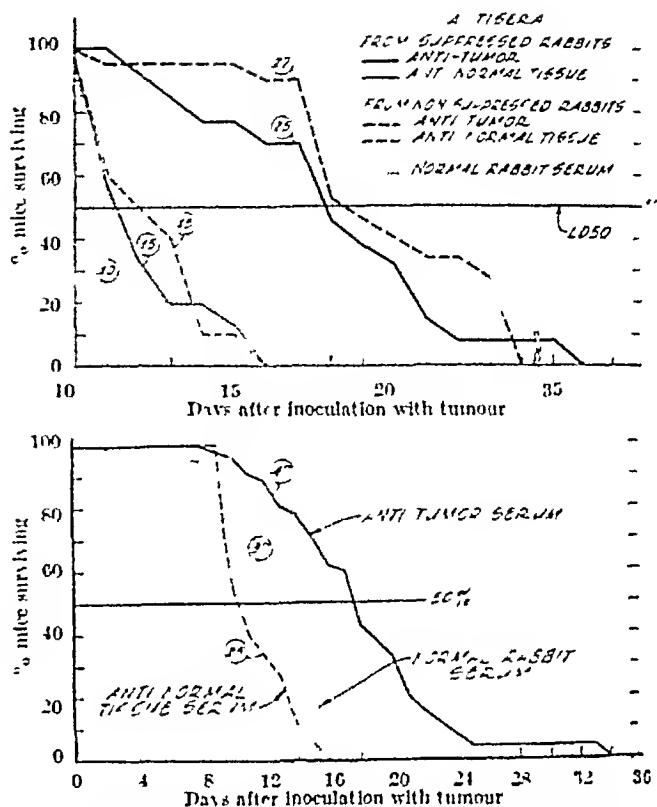
The Ehrlich ascites tumour was used and maintained in closely inbred C3H mice. The tumour is antigenically so like the normal tissues of C3H mice that antisera directed against it are also highly toxic for the normal mouse. The production of antisera of increased toxicity for the Ehrlich tumour without corresponding toxicity for normal C3H tissues was demonstrated by the following four-step method.

(1) Within 12 hr after birth New Zealand and Dutch rabbits were given the first of a series of suppressing injections composed of homogenized normal tissues (unperfused spleen, liver, lung, thymus and mammary gland) taken from 24 or more mice. Injections were then continued for 21 days, each animal receiving a total of 1.55–1.98 gm wet weight of homogenate containing 380–496 mgm protein. Uninjected litter mates served as controls.

At 12 weeks of age sera from the injected (presumptively suppressed) animals and from the controls were injected into mice inoculated with a standard dose of Ehrlich ascites tumour. Neither type of serum had any perceptible influence on the growth of the tumour, which killed the mice within the usual time (LD 50, 12 days). Skin tests were carried out on the rabbits by injecting supernatants from the normal tissue homogenate and the Ehrlich tumour. 8 of the 11 presumptive suppressed rabbits showed no cutaneous reaction.

(2) The 11 presumptive suppressed rabbits and 6 normal controls were then injected intraperitoneally with 200 mgm wet weight of the same normal tissue homogenate previously injected with the aim of suppressing the antibody response. The 3 rabbits with positive skin test and one with negative skin died 8–12 days after injection, with autopsy findings indicative of serum sickness. Sera obtained from the survivors at 5 and 14 days after injection were tested in tumour inoculated mice and showed no effect upon the growth of the tumour as indicated by the average survival time of the mice. Skin tests of the rabbits, using supernatants from both normal and tumour tissue, were now negative in all suppressed rabbits and mildly positive in the 6 controls.

(3) The suppressed rabbits, which had by this time failed to show anti-tumour sera in two successive tests, were now divided into two groups. (A) Three rabbits received each a total of 280 mgm protein of normal tissue homogenate and (B) four rabbits received each 260 mgm protein of tumour. The normal (non-suppressed) rabbits received equivalent amounts of



Figs 1 (above) and 2 (below) Survival of mice inoculated with Ehrlich ascites tumour after a single dose of rabbit anti-tumour serum administered shortly after the tumour. In Fig 2 the results using anti-tumour and anti-normal tissue sera are grouped together irrespective of their origin in suppressed or non-suppressed rabbits.

(C) normal tissue and (D) tumour. The amounts of tissue indicated were distributed among 6 injections given on alternate days. All rabbits were bled on the 5th and 14th days after the last injection and the sera used fresh or stored at 4–6° C without preservative. The antisera obtained at 14 days were tested for anti-tumour activity by injection of 0.2 ml intraperitoneally per mouse inoculated one half hour previously with a standard tumour dose (8×10^6 cells in 0.2 ml).

As shown in Fig 1, the single dose of anti-tumour serum, whether from suppressed or non-suppressed rabbits, protected the mice to a significant degree. On the other hand, antisera against normal tissues had little effect or seemed to decrease survival in comparison with controls given normal rabbit serum or saline. The reproducibility of these results is indicated by another experiment summarized in Fig 2 in which

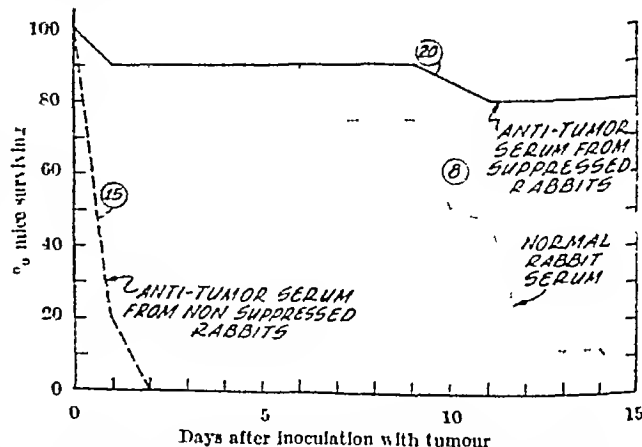


Fig 3 Effects of multiple doses of anti-tumour sera derived from suppressed or non-suppressed rabbits upon the survival of tumour inoculated mice.

mice receiving anti tumour or anti normal sera are grouped together, irrespective of the origin of the sera from suppressed or non suppressed animals. The tendency of anti normal sera to decrease survival is again evident.

(4) The striking advantage in the use of anti tumour sera produced by suppressed animals is shown in Fig 3. In this experiment multiple doses of serum were given in the attempt to enhance the survival of tumour inoculated mice. Three doses each of 0.4 ml. were injected during the first few days after inoculating the tumour and in some instances, depending on survival three others on days 7, 8 and 9. The antisera from non suppressed rabbits proved uniformly lethal within 48 hr, since the tumour never kills mice within this short period, death must be attributed to the toxicity of the antiserum for C3H mice. In conclusion supported by autopsy. Mice receiving normal rabbit serum were all dead within 15 days with abdomens distended by tumour growth. In contrast mice receiving anti tumour sera produced by suppressed rabbits showed 80 per cent survival on the 16th day.

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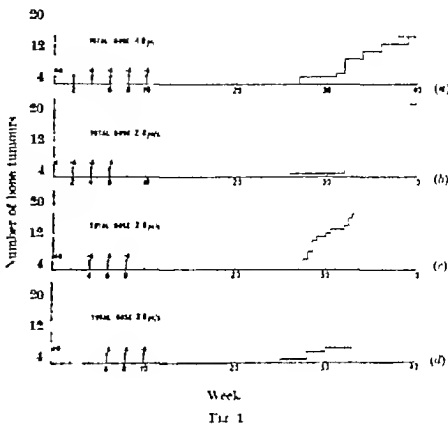
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An Effect of Dose Fractionation on the Incidence of Bone Tumours using Radioactive Phosphorus

CARCINOGENIC studies with rats using 'bone seeking' radioactive isotopes have shown that if the isotope is administered in several doses at intervals from a few days to one month a larger number of bone tumours develop than for a single injection of the same quantity of isotope.^{1,2} This increase in the number of tumours is due to an increase in the probability of tumours developing and also to a reduction in the mortality of the rats from other causes both before and after the time of appearance of the first tumour.

Similar results have been obtained using radioactive phosphorus phosphorus 32, (Bensted *et al.*, to be published). With this isotope the injection of 1.0 $\mu\text{g/gm}$ body weight followed by five doses of 0.6 $\mu\text{g/gm}$ (total dose 4 $\mu\text{g/gm}$) at intervals of two weeks resulted in 13 rats in a group of 15 developing bone tumours, Fig 1a. The two rats without tumours died at three months, one while under other anaesthetics. The tumours appeared between 26 weeks and 39 weeks after the first injection and a high proportion of the animals had more than one tumour.



In order to determine to what extent the various repeated injections contribute to the increased tumour incidence in smaller total dose of 2.8 $\mu\text{g/gm}$ phosphorus 32 was administered as 1.0 $\mu\text{g/gm}$ followed by three injections of 0.6 $\mu\text{g/gm}$. In one group of 20 rats these injections each of 0.6 $\mu\text{g/gm}$ were given at 2, 4 and 6 weeks respectively after the first injection. In a second group of 20 rats the injections were given at 4, 6 and 8 weeks and in a third group at 6, 8 and 10 weeks. The times of appearance of bone tumours are shown in Fig 1b, 1c and 1d. At 30 weeks the number of tumours in the three groups of 20 rats was 1, 10 and 4 respectively and at 33 weeks 3, 17 and 4. This demonstrates that the mean time of tumour development may be altered considerably by changes in the timing of the injections for the same total dose of phosphorus 32. Since tumours are still appearing in the surviving animals it is not yet possible to say whether there will be a difference in the final tumour incidence. Up to date of these 60 animals only one rat has died without developing a tumour; this animal was in the second group of rats and the death occurred after the second injection before there was any reasonable possibility of a tumour having developed. The present data are not sufficient to determine the effectiveness of the individual injections in producing bone tumours. Nevertheless they do suggest that injections at 4, 6 and 8 weeks after the first injection are particularly effective while those at 2 and 10 weeks have little effect or may even inhibit tumour formation.

Discussion of the results solely in terms of the timing of the injections is likely to be superficial since the distribution of the radiation dose within the bone varies in a complex manner with the timing of the injections. These complexities arise in part from the non uniform distribution of the isotope and the continued growth of bone during the period of injection. The type and number of cells being irradiated at any particular time will also depend on the amount of previous damage produced and on the extent to which repair mechanisms are operating. In order to investigate these effects further, the distribution of the radiation dose in bone is being determined by means of thick section autoradiography. The histological changes occurring with the different dosages

schemes are also being studied and will be reported elsewhere

I should like to thank Dr L F Lamerton for his interest and support in this work

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BACTERIOLOGY

Distribution of Nucleic Acids among Different Stable L Forms of *Proteus P 18*

In previous work, we have studied some enzymatic activities of various morphological kinds of stable L forms derived from *Proteus P 18* (ref 1) These enzymatic activities were highest in the fraction of small size (fraction 3, 1.9–3.8 μ) and lowest or absent in fraction 4 ($\leq 0.95 \mu$) containing the smallest forms invisible with the phase-contrast microscope

We decided to inquire into the distribution of ribo- and deoxyribonucleic acids in the various L forms separated by differential ultra centrifugation Four groups of different sizes were used fraction 1, 7.6–11.4 μ , fraction 2, 3.8–7.6 μ , fraction 3, 1.9–3.8 μ , fraction 4, $\leq 0.95 \mu$ (ref 2)

L forms are grown suspended in a hypertonic medium by a technique already described³ After separation of the particles of different sizes², the micro-organisms are freeze dried and crushed in cold ether In the case of fraction 4, we examined separately the whole fraction and the fraction passing through a Chamberland 3L3 filter The acid-soluble phosphorus is removed by 7 per cent trichloroacetic acid and the lipids are extracted by Bloor's method The residue is hydrolysed using Schmidt and Thannhauser's technique⁴ In the acid-insoluble fraction of the alkaline digest, deoxyribonucleotides are extracted by normal perchloric acid at 80°C during 30 min and deoxyribose is assayed by the Burton modification⁵ of Dische's technique⁶ In the acid-soluble part of the alkaline digest, ribonucleotides are determined by the orcinol procedure of Bial modified by Mojbaum⁷ The results were confirmed by the use of phloroglucinol⁸ and assay of ribonucleic acid phosphorus after adsorption of the ribonucleotides on a charcoal column followed by elution with alcohol-ammonia

Results are given for nuclear phosphorus (Table 1) The reference curve for deoxypentose has been established with a thymus deoxyribonucleic acid purified to Kay, Simmons and Dounce's methods⁹, that of ribose with a yeast ribonucleic acid purified by Smith and Markham's method¹⁰

Table 1 shows that fraction 3 has the highest ribonucleic acid content 1943 $\pm 125 \mu\text{gm}$ phosphorus, then come fractions 2 (1418 $\pm 222 \mu\text{gm}$) and 1 (1132 $\pm 99.7 \mu\text{gm}$), followed by fraction 4 obtained by centrifugation (439 $\pm 81.7 \mu\text{gm}$) and finally fraction 4 by filtration (235 $\pm 28.3 \mu\text{gm}$)

The deoxyribonucleic acid content is highest in fractions 1 (520 $\pm 40.9 \mu\text{gm}$) and 2 (485 $\pm 75.1 \mu\text{gm}$),

Table 1 DISTRIBUTION OF NUCLEIC ACIDS AMONG DIFFERENT L FORMS OF *Proteus P 18* BACILLUS
Results are reported in μgm of phosphorus for 100 mgm of dehydrated weight

| | Ribonucleic acid phosphorus | Deoxyribonucleic acid phosphorus | Col 2/Col 3 |
|---------------------|-----------------------------|----------------------------------|-----------------|
| Whole | 1450 \pm 41.0 | 515 \pm 10.13 | 2.83 \pm 0.10 |
| Fraction 1 | 1132 \pm 99.7 | 520 \pm 40.9 | 2.18 \pm 0.14 |
| Fraction 2 | 1418 \pm 222 | 485 \pm 75.1 | 2.93 \pm 0.41 |
| Fraction 3 | 1943 \pm 125 | 71 \pm 7.8 | 27.2 \pm 1.73 |
| Fraction 4 | 439 \pm 81.7 | 61 \pm 6.4 | 7.22 \pm 0.35 |
| Fraction 4 filtered | 235 \pm 28.3 | 389 \pm 21.5 | 0.73 \pm 0.05 |

much lower in fractions 3 (71 \pm 7.8 μgm) and 4 (61 \pm 6.4 μgm) In contrast, there is a high deoxyribonucleic acid in those elements of fraction 4 which pass through the Chamberland filter (389 \pm 21.5 μgm) It follows that the ratio of ribo- to deoxyribonucleic acid is lowest in the filtered fraction 4 (0.73 \pm 0.05) which shows the lowest enzymatic activity The ratio is highest in fraction 3 (27.2 \pm 1.73) which possesses the highest enzymatic activity¹

In summary, the distribution of ribo- and deoxyribonucleic acids differs in L forms of different sizes It is noteworthy that the ratio of ribo- to deoxyribonucleic acid is highest in fraction 3 which is enzymatically very active and lowest in the filtered fraction 4 However, what is most striking is the high deoxyribonucleic acid content in the filtered particles of fraction 4

We thank Prof R Tulasne, professor of bacterial biology in the Faculty of Medicine Strasbourg, for invaluable advice during this investigation

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ANIMAL PSYCHOLOGY

Effect of a Signal Contingent upon an Avoidance Response

CONVENTIONAL shock-avoidance training usually takes the form signal-shock-response which becomes signal-response when the appropriate behaviour is learned This operant technique has been shown to produce faster learning than the classical procedure in which the unconditioned stimulus (shock) inevitably follows the conditioned response^{1,2} and is most effective when the response terminates the signal as well as avoids the shock^{3,4}

Under this latter condition two events occur: an exteroceptive stimulus change precedes a potentially noxious event, and an exteroceptive stimulus change follows the response which escapes from or avoids this event. These changes are almost invariably the onset and offset of the same stimulus. It is widely thought that both these events are necessary for successful avoidance learning to come about.^{1,2} The stimulus onset preceding shock is said either to arouse fear, or to become aversive, and the stimulus offset contingent upon the response is said to be reinforcing either by virtue of reducing fear or simply through the removal of the aversive stimulus.

It has been shown, however, that avoidance responses can be learned when there is no exteroceptive stimulus change contingent upon these responses.³ On the other hand Kamrin⁴ has demonstrated that avoidance learning is the poorer the greater the time-interval between the response and the offset of the warning stimulus, and has interpreted this finding in terms of delay of secondary reward. It is equally reasonable, however, to interpret his results by reference to the degree of stimulus change contingent upon the response.

It is possible to fractionate the discriminatory and reinforcing effects of the termination of a warning signal by introducing a second stimulus contingent upon the occurrence of an avoidance response, while leaving the original stimulus unaltered for a certain period. To this effect we utilized a procedure similar to that of Kamrin except that a second stimulus came on when an avoidance response was made, and was terminated at the same time as the warning stimulus. Twenty-four naive male albino rats from 60-120 days old were divided into four equal groups (I, II, III, IV) and trained to avoid shock (110 V, 100 k Ω limiting resistance) by turning a small treadmill within 5 sec after the onset of a weak light. Each animal was trained in a single session until it made two avoidance responses. Inter-trial interval times were 50, 60 or 70 sec according to a predetermined random schedule with a mean of 60 sec.

When shock was not avoided the escape response terminated both shock and light immediately for all animals. When shock was avoided by experimental animals (groups I and II) the avoidance response turned on a buzzer. Both light and buzzer were terminated after about 0.5 sec for group I, and after 10 sec for group II. No buzzer accompanied avoidance responses made by groups III and IV. The light was terminated immediately after these responses

for group III, and after 10 sec for group IV.

Within the first ten trials behaviour was 'shaped' to facilitate escape learning, that is to say, shock was terminated when an animal approached the treadmill irrespective of whether it turned it or not. All animals learned to escape promptly within these ten trials, and thereafter only treadmill turning served to avoid or escape from shock. Spontaneous inter-trial responses were allowed, but served no purpose.

Table 1 shows the trial on which each animal made its first avoidance response and the number of subsequent trials prior to the second avoidance of shock. As differential treatment between the groups began when shock was first avoided, the number of shocks between the first and second avoidance responses provides a measure of the effect of one application of the differential treatment. Such a measure is the cleanest test of the effect of post-avoidance conditions because behaviour on subsequent trials is a consequence of a mixture of shock and no shock trials temporally distributed in different ways for different animals.⁵ Application of the Mann-Whitney *U* test to the results in Table 1 yields the following conclusions: (a) there is no significant difference between the four groups on the number of trials to the first avoidance response; (b) significantly fewer ($P < 0.05$, one tail) shocks intervened between the first two avoidance responses of the animals in group III than between those of the group IV animals, (c) significantly fewer ($P < 0.05$, one tail) shocks intervened between the first two avoidance responses of the animals in group II than between those of the group IV animals, and (d) the number of shocks between the first and second avoidance responses of the animals in groups I and II do not differ significantly.

As there were no significant differences between the trials to first avoidance between the four groups it is supposed that no systematic variations between the groups occurred prior to this point. The fact that significantly fewer shock trials intervened between the first and second avoidance responses when these responses immediately terminated the pre-shock signal than when the offset of this signal was delayed by 10 sec confirms earlier findings that immediate termination of a warning signal facilitates avoidance learning. The finding that this difference vanishes when a second signal immediately follows the avoidance response in both cases suggests that the effects of different delays before termination of the warning signal are not directly dependent on this event. Those animals given a buzzer immediately after making an avoidance response performed equally well whether the pre-shock stimulus was immediately terminated or not. The superiority of the 10 sec delay group with buzzer over the 10 sec delay group without buzzer leads to the same conclusion.

Although avoidance learning is facilitated by the termination of the warning stimulus contingent upon the performance of the correct response it is not the termination of this stimulus *per se* that is crucial but the changed stimulus conditions after the response has been made. The effects upon the efficiency of avoidance learning seem to be about the same whether avoidance behaviour changes the pre-response stimulus itself or not, so long as some stimulus change

| Animal | First avoidance | Trials between | Animal | First avoidance | Trials between |
|--------|-----------------|----------------|--------|-----------------|----------------|
| I 2 | 0 | 1 | III 2 | 5 | 1 |
| I 2 | 0 | 4 | III 2 | 8 | 1 |
| I 3 | 5 | 1 | III 3 | 31 | 1 |
| I 4 | 30 | 3 | III 4 | 6 | 1 |
| I 5 | 4 | 0 | III 5 | 9 | 3 |
| I 6 | 8 | 1 | III 6 | 4 | 0 |
| II 1 | 0 | 0 | IV 1 | 4 | 3 |
| II 2 | 2 | 0 | IV 2 | 6 | 16 |
| II 3 | 8 | 0 | IV 3 | 0 | 15 |
| II 4 | 8 | 0 | IV 4 | 13 | 4 |
| II 5 | 17 | 6 | IV 5 | 4 | 0 |
| II 6 | 2 | 0 | IV 6 | 0 | 2 |

In the Animal column Roman numerals refer to training groups. Arabic numerals to the individual animals in those groups. First avoidance is the trial of which the first avoidance response was made and 'Trials between' is the number of escape trials between the first and second avoidance responses made by the respective animals.

follows the response. Avoidance behaviour cannot, therefore, be simply interpreted in terms of the secondary reinforcing effects of the removal of an exteroceptive warning stimulus, but must make reference to the stimulus compound both before and after a response is made.

We wish to acknowledge our indebtedness to the Rockefeller Foundation which supported this investigation through a grant to the Arts and Sciences Division of the American University of Beirut.

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ARCHAEOLOGY

Pleistocene Climatic Significance of Calcretes and Ferricretes

CALCRETES and ferricretes are widespread features of African soils. They have attracted attention from both soil specialists and archaeologists, for they frequently occur in soil profiles containing Stone Age artefacts and fossils. The calcretes and ferricretes have been generally assumed to have climatic and stratigraphic significance. Archaeologists and geologists have dated them in terms of associated artefacts or fossils, just as other geological horizons are dated by *in situ* cultural or organic objects. R. F. Flint¹ has summarized recent views on the climatic interpretation of ferricretes and calcretes. Flint suggests that ferricrete formation requires rainfall 'above a certain minimum, stating that ferricretes "seem to indicate Pleistocene climates that were wetter than those of to-day, provided Pleistocene age is established", while calcretes imply low rainfall, perhaps less than 18 in (45.6 cm) per annum.

An interpretation of this kind was given to the soil profile at the Skoonheid 1520 Later Pleistocene archaeological site, long 29° 27' E, lat 24° 7' S, 40 miles (64.7 km) east of Potgietersrus in the Central Transvaal. Here an erosion gully has exposed Stone Age artefacts in a way frequently found in Africa. A number of archaeologists and geologists agreed with the observation and climatic deductions set out by one of us², but soil specialists found they could not accept the interpretation. Accordingly, we returned to the site in May-June 1959 for a fortnight's field study. We excavated a number of sections in the gully and examined borehole profiles drilled for the purpose adjacent to the gully.

The excavations showed that ferricrete concretions are scattered throughout the profile, though they are concentrated in the horizons given in ref. 2. Contrary to the views expressed there, these 'ferruginized zones' have no Pleistocene stratigraphic or climatic significance. For example, 'Ferruginized Zone 2' both underlies and overlies the same Pleistocene Stone Age horizon at different parts of the site. 'Ferruginized Zones 2 and 3' must have formed

recently, when the entire soil profile was established but before erosion of the present gully. The occurrence of all 'ferruginized zones' at the site in Stone Age horizons is purely coincidental, for they formed tens of thousands of years later than the dates of the artefacts they encase.

Ferricrete may be seen actively forming in some parts of the gully floor to-day, where water seepage along the granite bed-rock surface is producing a sesquioxide sheet or ferricrete in the overlying permeable sediments under impeded local drainage³. This recent ferricrete has cemented ancient Earlier Stone Age gravel in other parts of the site, thus—assuming a quite misleading age. Elsewhere on the site, excavation proved that the same gully floor ferricrete, named 'Ferruginized Zone 1' in ref. 2, lies several feet above the Earlier Stone Age gravels, clearly showing its more recent origin. In ref. 2 it was assumed that 'Ferruginized Zone 1' formed immediately after Earlier Stone Age but its origin post-dates formation of the present gully. In June 1959, at the height of the local dry season, ferricrete concretions appeared to be forming continuously in one part of the gully floor where nocturnal water seepage to the surface ceased during the day.

Like ferricrete concretions, calcrete concretions also occur throughout the profile, but not in the limited horizons stated in ref. 2. Calcrete formation has continued in the less permeable horizons throughout the history of the profile, from Earlier Stone Age times to the present day, concurrently with ferricrete formation. To-day the area receives 21 in (53.25 cm) of rainfall per annum, while daily average temperature varies from 80° F (27° C) to 36.6° F (2.6° C), so at Skoonheid it is clear that ferricretes and calcretes reflect soil climate, not external climate. Wet conditions are necessary for the formation of ferricretes, but these occur within the soil itself, not above it. Soil evidence at Skoonheid 1520 therefore gives new evidence of the wide range of variation of conditions favouring ferricrete and calcrete development. Finally, study of the stratigraphy of the site in relation to present river action in the nearby Chumies River suggests that sedimentation on the site may have been controlled by the nearby gap in the Strydpoort Mountains known as Chumiespoort, and need have no relation to Pleistocene climatic change. The climatic interpretations and correlations set out in ref. 2 are accordingly withdrawn. The Pleistocene climatic and stratigraphic value of the calcretes and ferricretes at the Skoonheid 1520 profile have now been placed in truer perspective. There is little doubt that archaeological interpretations of these features elsewhere in Africa should be reviewed in this light.

The work at Skoonheid is part of the Archaeological Survey's Cave of Hearths-Makapan Valley project generously supported by the Wenner-Gren Foundation for Anthropological Research.

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EXPANSION OF EDUCATIONAL AND TRAINING FACILITIES IN BRITAIN

WHEN moving the second reading in the House of Lords on April 28 of the Factories Bill, which amplifies and amends the Factories Act, 1937, the Earl of Dundee pointed out that it empowered the Minister, under Clause 25, to improve his advisory services by the collection of information, the investigation of problems of health, safety and welfare, including the establishment of laboratories not only for research but also as Mr Ian MacLeod had explained in the House of Commons, for wider purposes and the dissemination of the results to industry. The Bill, in fact, constituted a new departure in factory legislation and he emphasized the constructive and co-operative aspect of the work of the factory inspectorate. There are now 409 inspectors and it is hoped to have 445 very soon, but quality and experience are regarded as more important than numbers. Other innovations in the Bill which received the Royal Assent on July 29 empower the Minister to make special regulations as to the measures to be taken in factories to reduce the risk of fire including regulations prescribing requirements as to the internal construction of a factory and the materials to be used, and call for the provision and maintenance in every factory of appropriate and readily available means for fighting fire.

In the debate Lord Wilmot of Solihull remarked that the Bill is an outstanding example of Parliament at its best in the active co-operation of Government and Opposition in pursuit of a common aim. Lord Stonham expressed the hope that in promoting a partnership of safety in the factories, the Government would greatly strengthen the provisions for consultation and research into safety and suggested that full information was a prerequisite of confidence. Lord Taylor estimated that sickness and accident in industry in Britain represent a loss of £780-£1,000 million a year mostly through minor illness and minor accident, and he stressed the importance and value of an efficient industrial health service, including such a co-operative and mobile industrial health service as had been created at Harlow. The Earl of Dundee particularly welcomed this suggestion as providing a solution to the problem of making trained assistants available to the smaller type of factory.

The Bill obviously strengthens the contribution which science can render to industrial health and safety. On the second reading of the Bill in the House of Commons last November, the Minister of Labour and National Service emphasized the critical importance of the strength and efficiency of the factory inspectorate and this was recognized on all sides. Mr Robert Carr, however, directed attention to the way in which the growing complexity of industry has increased the difficulty of progress simply by enforcement. It has become more and

more impossible for a general inspectorate to possess all the technical qualifications needed to cover the whole range of industry in its area. With all the help it can draw from a more or less centralized and specialist branch, to which we must look increasingly for encouragement and advice for major advances in the future, we are once again reminded of the importance of the continual expansion of education and training facilities in Britain.

Three other recent debates have also stressed the importance of this factor, and particularly the need to implement the recommendations of the Carr Report on recruitment and training of young workers in industry. Intervening in the debate on secondary education in the House of Lords on February 26 Lord Rochester urged that the employment of young people, and particularly their training as apprentices should be regarded just as much a part of their education as that which they receive at school, and that before steps were taken to raise the school leaving age further, the possibility of industry absorbing them all at any one time each year instead of three times as at present, should be examined. Lord Rochester thought that to limit intake to one occasion in the year might in practice prove a retrograde step even to the technical education of the boys, but he urged that from the point of employment the problem is much too important to be handled without the closest consultation both with the trade unions and the employers.

That aspect was also stressed in a debate on the effects of automation, on a motion of Mr F. Lee in the House of Commons on May 1. Mr Lee's motion, recognizing the need for British industry to keep abreast of modern production methods, and also the need to allay fears of heavy unemployment, urged an intensive study of the probable consequences of automation and that the Government should invite industry to co-operate in introducing the necessary changes with a minimum of hardship to its employees and in supporting the motion Mr Austen Albu emphasized the bearing of technical education. Mr MacLeod, in his reply, referred to the survey which had been made by the Department of Scientific and Industrial Research in 1954 and to the general endorsement of the conclusions of the report in July 1956 by the National Joint Advisory Council. A subsequent inquiry by the Board of Trade, the results of which were published in the *Board of Trade Journal* of February 1958, suggested that automation would tend to decrease the number of unskilled labourers but increase the number of skilled technicians of all kinds. Firms did not expect automation to lead to any severe reduction in the size of their labour force, partly because that force would be re-deployed substantially within the factory, and partly in consequence of an increased level of

activity Mr MacLeod believes, however, that increase in apprenticeship training is the responsibility of industry, and that the Government can only indirectly stimulate that. He referred to the studies of technical change which the Department of Scientific and Industrial Research is already sponsoring and thinks that this work on the social aspects of technological innovation might be better co-ordinated and given more publicity. He undertook to raise this question with the National Joint Advisory Council.

In opening a debate on youth employment problems on April 30, Mr A Robens suggested that the future of Britain is based on the development of our technical skills, and that we must take firm action to ensure that our people are highly skilled and able to make full use of the possibilities offered in electronics, nuclear power and transfer machines. Our educational programme, including the development of technical education, contemplates an output of about 20,000 scientists and technologists a year by 1970, and to make full use of the technologists some five or six technicians are required for each technologist. The production of these technicians and craftsmen is regarded by Mr Robens as the key problem, and to meet the needs of the increased number of school-leavers we should be taking about 135,000 into skilled apprenticeship a year. The evidence of recent months, he asserted, is that there are insufficient vacancies for boys who have the necessary educational qualifications, and he believes that only by persuasion or legislation will industry be induced to provide the extra training places required, many of which would be surplus to present requirements. He said that the trade unions have a responsibility here—in the printing trade and in the shipbuilding industry the number of apprenticeships is strictly limited.

Mr Robens advocated re-examination of the length of time required for an apprenticeship and challenged the practice of restricting entry to those leaving school at fifteen or sixteen. He believes the older boy with added educational qualifications would be likely to acquire his craft skill more rapidly, and further, that full employment could not be guaranteed on the basis of an inevitable job. Mr Robens suggested that since industry could not do this on its own, the Ministry of Labour should assist by making use of redundant Royal Ordnance factories or Ministry of Supply factories, so as to meet the needs of the small firms for training apprentices. Something more was required than had been recommended by the Carr Committee.

The Parliamentary Secretary to the Ministry of Labour and National Service warmly welcomed Mr Robens's speech, though he thought the prospects of employment for boys and girls depend on economic expansion and not merely on the size of the bulge, and he was not convinced that opportunities for apprenticeship are as limited as Mr Robens suggested. He believes that the Government's part should be, first, to provide adequate facilities for technical education, and secondly, to shape the conditions in

which industry can best play its own part. The Industrial Training Council should take a most important part in developing a strong and effective leadership in industry towards expanding training opportunities in each individual industry, and the Council has, in fact, already asked both employers and trade unions to examine urgently the Carr Report. The Government also proposes to make a grant of £75,000 to the Council to further the appointment of training development officers, either by the Council itself or by employers' organizations, joint industrial councils or similar bodies. He was confident that the Carr Report has already had a profoundly beneficial effect on the situation.

Mr Robert Carr, who also spoke, explained that the Carr Committee was influenced in its recommendations by the view that more rapid progress would be achieved by building on practice and tradition rather than by breaking completely with the present system, even if the Committee did not condone the present rigidity of much of it. He believes that it is essentially in the smaller and medium sized firms that an increase in training could take place in the skills we need, and that help with the first year's training of an apprentice is particularly desirable. Pre apprenticeship courses could be developed in technical colleges, but the development of group apprenticeship schemes requires further attention, and small and medium-sized firms could be helped by more block release in technical colleges as an alternative to day release. While welcoming Mr Wood's announcement, Mr Carr said he thinks there might be a capital grant towards the establishment of joint training centres and tax remission to firms in respect of the number of their apprentices, and finally he stressed the importance of quality.

Mr A Albu, who pointed out that only between 20 and 30 per cent of school leavers receive any further training at all—and in some occupations only 2-3 per cent receive any serious training for their employment—quoted an estimate that we would need 1,300,000 skilled workers and 450,000 technicians by 1966. To provide these, about 86,000 extra apprenticeships would be needed each year, or nearly three times the present number. He suggested a levy, based on the number of skilled workers employed, to enable training workshops to be established in technical colleges, and also that the Industrial Training Council should be reconstituted under an independent chairman, with a specialist and highly qualified staff. Stress was laid by Miss Elaine Burton and by Miss Joan Vickers on the importance of the Youth Employment Service, and the need to see that this is properly supported, and that youth employment officers are sufficiently well paid to attract able and really qualified people to such posts.

Sir Edward Boyle, who replied on the debate, said that to achieve the objectives laid down in the 1956 White Paper on Technical Education, we must achieve an average increase in the number of part-time day release students of about 40,000 a year. Although in 1958 there had been a recession of

17,000 part-time day releases, the advanced levels in technical colleges are progressing well and the colleges are also diversifying their courses and providing new types of courses for the ordinary craft apprentices and technicians. The teaching force of the colleges is increasing and in 1958 reached a record total of 13,500. The technical colleges, however, cannot do their best without the active co-operation of industry and Sir Edward stressed the need for close and regular contact between the staff at the technical college and the training officers and apprentice supervisors in the factory.

It is against the background of these debates that the report of the Ministry of Education for 1958* is appropriately considered, particularly the important chapter which reviews developments in technical education since the War, and more especially progress since the White Paper on Technical Education was issued in 1950. Some further information bringing the report more up to date was given in speeches of Lord Hailsham in the House of Lords debate on February 26 and in that of Sir Edward Boyle in the House of Commons on April 27. Sir Edward Boyle pointed out that during the past four years the number of pupils per full time teacher in primary schools has declined from 32.1 to 30.0, while the number of pupils per full time teacher in secondary classes has only risen from 20.9 to 21.4 in spite of the movement of the hulse from primary into the secondary schools. From now onwards, apart from the year of intermission in 1962, the increase in the teacher force should more than match the increase in school population, and Sir Edward Boyle anticipated that primary classes of more than forty children should be virtually eliminated by the middle 1960s with no deterioration in staffing standards in secondary schools.

From 1959 Sir Edward thinks that an annual net increase of 6,000 teachers can be assumed, as 10,000 students should complete teacher training courses in 1959 and 17,000 in 1960, and this output should be maintained. An increased number of graduates is also expected to enter the schools, and wastage is unlikely to increase. More recently, on June 26 Mr Geoffrey Lloyd the Minister of Education said that in addition to the programme for 12,000 places announced last September, he has authorized forth with a programme of 4,000 training college places which should be effective by 1964. Sir Edward Boyle also said that the selection of highly qualified entrants who could complete a course in two years instead of three was being considered.

"Education in 1958" records that although in January 1958 there were nearly 840,000 children in maintained and assisted schools, the rate of increase has fallen by nearly half. The rise in the number of children older than fifteen was more than double that for the previous year. Nevertheless, the percentage of senior children in over size classes remained the same although the number of over size senior

classes was slightly larger in January 1958. The total number of students taking advanced courses at technical colleges has increased from 9,500 at the time of the White Paper to more than 11,000, and of these nearly 6,500 are enrolled in sandwich courses compared with about 2,300 early in 1956. During 1958-59, more than 19,600 out of 23,000 students admitted to universities in England and Wales, excluding those from overseas, were receiving awards from public funds, compared with 14,000 during 1954-55.

Apart from the firm expression of the Government's conviction that anything like a uniform pattern of secondary education throughout Britain would be wrong, and that instead wide experiment and flexibility in organization should be encouraged, the two chapters on further education are those of most direct interest to the scientist and technologist. The first of these provides a convenient concise summary of the progress that has been achieved in technical education during the past five years without however, distinguishing as clearly as had been done in some recent debates in Parliament between the technician and the technologist. One encouraging feature is the decreasing proportion of part-time education at the advanced level. In the mid 1950s, more than three-quarters of technical college students who obtained professional qualifications did so by part time study only. By the late 1960s about one half of those qualifying each year as scientists and engineers will probably have come from a technical college and less than one third of these will have taken part-time courses.

The review refers to the shedding by the colleges of advanced technology of the less advanced work and there is some discussion of the problem of broadening a technological course. It is recognized that a concept of teaching is needed in which the mere imparting of information is replaced by a more active handling of the student's mind and interest through the personal help and guidance of the teacher and it is the Government's policy that the colleges of advanced technology should be staffed on a basis generous enough to enable them to provide a tutorial system throughout a diploma of technology course. Apart from the great benefit to the students this should encourage the staff to adopt teaching methods which will increasingly encourage students to work on their own and to think for themselves. Of the £70 million authorized for investment in technical college building in Britain during the quinquennium ending in 1961, the colleges of advanced technology claimed about £10 million. Encouraging progress is recorded in regional co-ordination at the advanced level, in co-operation between the colleges and industry and in the development of research and postgraduate studies, and to a lesser extent in the development of courses in management studies. The need for residential accommodation however will only partly be met by the 3,000 places to be provided under the five-year programme of which nearly 2,000 will be at the colleges of advanced technology including about 1,000 at the entrench-

* Education in 1958. Being the Report of the Ministry of Education and Statistics for England and Wales. Pp. v+261. (Cmd. 777.) (London: H.M. Stationery Office 1959) 12s. net.

college at Loughborough Recruitment of suitable teaching staff for advanced scientific and technical courses is likely to remain a serious and urgent problem, and related to this are the conditions of service for such staff Here the improvement in the climate of opinion about advanced technological education could well be a decisive factor

The report stresses the distinctive functions of the colleges of advanced technology and of the universities and rightly urges that both are needed It would be more reassuring, however, to see the distinctive functions of the technical colleges and of the colleges of technology clearly recognized, and the need to keep the supply of technicians and craftsmen in balance with the expansion in numbers of both technologists and scientists This could well prove a major weakness, and although the apprenticeship system receives notice in the report, the Carr Report is merely noted and its implications even for technical education are not discussed Lord Hailsham's speech in the House of Lords on February 26 was limited essentially to secondary education, and although he referred to the improvement of facilities for teaching science, he did not touch on this vital aspect Between 1947 and 1957 the number of advanced level passes in the General Certificate of Education rose from 10,000 to 14,000 in mathematics, from 8,000 to 15,000 in physics, and from 7,000 to 13,000 in chemistry, and since the War more than £20 million has been spent on the provision and equipment of science laboratories at new and enlarged maintained secondary schools of all kinds and £3 million has been spent in three years on independent and direct-grant schools by the Industrial Fund for the Advancement of Scientific Education in Schools

This report from the Ministry of Education, and the debates in Parliament referred to earlier, demonstrate that the Government is aware of the many problems involved in expanding technical and technological education in Britain; it is the duty of professional associations and similar bodies to impress on those concerned the importance of striking a true balance between the diverse interests involved

CONCEPTUAL FOUNDATIONS OF SCIENCE

Patterns of Discovery

An Inquiry into the Conceptual Foundations of Science By Prof Norwood Russell Hanson Pp 1x+241 (Cambridge At the University Press, 1958) 30s net

THE general thesis of this book is that observational data become significant only when seen against a given conceptual background or *Gestalt* (p 90). The theme is worked out at various levels. Thus Chapter 1 discusses interpretative activity of plain observers, Chapter 2 illustrates, through a historical discussion of the work of Galileo, Descartes and Beekman on the problem of free fall, the influence of purely geometrical as against physical attitudes on the direction of research, and Chapter 4

emphasizes the unimportance of physical (as compared with purely mathematical) preconceptions in their hold on Kepler's astronomical thinking Comparatively, these are historical issues, though Prof Hanson here sometimes flirts with something more important, as when he writes that "conceiving of an hypothesis has a logic" and is not merely a matter of intuition or hunches (p 71) Of course it is not But as to "logic", when we inquire further we are after all given no more than the tame if correct remark that the physicist's task is to find the simplest formula which will include all the known data (p 84)

Hanson's conceptualist thesis is indeed mostly intended to throw light on a number of traditional philosophical issues such as the nature of causal relations (Chapter 3 causes being interpreted as "theory-loaded" (p 54) entities), the logical status of the laws of classical dynamics (Chapter 5 whether they are considered as definitions or as conventions or as empirically testable statements depends on "the organisation of concepts" (p 96)), as also the question whether the Indeterminacy Principle states "merely a technical" or rather "a conceptual impossibility" (p 136, Chapter 6) This last question, perhaps the most interesting in the light of recent discussions on the ideas of Bohm and others, does not receive much clarification, being discussed merely as a further illustration of a philosophical thesis

Altogether, though this book abounds in a wealth of illustrative studies, remarks and quotations, at the end one is left with the feeling of a somewhat hazy and impressionist picture There is a great deal of trailing of the coat, the *bête noire* being "the philosophers", who now fail to grasp the elementary facts of physical reasoning (p 88); now "think physicists confused" about the use of law-statements (p 109), and who are finally told that not they but men like Kepler, Galileo, Newton, Einstein and others have developed physics (p 113) Sneering was never a good substitute for argument, it is never certain who these philosophers are that so dismally mis-understand, and on the few occasions when they are named, their arguments are peculiarly misrepresented Thus some contemporary logicians are chastized for having represented physical theory either as an inductive generalization, or as a piece of pure deduction, or, again, as inverse deduction, namely, the postulation (the "thinking up") of hypotheses accounting for the facts (pp 86 ff) Armed with this logical terminology, Prof Hanson imputes to the logician the absurd doctrine that the physicist first thinks up hypotheses at random and then sees what he may perchance deduce from them (pp 71 ff) Surely it was perfectly obvious that what the logician meant was think up hypotheses in the light of the problems they are meant to solve

Disentangling the puzzles and paradoxes of the language of science is a delicate operation, the statements that emerge after due reflection, when honestly put, are deserving perhaps of slightly more respect than a hasty misreading of the evidence might suggest Prof Hanson writes that "because of the inadequacy of philosophical discussions" of the topics dealt with in his book, he proposes to use physical theory and theorizing as "the lens through which these problems will be viewed" (p 2) One reader at least has certainly gained the impression that the method is, on the contrary, the perfectly standard one of running a definite philosophical line

But no greater damage could be done to genuine philosophy of science than to suggest that there is an easy way to a solution of its problems, let alone that they may be settled by simply inspecting the metaphysics and the language of science.

The book seems most stimulating in its discussion of some of the case studies referred to, even though one might have wanted some explanations on occasion which would have made the matter less mystifying to the general reader. (Who of these understands the theory of the hodograph? (p. 106).) It can certainly be warmly recommended as accompanying reading to more sustained studies in the subject.

GERD BUCHDAHL

THE INVERTEBRATES

The Invertebrates Vol 5

Smaller Coelomate Groups—Chaetognatha, Hemichordata, Pogonophora, Ploronida, Ectoprocta, Brachiopoda, Sipunculida, The Coelomate Bilateria. By Libbie Henrietta Hyman (McGraw Hill Publications in the Zoological Sciences.) Pp viii+782 (London: McGraw Hill Publishing Company, Ltd., 1959.) 10s. 6d.

THE fifth volume of Dr Hyman's series on animal phyla is devoted to the smaller coelomate groups except the Echinurida. These she divides into three sections: the enterocoelous coelomates or Deuterostomia (Chaetognatha, Hemichordata and Pogonophora), the lophophorate coelomates (Ploronida, Ectoprocta and Brachiopoda) and the protostomatous coelomates (Sipunculida). It must have been a difficult task mastering the literature on such widely varied forms of life, the bibliography is excellent.

Each chapter is arranged on the same lines as those in previous volumes—history, general characters, classification, morphology, embryology, ecology and physiology, geographical distribution and relationships so that it is easy to find a particular section. The illustrations are good on the whole, mostly copied from original papers but a few have deteriorated in reproduction such as *Bathyspadella*, Fig. 15A, and the nervous system of ploronids, Fig. 87. Lettering by numbers enables the reader to test his knowledge, and this is applied uniformly throughout the book.

Some phyla have been exhaustively dealt with elsewhere, such as the Hemichordata by van der Horst, others are little known or have not been adequately treated in available books and monographs. It is to the latter groups that the zoologist will gratefully turn first. Here for the first time we have a clear account, largely translated from the Russian, of the now phylum Pogonophora the beard bearers, deep sea worm like creatures with a heart and vascular system but no digestive canal. The dredging of twenty two species of pogonophores chiefly from the Behring and Okhotsk seas and from the Skagerrak off Norway is one of the most remarkable finds in modern zoological research, comparable with the discovery of *Lamerna* and *Neopilina*.

More than a third of the volume is devoted to the Ectoprocta, a group which "is burdened with a large and fantastic terminology." Dr Hyman therefore has correlated the terms used for the parts of the colony with those employed in invertebrates generally. For her study of the Ectoprocta she travelled to Brazil, to consult with Prof F. Marcus, who had worked so extensively on that group. The result is an excellent account. Dr Hyman prefers to call the phylum Ectoprocta and to use Bryozoa in a popular sense only since the latter name included the Ectoprocta, which must now be removed from close association with the Ectoprocta.

The chapter on Brachiopoda is also a competent piece of work, especially for the palaeontologist. It is strange that the name is misspelt on the dust cover and the title page.

The final chapter, entitled "Retrospect" enables the author to correct a few mistakes in the earlier volumes, to add short accounts of recent work not previously known and to state her views on current trends in zoology. The last she does very forcibly.

THE WEEVILS OF FRANCE

Faune de France, Vol 62

Coléoptères Curculionides (Troxidinae Partio). Par Adolphe Hoffmann. Pp ii+1200-1840 (642 figures) (Paris: Editions Paul Lechevalier, 1958.) n.p.

IT is now more than forty years since the last comprehensive work on European beetles appeared. The present volume in this well known series deals with the remaining weevils occurring or likely to occur, in France and Corsica. It is issued, unusually, in a stout and durable cloth binding. Keys to all groups, including sometimes the varieties of a single species, are given. Each couplet usually contains several easily observed characters and the keys appear to be reliable. There is a full description of each species together with many references.

The figures are even more numerous than in the earlier parts, averaging more than one per page. They exhibit a variety of styles and techniques but seldom reach the standard one expects nowadays in a work of this kind. Some of the figures of antennae and tarsi are particularly crude, stippling and shading are frequently used where a simple line drawing would be far more effective.

The author's system of classification is rather individual and open to criticism. Following Reitter (1912) he has included some twenty or so subfamilies as tribes under the name 'Calandrinae'. Also the Attelabidae are denied their full family rank. *Alysi chites* was even used as an example of the Pluronid gnathii in the introduction (Part I). In addition a number of long established generic names (for example *Dorytomus*) have been sunk though in such cases an explanation is given and the reader can form his own opinion with the aid of the references. The fact that the general classification of weevils has not been studied since 1866 and that the now Code of Zoological Nomenclature has yet to appear in print reduces the weight of these criticisms. Furthermore, this work is essentially a faunistic study, not primarily intended to make a fundamental contribution to anatomy or taxonomy.

It is in its faunistic aspect that the value of this work lies. The author has taken the greatest pains to record accurately and often in great detail both the distribution and the biology of every species as far as these are known. Again many references are given. Many galls etc. and leaf rolling techniques are illustrated.

Following the main body of the text is a lengthy list of additions and corrections to the whole work, also a list of food plants with their associated weevils and a general index.

R. T. THOMPSON

"Hemichordata must be removed from Chordata and made an independent phylum of invertebrates", "The concept Gephyroa must be obliterated from zoology", "Ctenophora are a sharply delimited group with definite characteristics that entitle them to separate phyletic rank. It is even not at all settled that they have originated from Cnidaria", "The Entoprocta are maintained as a phylum distinct from the Ectoprocta"

The volume reaches the high standard of all McGraw-Hill publications. Its cost in Britain is certainly very high, but its value as a compilation of up-to-date knowledge is undoubted. All zoologists will wish Dr Hyman renewed health so that she may complete the great task she has set herself, and will look forward to the next volume, which is to deal with the Mollusca.

N. B. EALES

MODERN THEORY OF THE INTEGRAL

An Introduction to the Theory of Integration

By Prof. Adriaan C. Zaanen. Pp. ix+254. (Amsterdam: North-Holland Publishing Company, New York: Interscience Publishers, Inc., 1958) 50s.

PROF. ZAAZEN'S reason for adding to the considerable number of books surveying the field of modern integration, from the classical Lebesgue theory to the developments of Radon's extension of this theory to abstract spaces, is that such accounts generally rely either on the approach through measure theory or on the concept of the linear functional; he wishes the young analyst to be familiar with both procedures. Thus after a brief preliminary section on set theory, he defines measure over a semi-ring and builds up a more general measure by an extension procedure, then Stone's method of defining the Daniell integral as the extension of a linear functional over the class of step functions is seen to be practically a special case of the extension procedure for measure. The author gives plenty of illustrations, particularly helpful in showing how the older theory fits into the more modern, so that, for example, the extension procedure applied to the Riemann integral yields the Lebesgue integral. Fubini's theorem on the reduction of a multiple integral to repeated integrations is carefully studied, as is the tedious but important Radon-Nikodym theorem, which may be regarded as a very high-level version of the change of variable in an integral. Later chapters give some applications, such as unitary transformations in Hilbert space, and ergodic theory. Measure over a Boolean algebra is excluded, but Carathéodory's book is available, and integration over a locally compact space and the related Haar measure are omitted, since an account of the relevant topology would have substantially increased the size of the volume.

The exposition is clear and precise, provided the reader pays unremitting attention, and provided he does not neglect the exercises, an integral part of the text. "The student who omits them is like the man who, when attending an excellent dinner, wants to race through the main courses only, and (under the misapprehension that it is merely the nourishing value that counts) refuses to touch the wines and little delicacies which are offered him", and the author is offering Montrachet, not Coca-Cola.

INTERNATIONAL CYTOLOGY

International Review of Cytology, Vol. 7

Edited by Prof. G. H. Bourne and Prof. J. F. Danielli. Pp. x+684. (New York: Academic Press, Inc., 1958) 16 dollars.

THIS volume, issued under the auspices of the International Society for Cell Biology, is probably the most valuable and interesting of the series, of which it is the seventh. Among the well-known contributors are Don W. Fawcett, Françoise Haguenau, Johannes Rhodin, F. G. Spear and Paul Weiss. The articles by Spear on the biological effects of radiation and by Ilse Lasnitzki on carcinogens, hormones and vitamins in organ cultures are topical in view of widespread interest on the effects of atomic tests, and of cigarette smoking. Spear gives a comprehensive historical review on radiation physics, the general response of living tissues to radiation and radiation chemistry, and has cleared the ground for a new approach to this field. He quotes J. A. V. Butler: "We are at the moment in the position of a man who tries to elucidate the mechanism of a telephone exchange by throwing bricks into it and observing some of the results." Naturally, Spear's section on the possibilities of chemical protection against radiation effects is of considerable interest. A number of chemical and physical agents are claimed to have such protective action in certain cases. He lists cysteine, glutathione, BAL, thiourea, glucose and ethanol. The intimate cytological results of radiation could not be examined more than cursorily by Spear. Many years ago M. J. D. White discovered as a by-product of his work on the effects of X-rays on the maturation phase of locusts that in many cases the single sperm 'middle piece' became double, triple or even quadruple. Recent work at the Argonne National Laboratory, by Talmisman's group, working under the auspices of the U.S. Atomic Energy Commission, has shown that the insect 'middle piece' arises from a number of separate bodies which normally fuse to form the 'neck body', radiation prevents their fusion, but does not prevent their growth. Further work along these lines with electron microscopy should be fruitful.

Ilse Lasnitzki, using the watch-glass plasma extract clot technique of Fell and Robison, has investigated the effect of carcinogenic hydrocarbons on human foetal lung, and mouse prostate, the influence of sex hormones on embryonic development of sex organs, and the changes produced by vitamin A. Lasnitzki provides some remarkable photomicrographs of the effects of 3,4-benzopyrene from cigarette smoke, on the bronchiolar epithelium. Carcinogenic hydrocarbons and sex hormones stimulate cell division in basal cells of skin and vagina, and thus induce abnormally high proliferation.

The section by Françoise Haguenau, a distinguished member of the French School of electron microscopy, goes into the question of orgastoplasm or endoplasmic reticulum. The name orgastoplasm was coined by Garner (1897, 1899) for the *Nebenkerne* in gland cells. His work was amplified by other members of the Nancy School of Histology, such as Prenant and Bounin. Copies of their figures occur in many of the major works on histology. Happily, Haguenau also mentions the contributions of the Japanese cytologist Sakae Saguchi in this connexion. Electron microscopists entered the field, and by about 1947 really good electron micrographs

of gland cells had begun to appear, pioneer work being carried out at the American National Cancer Institute by Dalton *et al.*, and at the French Cancer Institute at Villejuif by Oberling's group. The way was then open for the excellent high resolution studies by the Swedish workers under Sjöstrand, and by the active Rockefeller group led by Porter. During this enriching period a controversy arose on nomenclature as a result of the continued use of Porter's term 'endoplasmic reticulum', which the Americans in particular believed proper to describe the ultrastructure of the classical ergastoplasm discovered by the French. Space allowed to the reviewer does not permit further reference to this topic, but Huguenuau remarks, 'It has been emphasized that the general acceptance by electron microscopists of the word *ergastoplasm* in its original context would do much to bring order to the present terminological confusion'.

Don W Fawcett writes on the structure of the mammalian sperm as determined by electron microscopy. Naturally with the higher magnification and excellent resolution of the modern electron microscope recent authors provided with these blessings have been able to better the often pathetic past efforts of the optical microscopist in this field. Nevertheless the electron micrograph has not produced any new basic facts except possibly for recognition of the peculiar lamellation of the Golgi apparatus—yet Pollister (Vol. 6 of this series) claims that Jan Hirschler did understand that the Golgi apparatus was essentially a lamellated structure. Of great interest to day in the structure of the metamorphosing spermatid is the neck region. Fawcett holds that the base of the flagellum is connected to the head by a segmented body that is probably a highly modified distal centriole, but the reviewer has yet to see any micrograph of this region which does not show a special neck body, centriole adjunct archoplasm (Grassé, Carnasso and Favard), etc., which is material separate from the proximal centriole. In fact, the electron microscope has shown that the head centriole is not the major attachment area of head and flagellum—there is a separate structure or packing which reaches its highest state of development in insects. There seems to be no recent evidence that the centriole divides more than once in normal spermatogenesis. It must now be admitted that the mammalian post-nuclear body and the neck body or centriole adjunct are different structures.

Paul Weiss discusses cell contact—that is, (1) contact relations between cells and their physical substratum (2) the mutual reactions of cells on contact with one another and (3) the transmission of specific agents and influences from one cell to another by direct contact. Weiss considers a cell to be in contact with another body not only if the two surfaces are in direct apposition but also if they are separated by a narrow space occupied by a molecular population the free mobility of which is restrained. In his usual suggestive manner, Weiss has investigated the 'bobbin' structures at cell interfaces of epidermal units and goes on to discuss the possibility that in cancer cells undergoing metastasis there is a close relation between loss of specific surface contact on one hand and mobilization and proliferation on the other. Mobilized normal cells, after recovering co-optive relations (for example, epithelia meeting their own kind), cease to proliferate, whereas cancer cells under comparable conditions evidently do not.

Weiss omits mention of the paper by Dalton, Kahler and Lloyd (*Anat Rec* 111, 1951).

Papers emanating from Sjöstrand's laboratory have been marked by helpful interpretative drawings which can only be made up by close study of many micrographs. These drawings will be used gratefully by authors of histology books. Johannes Rhodin's study on the anatomy of kidney tubules is a good example of Swedish work, the diagram on page 506, Fig 14, being excellent. The studies on kidney by Pease, Dalton, Rhodin and others can now be followed by experimental work.

Another paper from the Karolinska Institutet is by Hans Engström and Jan Wersäll. Engström is a practitioner in the ear, nose and throat clinic of the University of Gothenburg, yet has managed to collaborate in this erudite study of the structure and innervation of the inner-ear sensory epithelia.

A further paper is by L M J Rinaldini of the University of Cordoba, Argentina, whose work was carried out at the Strangeways Research Laboratory, Cambridge. No doubt Rinaldini will read Weiss's article with appreciation, as the two valuable papers have certain meeting points. Rinaldini has covered a great deal of difficult ground in an interesting manner, and of all the papers here mentioned this has needed the widest grasp of the international literature on biochemical and biophysical cytology.

The supposed hypothalamo-neurohypophyseal neurosecretion has been carefully considered by J C Sloper, of the Charing Cross Medical School, London. The subject of neurosecretion is one that is largely made up of doubtful histology and worse cytology. Degenerate and effete cells stain darkly in toluidine blue, iron haematoxylin, etc.—these are supposed in some cases to be neurosecretory, whereas to the reviewer the most convincing vertebrate nerve cell secretions are those demonstrated by electron microscopy by Palay, Van Breemen, J D Green and others. In the case of the sympathetic neurones of the mouse, similar fine 'secretory' bodies exist in animals a few days old, and soon disappear. Older cells become packed with formed bodies which are hooped aggregations of effete mitochondria lying mainly at the axon end of the nucleus. Sloper remarks that future investigations will be facilitated by a more exact knowledge of the nature of 'neurosecretory' material, and he feels unable to equate the several categories of inclusions demonstrated by various workers.

The remainder of this volume has papers on the 'Lymphocyte', by O A Trowell of the Radiobiological Unit at Harwell, on 'Autoradiographic Studies with S^{35} Sulphate', by D D Dziewiatkowski of the Rockefeller Institute, on 'Recent Advances in the Study of the Kinetochore' (centromere), by A Lima-de Faria, of the Institute of Genetics of the University of Lund and finally on 'Lamellarbranch Muscle', by J Bowden, of the Anatomy Department of the Queen's University Belfast. These valuable studies are all of the highest standard and it is regrettable that they cannot be reviewed here at length.

Looking back on the various volumes of this series which have appeared under the guidance of Bourne and Danielli, one is impressed with the fact that the problems encountered in the study of the living cell nowadays seem to become more complex and more insoluble. It would be pretentious for us to think otherwise.

J BRODIE GATEWAY

A Defence of Free Learning

By Lord Beveridge Pp xiv+146 (London Oxford University Press, 1959) 18s net.

IN this book Lord Beveridge has drawn in the main on the documents collected for their work by the Academic Assistance Council and the Society for the Protection of Science and Learning to give a sober but moving narrative of twenty-five years work in Britain to help university teachers and scholars driven from their work on political or racial grounds. It is not a philosophical or theoretical argument for academic freedom but a factual account of what has been done in Britain alone, beginning with the expulsions from Germany initiated by Hitler in 1933 and continuing down to the problems presented by the intolerance persisting after the Second World War, including the Hungarian persecution of 1956-57. It is a story little known outside the universities and is told without embellishment, save, perhaps, where in his concluding chapter "The Folly of Tyrants", Lord Beveridge, summarizing, points to the rich harvest which Britain has reaped by her reception of these refugees. There are indeed some dark places in the story and Lord Beveridge does not attempt to conceal them. On the other hand, he does not overstress them and points out fairly enough that, even in the darkest hour of 1940, there were always those in Britain ready to protest vigorously against administrative error or tardiness and to insist on the revocation of stupid decisions. Five debates in the House of Commons in less than eight months of desperate war testify to a sense of justice and a vigilance of which Britain has a right to be proud. The most moving chapter is, perhaps, that entitled "Wandering Scholars", in which Lord Beveridge sets forth some of the typical experiences of these scholars collected from their replies to an inquiry sent out in June 1958. No eloquence could make the human issues plainer, nor is more needed by way of argument to demonstrate that here is a continuing problem calling for forethought and imagination, as well as practical help if its difficulties are to be resolved and some of the existing gaps, notably in relation to professional work, are to be closed.

In writing this book, Lord Beveridge has added to the debt which Britain as well as wandering scholars owe him and his colleagues, first on the Academic Assistance Council and then in the Society for the Protection of Science and Learning.

R. BRIGHTMAN

Systematic Mineralogy of Uranium and Thorium (Bulletin 1064, U.S. Geological Survey) By Clifford Frondel Pp viii+400 (Washington U.S. Govt. Printing Office, 1958) 1.50 dollars

FOR the past ten years an intensive investigation into the mineralogy of uranium and thorium, undertaken in connexion with economic studies of radioactive ore supplies, has been in progress in the laboratories of the U.S. Geological Survey, the U.S. National Museum, and the Mineralogical Department of Harvard University. The vast amount of new information forthcoming from these researches has now been assembled by Prof. Frondel of Harvard, in a monograph which is quite the most outstanding work among the half-dozen or more major text-books on radioactive mineralogy that have appeared in the U.S.S.R., North America and France during the past two years. Each of close on a hundred mineral species is very fully described according to its

synonymy, composition, crystallography and crystal habit, physical and optical properties (with X-ray powder diffraction interplanar spacings), synthesis, criteria for identification, mode of formation, and natural occurrence. Comprehensive determinative tables are given in an appendix and there is a bibliography of 800 items. Although the work has been three years in the press and thus gives no account of the most recent discoveries, no earlier book in this field has achieved anything like the same coverage and certainly none can parallel this inexpensive Bulletin in accuracy of data and freedom from misprints. Most of the opaque multiple oxide minerals of uranium, other than species of economic importance such as brannerite, davidite, and the pyrochlore-microlite series, have still to be studied in detail, for the rest, the many geologists and mineralogists now concerned with uranium ores will unhesitatingly accept this monograph as their foremost authority.

C. F. DAVIDSON

Numerical Analysis and Partial Differential Equations

By George E. Forsythe and Paul C. Rosenbloom (Surveys in Applied Mathematics, Vol. 5) Pp x+204 (New York John Wiley and Sons, Inc., London Chapman and Hall, Ltd., 1958) 60s net

THIS survey contains two unrelated essays. In the shorter of the two, Forsythe summarizes recent work in numerical analysis, with special references to developments in the U.S.S.R. There is an account of the chief Russian automatic computers, details of which have been available only in the past two or three years. Forsythe also stresses the skill with which Russian workers have brought to the service of numerical analysis some of the most up-to-date tools of pure mathematics, such as constructive function theory and functional analysis. The bibliography is helpfully selective rather than blindly comprehensive, and the author's comments on the various items are crisp and efficient.

Rosenbloom's essay does not attempt to describe all recent contributions to the study of partial differential equations, but it gives a valuable indication of the way in which the theory of function spaces and the transform calculus have yielded fresh results about elliptic and parabolic equations. The young research worker should find this a helpful guide to some of the main lines of advance, the bibliography, of some 700 items, may well lighten the novice, and some further annotation would have been an advantage.

T. A. A. BROADBENT

Clinical Biochemical Method

By Dr A. L. Tarnoky Pp x+239 (London Hilger and Watts, Ltd., 1958) 50s net

MOST large clinical biochemistry laboratories have their own particular methods for routine examinations, or more likely use modified classical ones in the light of their experience. Dr A. L. Tarnoky's book describes the methods used routinely in his laboratory at the Royal Brompton Hospital. It is a straightforward bench manual giving most of the usual tests arranged in alphabetical order. Each test is described under the headings of principle, specimen required, method, result, normal value, reagents required and remarks. There is a small but valuable appendix which gives procedures for checking analyses in a laboratory, lists of books and references and a list of manufacturers. There are

only a few diagrams for the class of worker who would most depend on this book: spectroscopic charts and illustrations of electrophoretic patterns, for example, would have been of great value. Again, the omission of any mention of paper chromatography or of serum transaminase tests is noticeable. On the other hand, the directness and simplicity of the text are much to be commended.

This book will be very useful to technicians, clinical pathologists and doctors in smaller hospitals in Britain and overseas, and to medical research workers who need to do routine clinical biochemical tests as part of a larger research scheme. It forms a useful addition to the larger and more well known text books of clinical biochemistry.

D S H W NROOL

Biological Laboratory Data

By Dr L J Hale (Methuen's Monographs on Biological Subjects). Pp x+132. (London: Methuen and Co., Ltd., New York: John Wiley and Sons Inc. 1958.) 15s net.

BOOKS intended as laboratory aids are by no means rarities and cover a great variety of subjects, while they range in their appeal from the beginner to the advanced research worker. This book falls rather into the latter category and it has some unusual features which single it out among those devoted to the biological sciences. The emphasis on the mathematical aids, for example, is conspicuous. Out of a total of one hundred and twenty-seven pages, twenty-three deal with mathematical data, twelve are devoted to statistical data and formulae and thirty-five to physical and chemical data. This is not an overbearing proportion but it is more extensive than in most books of this size and type and the material is very handily presented.

The result, however, has been somewhat to repress the more strictly biological matter, so that cultural methods for the laboratory get only seven pages, inclusive of a page of references to other works, while histological and histo-chemical data cover only fourteen pages. This seems more considering the enormous amount of such data available and a better balance might easily be achieved. There is no doubt, however, of the value of the material which the book contains and the mathematical sections alone should ensure it a wide popularity among biologists who so often feel the need of guidance in that field.

R C McLEAN

The Salmon

By Dr J W Jones (New Naturalist Special Volume). Pp xvi+192+12 plates. (London: William Collins, Sons and Co., Ltd. 1959.) 15s net.

ON the whole Dr Jones has written a readable book. The chapters dealing with the spawning of adult salmon and young moles are the best in the book, as it is there that Dr Jones has drawn largely from his own work and experience. An important chapter is devoted to scale reading from which many of the details of the life history of the salmon have been discovered.

The chapter on "Salmon in the Sea" is frankly disappointing, as sufficient use has not been made of the information amassed in the past thirty years so the reader does not get a clear picture of the long migrations which salmon often make when returning to the river of their birth.

Other chapters deal with the early life of the salmon, the return to the river, the return to the sea

and the salmon river. The book is completed by four useful appendices dealing with the characters of salmon and trout and their hybrids, a key to the genera of the Salmonidae, etc., a description of the parasites of salmon and methods of estimating lengths from scales. Serious readers will also find the bibliography of value in their more extensive reading.

One serious criticism of the book I have to make is that many of the illustrations are poor. The publishers inform us in a note opposite the title page that in this series of publications 'the animals and plants are described in relation to their homes and habitats with the help of fine photographs'. The italics are mine. Plates 4, 5, 6 and 7 are certainly not based on fine photographs as I have often seen better in angling magazines.

ARTHUR E J WENT

Nitration of Hydrocarbons and other Organic Compounds

By A V Topoliev. Translated from the Russian by Catherine Matthews. Pp vi+329. (London and New York: Pergamon Press, 1959.) 90s net.

TRANSLATIONS of foreign texts are seldom successful unless carried out by workers in the same field with freedom to incorporate recent material. The pitfalls are well illustrated by this book, which is both out of date and unreadable. There are one or two references to papers published early in 1954 but none to the more recent literature. Since much work of fundamental importance to this field has been published during the past five years the book is of little value as an account of the subject. Although it does contain a rather complete account of the earlier literature and a useful summary of Russian papers that are not readily accessible in Britain.

It is most unfortunate that the distinguished author of the book could not have been persuaded to revise it during translation.

M J S DEWAN

Commonwealth Universities Yearbook, 1959

Pp xxvii+1407. (London: Association of Universities of the British Commonwealth, 1959.) 8s 13 dollars.

THE invaluable 'Commonwealth Universities Yearbook' is now in its thirty-sixth edition. There are no major changes from last year's edition when the new enlarged format was introduced, but the size has increased from 1305 to 1435 pages, mainly in order to accommodate expansions in university staff.

The University of Sherbrooke in Canada and Sardar Vallabhbhai Vidyapeeth in India are mentioned for the first time and the University College of Fort Hare in South Africa now has a complete entry. Two events which occurred in Australia as the book was going to press are also mentioned briefly: the founding of Monash University in Victoria and the transformation of the New South Wales University of Technology into a multi-faculty University of New South Wales.

The valuable essays in higher education in the various countries have been brought up to date and where necessary additions have been made to the maps showing where the universities are located.

New features of this edition include a full length summary of admission requirements by the Canadian Universities and information on the transfer courses at certain British universities whereby students who have previously studied arts subjects can switch to science.

BEHAVIOUR IN CONVENTIONAL AND EXTRA-TERRESTRIAL FLIGHT

SOME FUTURE ASPECTS OF AVIATION MEDICINE

By AIR COMMODORE W K STEWART, C B E, A F C

Royal Air Force Consultant in Aviation Physiology, Institute of Aviation Medicine,
Royal Air Force, Farnborough

AVIATION medicine is the normal clinical practice of medicine as applied to the special circumstances of flight, but in this survey it refers to the basic sciences of physiology, psychology and biochemistry.

The growth of aviation medicine has been largely due to preceding advances in combustion, aerodynamics and metallurgy, in turn, these advances were the result of operational plans, either civil or military. At the present time, most aircraft or missiles appear to have a cycle of approximately ten years for the stages of planning, development and production, and it is reasonable to assume that some such cycle will be entailed in the future. Past experience in the conduct of biological research has indicated that such a period should be sufficient for the production of the major contributions from aviation medicine. It is also sufficient for the design and installation of the capital equipment required, both for fundamental and applied work.

It has become clear, however, that a significant contribution to a particular phase of the programme will depend on adequately trained staff. No institute or laboratory of aviation medicine will survive in the future if it lacks staff of the proper orientation in the relevant biological disciplines.

Since these are likely to be of a complex kind, skilled research workers will be correspondingly few in number. It is held, therefore, that it is necessary to plan future activities in aviation medicine so as to ensure the early derivation of biological information.

Survey of Some Future Problems

For the purpose of this review, it will be assumed that manned aircraft will continue to be used in an era of unmanned ballistic missiles, or vehicles, and later in an era of orbital-manned vehicles. Such aircraft may be hypersonic, may operate at low altitudes, or in the outermost layers of the atmosphere, for short or very long durations. They will subject their occupants to stresses and environmental changes, different in degree, but on the whole basically similar to those of contemporary aircraft, and this, to some extent, may be also true for orbital-manned vehicles.

The experience gained in the past fifteen years in applied physiology and psychology is sufficiently extensive to encourage the belief that problems arising in these disciplines can be successfully solved, since the techniques involved and equipment necessary can be foreseen to a considerable extent.

For extra-terrestrial flight, many of the problems, weightlessness, for example, can only be solved either

by extrapolation from poorly quantified data, or by direct experience.

Hazards such as the effects of corpuscular radiations and cosmic rays will almost certainly be a more worthwhile sphere for laboratories of physics than for an institute of aviation medicine. In considering the philosophy of extra-terrestrial flight, it is always difficult to justify biological participation since apart from the remote possibility of acquiring data of importance to microbiology, it is unlikely that purely physiological studies will advance general knowledge in proportion to the cost of the venture.

The proper function of biological researches is undoubtedly to further manned exploration of the upper atmosphere or beyond, and even here it is wise to hesitate in considering, not whether this is feasible, but whether it can ever lead to more than an *ad hoc* determination of the ultimate limits of man's endurance.

However, the value of manning a satellite may ultimately depend on those functions of the central nervous system which are difficult to simulate, either in absolute terms or in size and weight. It is probable that what a man can be expected to do in a satellite could only be determined by actual experience, but it is unfortunate that the environmental conditions which he will encounter are those most likely to affect the logical and purposive functioning of the brain.

The problem here is that the behaviour of animals and man is still very far from being understood, aberrations of behaviour in flight are still more difficult to investigate, and if any occur in the occupant of a satellite the determination of their basis might be quite impossible. Clearly, advancement of such knowledge would be of benefit, not only to those nations with official programmes of the 'man in space', but also to aviation in general, and would constitute a field in which expenditure of effort and money would be justified.

Every practitioner of aviation medicine has some acquaintance with cases of abnormal behaviour in flight. For many of these cases, no simple answer can be given, although they are commonly referred to as 'manifestations of disorientation', but analysis of near accidents has shown a higher frequency than suspected of misinterpretation of visual information and illusions of different kinds.

Some of these illusions were hypnagogic in nature others led to panic or startle reactions. Some were obviously associated with reduction in sensory input and probably an element of perceptual conflict. In future manned flight, there will be an increased exposure to the factors probably initiating such

changes in behaviour. It has therefore become mandatory to review their relationship to physiological mechanisms, and to try to determine the primary stimuli for chains of reaction. Do disorders in behaviour determine physiological events or is it necessary to postulate underlying abnormalities in the neurophysiological or homeostatic spheres? Probably both mechanisms are implicated at different times.

The classical problems of behaviour in flight, such as fear and fatigue, are entirely material to this argument. Hence it is essential to derive such advances in knowledge that adequate theories can be constructed, adequate in the sense that they can produce methods of prediction of alterations in learned behaviour under stress whether this stress be noxious or systemic in origin. The purpose of this review is to indicate some avenues of research which could be explored and which might prove of value not only in conventional aviation medicine, but also in what is rather loosely termed 'space medicine'.

Survey of Brain Mechanisms

It is impossible to prophesy how far theories of integration of nervous action will have advanced in the era of the hypersonic aircraft and manned missiles, and it is therefore probably legitimate to commence with Hobb's¹ ideas concerning the conceptual nervous system. He related the function of the brain-stem, or arousal system of Moruzzi and Magoun², to the level of the 'cue' function in learning. For general reviews of the physiological and psychological aspects of those of Jasper, Gloor and Milner³ or Duffy⁴ should be consulted.

Stress. It is proposed to regard stress from the point of view of Fortier⁵ and Fortier *et al.*⁶ namely, that there are basically two types of stress—neurogenic initiated through perceptual processes, and systemic, initiated through chemical and metabolic processes. In both, the hypothalamus appears to influence anterior pituitary secretion via the hypothalamic portal vessels. Permanent interruption of these vessels lowers the normal rate of secretion of adrenocorticotrophic hormone, abolishes reflex secretion of adrenaline in response to stress and also that of the gonadotrophic and thyrotrophic hormones. There are indications that the tasks of flight can be regarded in these terms as a stressful occupation, with enhancement of the secretion of adrenaline and noradrenaline of the output of 11 and 17 ketosteroids, or α -peptinogen accompanied by alteration in gastric function.

It has not however been possible to state that the degree of stress represented by biochemical findings is of unusual severity or to relate them to the degree of fatigue experienced. The fact that narrow trainees hyperventilate more or excrete more ketosteroids than their instructors may merely represent higher levels of arousal than higher intrinsic levels of stress. If stress and arousal be synonymous, then it may be necessary to postulate that certain forms of learning set represent stress also. Unfortunately it is impossible to investigate the immediate physiological reactions of man exposed to an overwhelming event such as a major loss of control in the air.

Further the physiological parameters which had been investigated in the intact man are second or even third-order variables, but this does not deny the importance of techniques, such as those of Malm and his associates⁷. It would seem to be important

to extend their approach possibly by applying techniques such as Morton's⁸, in order to derive more fundamental knowledge of how anxiety may alter reflexive physiology.

If a given level of arousal be equated with stress then a reduced sensory environment should also, from some points of view, be regarded as stressful. In future aircraft or vehicles, in which such factors may well operate, and may be enhanced by fatigue there will also be the interposition of alterations in environmental and temporal rhythms. Both these states may be found in nuclear powered aircraft as well as satellite or orbital vehicles, and some understanding of their interrelationship is certainly necessary. The approach of Lewis and Lobban⁹ into biochemical aspects of alterations in environmental time should be combined with that of Bexton, Heron and Scott¹⁰ into the intellectual effects of perceptual isolation.

Behaviour during stress. In the future it will be important to ensure that memory and learning will remain as stable as possible during acute stresses occurring in a critical period of a sortie.

Tylhurst's¹¹ study of behaviour in disaster situations on the ground is especially significant in that 75 per cent of individuals affected showed definite impairment of decision taking, and it is likely that in any normal population of aircrew there must be a significant proportion of men who would evince similar reactions. Even if the motivation and training are different, it would be desirable for their safety to select crews in which the 'cue' function alters as little as possible with high levels of arousal. In order to do this, much more knowledge will have to be acquired by neurophysiologists.

Vogt¹² has pointed out that not only are the hypothalamus and the reticular activation systems of the brain stem particularly rich in sympathin content but also that loss of this content is accompanied by an increase in secretion from the adrenal medulla. It may also be significant that the non-specific thalamic nuclei contain more than three times as much sympathin as the specific thalamic nuclei, since Mahut¹³ has demonstrated that electrical stimulation of the non-specific intralaminar nuclei can produce learning deficits in rats provided that stimulation occurs within a given period of the activation of the cell assemblies concerned.

Activity in the arousal system does not stop abruptly following a sensory stimulus, probably because of release of adrenaline. Rothkall¹⁴ has determined that the system is likely to be composed of adrenaline sensitive elements which give an immediate arousal effect upon the electroencephalograph and other adrenergic or transmitter elements, which are responsible for the long lasting effects. In any stressful situation such as flight, the level of arousal is probably at an optimum as a result of prolonged training, it is also envisaged that the level of circulating adrenocorticotrophic hormone and the feed back control of the blood value of adrenocortical hormone are also stabilized at a high normal value. What happens to this system when a new situation arises in flight which may have originated from lapses in attention or perceptual conflict?

It can be postulated that corticofugal impulses along the descending pathways to the arousal system¹⁵ may reduce its noradrenaline content and initiate the reflex discharge of adrenaline from the adrenal medulla and the new level of circulating adrenaline

may affect adversely the stability of the arousal system

It is important to consider that the neurogenic stimulus must be maximal, and the rate of build-up of disorganization of perception must be sudden. Too often one elicits histories of near-accidents of this type "I have been teaching jet instrument flying for some time with complete confidence in the right things happening if the right control movements are made, but on this occasion, panic and delusion completely took control of my faculties, and I was unable to think and act as I knew I should" Here is a sudden misapprehension leading to a sudden effector activity and the rapid rate of loss of control in high-performance aircraft only reinforces the "panic and delusion"

Despite the fact that the injection of adrenaline into the lateral ventricles of cats produces behavioural effects similar to light barbiturate anaesthesia¹⁴, and despite the probable existence of neurohumoral loops as postulated by McDermott *et al*¹⁷, how does the disorganization of integrated behaviour arise?

Milner¹⁸ has further elaborated Hobb's theory in the light of recent advances in neurophysiology, and in particular with introduction of the concept of neural inhibition as an active process. This has been demonstrated in the spinal cord on mono-synaptic reflexes by Eccles and his co-workers¹⁹, both by physiological and pharmacological techniques (Curtis *et al*²⁰) and in the neurones of the motor cortex by Li²¹

Even if it is difficult to extrapolate from observations on single neurones by micro-electrode techniques to the organized behaviour of the whole animal and thence to man, the fact that active inhibition can be demonstrated in neurones is of extreme importance. But does one require to postulate the presence in the central nervous system of substances which appear to have an inhibitory action upon dendritic function²²?

The maintenance of efficient performance in future tasks will depend to a considerable extent on whether there is impairment of attention or vigilance by either fatigue or stress. Mackworth²³ has demonstrated the importance of vigilance in work tasks, and it may be postulated that in any form of ballistic vehicle there may well be increased lag in perceptual feed-back with an enhanced rate of impairment in vigilance.

This is related to two neurophysiological problems in the mechanism of attention. Where and how does the inhibition of a sensory input occur when a more effective perceptual stimulus is presented? And what is the relationship to habituation?

Sharpless and Jasper²⁴ have already shown that habituation occurs readily in the arousal system when a tone is presented repetitively, but that re-arousal occurs when the frequency of the tone is altered. This is a situation well known to aircrew, who may first gain cognizance of an impending emergency from aberrant noise in the engine.

In the conscious animal, neurophysiological techniques such as indwelling micro-electrodes are of the greatest importance to the elucidation of these problems, particularly when the experimental orientation includes psychological constructs. There are also indications that neuropharmacology may well be implicated.

Hobb²⁵ has summarized the data on the function of acetylcholine in the central nervous system by stating the situations or cell-masses to which it

appears to be limited. There may be significant contributions to theory if there were any relationship between the rich content of acetylcholine in the caudate nucleus and the selective impairment of the delayed alternation response in the monkey produced by stimulation²⁶. Acetylcholine, as well as adrenaline, has a direct action upon the neurones of the reticular system²⁷, and both drugs have no direct effect upon specific sensory projection systems. The use of micro-injection techniques might elicit much data which may elucidate the physiology of the central of sensory inflow. Dawson²⁸ has reviewed the evidence for the existence of mechanisms of this nature which suggests that there might be a continual control on afferent sensory transmission from centres in the cortex, brain stem or cerebellum.

Since attention is a much more subtle process than can be accounted for by the arousal system, a controlled sensory block is of great interest and may be the basis for the direction of perception or the selective use of cues. However, arousal does tend to depress evoked cortical potentials in an 'unattended' sensory modality and an element of behavioural alarm may be essential for some of the inhibitory changes which accompany shifting of attention²⁹.

Neurophysiological studies of such changes should further the establishment of psychological theories of attention.

Inter-Disciplinary Research

If it were possible to measure in any individual, values for learning or 'cue' functions, in relation to values of arousal as affected by environmental or emotional processes, then some estimate of the probable stability of an individual's behaviour during exposure to neurogenic stress might be obtained.

A general approach could be adopted initially in which pilots who have experienced certain types of near accident could be compared with pilots who have not had illusions in flight. Some techniques are more appropriate than others. Steinert³⁰ has shown that an inverted U relationship exists between performance level and level of arousal, using as criteria palmar conductance, electromyographic gradients and the alpha component of the electroencephalograph. It is probable that such techniques would merely give group identification, and the relative placing of any one individual within a group would not be sufficiently accurate for practical purposes.

For more detailed investigation, use could be made of flight simulators of modern type situated in a reduced sensory environment. The aim would be to repeat in some degree the observations of the Cambridge Cockpit Group, and when fatigue had resulted in lapses of attention, or decrease in vigilance³¹, to introduce a perceptual conflict in orientation. Not only would such methodology require development, but also physiological variables should be recorded which show less temporal independence than the electroencephalograph and palmar conductance.

In order to investigate the effects of neurogenic stress upon man, methods of inducing fear or anxiety are obviously required, other than the usual ones of incentives or pain³². Again, use can be made of isolation, by immersion in water³³. If it were possible, for example, to create an illusion of sudden reversion of bodily orientation, data of great interest could be derived from the recording of such variables as

electroencephalograph, pulse-rate, respiration, electro-myograph and muscle blood flow by electronic means.

The correlation of results with anterior pituitary and adrenal activity would be clearly desirable, but it would be essential to employ techniques which would give more direct functional measures than oesinophil counts or urine extractions. Bush and Sandberg¹⁴ have established by chromatography the identity of the major circulating adrenocortical hormone in human plasma as 17-hydroxycorticosterone (compound E) although the amounts are small. Nelson *et al.*¹⁵ found only 4–10 μ g per 100 ml of whole blood in resting normal subjects.

Even if the aggregate of data from such investigations would prove to be of considerable value, it is unlikely that their interpretation could adequately decide orders of precedence in events, so that considerable animal experimentation is clearly required.

Investigations on Animals

Rats. It has been postulated that the general stressful conditions of flight lead to a sustained increase in activity of the hypothalamic-pituitary-adrenal axis; it is known that an intravenous injection of adrenocorticotrophic hormone leads to an increase in output of hydroxycorticosterone within 10–20 min., and that continuous infusion of the same amount of adrenocorticotrophic hormone leads to a sustained rise in adrenal output.

Though enough is known about the peripheral or somatic actions of corticosteroids, very little is known about their action on the central nervous system and nothing about the stability of the feedback control of the enhanced level of cortico-steroids on man. It is evident from animal data that there is a neuro-humoral loop of some magnitude which should have some control as well as peripheral actions but which has a delay of minutes and is therefore probably concerned with metabolic rather than primary nervous activity. For example this loop might be concerned with the maintenance of arousal but scarcely with rapid alterations in the level of arousal.

Vogt has speculated that the rich content of sympathin, in the reticular system and hypothalamus may have a behavioural function: reduction in content is caused by the administration to dogs of drugs known to effect stimulation of the sympathetic nervous system and the reflex release of adrenaline. Purpur¹⁶ has demonstrated in cats with crossed circulations, the persistence of arousal or electrical excitability of the cortex, after cessation of stimulation of the bulbar reticular formation in the ipsilateral animal. He also demonstrated similar effects in the unstimulated animal but with a delay of 30–80 sec.

It is possible, therefore that stress, by causing increased activity in the brain stem reticular formation and a reflex secretion of adrenal medullary hormones influences cortical activity in a non-specific manner. Intense stimulation of this second hormonal loop within a generally stressful environment, which has already resulted in enhanced activity in the production of corticosteroids may have some relationship to abnormalities in behaviour.

There are many factors which are still unknown. The role of the limbic system of the brain has received much attention in various aspects of responses to

stress particularly with reference to emotional behaviour but little is known of its possible relationship to the hypothalamic control of hormonal output, except that the reticular system is probably implicated. Again, the relationship of the sympathetic adrenal medullary system to the pituitary-adrenal cortical system has many puzzling factors. In man, Sandberg *et al.*¹⁷ found no effect from the infusion of adrenaline on adrenocortical secretion but Harwood and Mason¹⁸ found a fairly marked effect on the dog.

It is therefore proposed that studies be carried out on the possible relationship of various aspects of behaviour and the activity of the brain stem reticular formation as determined indirectly by its sympathin content or by the output of cortico-adrenal steroids.

Beach¹⁹ found that morphine injections result in a significant increase in exploratory behaviour in rats, as compared to a control group but not as compared to a hungry group. He considered that this effect was probably due to lowering of perceptual threshold through increased activity of the reticular formation of the brain stem, but he did not relate his findings to those of Vogt¹⁶, who found that morphine caused loss of hypothalamic sympathin with concomitant secretion from the adrenal medulla.

Again, Petronovitch and Bolles²¹ found in studies on delayed alternation in rats that 12 out of 16 animals met the criterion of learning—the remainder could never learn to alternate their responses on the T-maze. These animals were subjected to a water deprivation schedule and it was found that in order to develop the delayed alternation response to its full a loss in body weight of 20 per cent was necessary. Although it was concluded that memory served as a cue for the correct response, no further investigation was made into the failure in training of the four rats which did not lose weight.

Thurst schedules are used in many comparative psychological investigations in order to induce a learning set, but the probable physiological processes involved are infrequently considered. Hunger is usually considered as a drive. However, Hebb²² has equated drive with arousal on the hypothesis that an increase in drive or arousal from a low to a moderate level and likewise a decrease from a high to a moderate level will favour the learning of responses.

All initial handling of rats should therefore be considered as stressful, and the physiological literature abounds in warnings that even methods of examinations involving taking of blood induce an oesinopenia. The literature of this aspect of psychology is also large not only does constant handling affect growth and resistance to stress, but it also affects behavioural performance, such as reduction of numbers of errors in re-learning on a water-filled closed field maze.

It would appear to be worth while investigating the influence of some of these methods used in physiological psychology on for example the corticosterone content of rats: adrenals the animals being killed by rapid decapitation, analysis being carried out by paper chromatography.²³ Holzbauer²⁴ has demonstrated that, in decapitated rats the hormonal stress of the adrenal cortex reflect the secretion rate at the time of death. She found significant variations between unstressed rats belonging to different colonies but the largest differences were between stressed and unstressed rats.

For example, the influence on intelligence of rearing rats in a free environment, as determined by the closed-field test of Rabinovitch and Rosvold⁴⁶, should be re-investigated, if there should be any correlation between corticosterone secretion and behaviour under these conditions, then it might be possible to show some relationship between the response of the adrenal cortex and 'brightness' and 'dullness' within similar strains

Dogs The biochemical properties of the adrenal cortex of each species are probably specific and genetically determined. The secretion of the rat is unlike that of most other experimental animals and also of man, but those of the dog and the monkey are sufficiently similar to man, since a large proportion of the total secretion would appear to be compound E

Consideration should therefore be given to the dog as an experimental animal, if results of significance can be derived from experiments with rats

The general plan of these further behavioural studies might well follow that of Thompson and Heron⁴⁶, who investigated the effects of early experience on both the problem-solving capacity of dogs and on exploratory activity. They found that the dogs reared in an environment which was restricted in perceptual content evinced significantly greater activity, but had a permanent decrement in intelligence compared to their litter mates which were reared in a normal environment

24-hr food deprivation schedules were used in trials on delayed reactions and it can be postulated that the stress of testing was different in the two groups

In four normal dogs, delays of 240 sec were achieved after an average of 230 trials, but the restricted dogs could not achieve any delay. If a modification of Vogt's technique⁴⁰ for the estimation of sympathin in the central nervous system were used, then it might be possible to relate the sympathin content of the reticular formation and the intralaminar thalamic nuclei to differences in behaviour

If the sympathin content were higher in the normal dogs, then it could be deduced that the impaired learning of the restricted dogs was related to the activity of the reticular formation, but further experimentation would be required to relate the strength of drive or of drive reduction to learning

A series of investigations on learning set might provide more data of significance. It is known that stimulation of the central median nucleus of the thalamus (non-specific) produces facilitation of cortical sensory neurones⁴⁷, also stimulation of intralaminar nuclei may interfere with learning. If these findings be related, then during the formation of learning set, two physiological processes may be involved—the determination of the motor response by the linkage of the appropriate active cell assemblies and the progressive reduction in the activity of the arousal system

Determination of this latter by Vogt's techniques might be more meaningful to behaviour studies than micro electrode techniques

Summary

The future problems in aviation medicine are subtle and difficult. Many are concerned with the determination of behavioural responses to neurogenic stress in conditions where it is impossible to reproduce

fully this stress on the ground. It would appear that studies on man should be supplemented by animal investigations and that a multi-disciplinary approach would enable adequate theories to be constructed on the relationship of alterations in perceptual learning to stress

With the verification of such theories or important parts of them, it should be possible to derive new selection processes for personnel involved in future flight or extra-terrestrial travel

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A BONE IMPLEMENT FROM STERKFORTEIN

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A MEASURE of controversy has been aroused by Dart's thesis that *Australopithecus* used bones, horns and teeth as implements. Evidence for this view has mainly come from Makapansgat but it is the purpose of this article to report the discovery of a bone implement at Sterkfontein. This single find supports Dart's view in proving that bone was employed artificially in the Transvaal during the known australopithecine period, on the other hand whether this new find represents australopithecine handiwork is quite a different matter.

The specimen under consideration was found on June 4 1958 during a five-month excavation season devoted to further exploration of the Sterkfontein extension site. This abuts on, and is continuous with the type site from which approximately a hundred specimens of *Australopithecus* have been recovered. As already reported^{1,2} the Sterkfontein deposit (type plus extension sites) consists of three different breccias: (a) lower or type site breccia, which has yielded numerous *Australopithecus* remains but neither stone artefacts nor *Equus*; (b) middle or red brown breccia, which has yielded 228 stone artefacts, a few small pieces of *Australopithecus* as well as remains of *Equus*; (c) upper or brown breccia, which is thin and patchy and has yielded *Equus* but neither *Australopithecus* nor artefacts. Where the upper breccia occurs in the area actually excavated, it is separated from the middle breccia by a thin drip-stone or stalagmite. The bone implement was wholly encased in solid red brown (middle) breccia a short distance below the stalagmite.

The maximum dimensions of the specimen are length 0.1 m., width, 3 cm. and thickness 1.5 cm. In most places the thickness is roughly a centimetre. It consists of a portion of a long bone which had been split longitudinally. One half was then apparently broken in a manner which left one end pointed. The surfaces resulting from the breaks which formed the point have become polished completely smooth, while most of the natural bone surface has retained its original appearance—except for an appreciable amount of manganese staining. The specimen was originally longer than at present. In excavating the breccia in which it was embedded it was broken into a number of pieces all but a very few small pieces being recovered. The butt end was apparently slightly longer before the recent breaking occurred. Evidence of ancient damage to this end suggests that the specimen had originally been over longer.

In view of the differences of opinion which exist about the reality of bone implements associated with australopithecines it is necessary to examine the reasons for regarding this specimen as an artefact. Two common groups of agencies may produce post-mortem alteration to the natural shape and appearance of a bone. These are (a) natural weathering agencies, and (b) animals including man.

Under (a) the following may be considered

(1) *Water* This could have acted by rolling and abrading the specimen while loose—in a stream bed, for example. This action would first affect all ridges or other prominences. This is not true of the specimen in question. The most marked smoothing is not on ridges, and at least one fairly delicate ridge is present and scarcely affected. Most of the surface has not been smoothed at all. Rolling may thus be discounted. But water may also have affected the specimen in another way. If the bone became partially exposed by weathering of the breccia the exposed portion could have been smoothed by sand bearing water flowing over it periodically while the protected portion remained unaffected. This can also be discounted, since the smoothed portions are related to the unsmoothed portions in such a way that the one could not have been exposed without at least some of the other also. Furthermore, the entire specimen was in solid breccia overlaid by a stalagmite as well as a later breccia. All other bone in the immediate neighbourhood was fresh and showed no signs of artificial smoothing.

(2) *Wind* Wind blown sand particles can readily smooth off rock, glass, bone and other such objects.

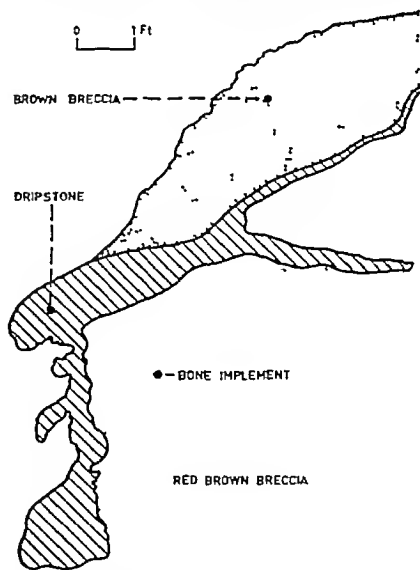


Fig. 1. Vertical section through a portion of the Sterkfontein extension site showing the position of the bone implement in relation to the middle and upper breccias and the drip-stone layer.

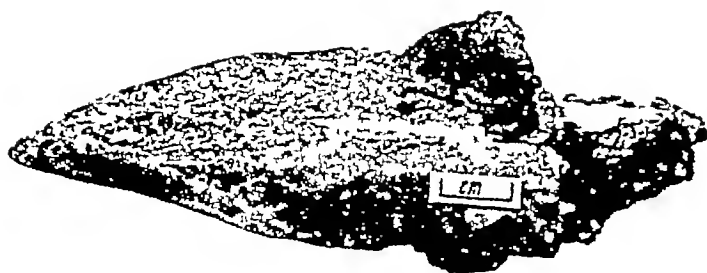


Fig 2 Bone implement from Sterkfontein. Some breccia is still adhering to the specimen



Fig 3 Enlarged view of apex of the Sterkfontein implement, showing one of the two main polished surfaces

However, this mechanism is indiscriminate in that all exposed parts are affected. The marked localization of the smoothed areas on the specimen and the relationship of smoothed to natural surfaces render wind action improbable in the extreme. Furthermore, the action of blown sand is to produce a fine frosting on the affected surfaces, not a smooth polish.

The nature, relative size and distribution of the artificial surfaces and the circumstances of preservation eliminate also the remote possibility of chemical weathering.

Under (b) may be considered

(1) *Carnivores* The carnivores which commonly chew bones and which could conceivably be concerned in this instance are hyenas, the larger cats and the dog group. All these splinter the shafts of long bones or consume them entirely. It is impossible to see how any of them could produce either the shaping or the polishing here involved.

(2) *Rodents* Some modern rodents gnaw bones found lying about, especially in caves. This is particularly true of porcupines, and many fossil bones bear witness to the antiquity

of this activity. Unwary observers may be misled by such bones as they are often gnawed along the shafts to produce a sharp edge or around the broken ends of shafts to produce chisel edges and similar effects. Examples occur among the bones found at Hopfield². However, the unmodified results of porcupine gnawing are fairly easy to detect since the marks made by the chisel-shaped incisors are visible. Where weathering has afterwards smoothed the bone, the gnawing may not be easy to detect—as in the case of some of the Hopfield bones which occur in shifting, loose sand where smoothing may thus occur easily.

This cannot be the explanation of the nature of the Sterkfontein specimen. There is no trace whatever of gnawing anywhere on the bone. If the smoothed portions are regarded as areas of weathered porcupine gnawing, then it is difficult to explain why the other parts of the bone are totally unweathered, since a marked degree of weathering would be necessary to remove all traces of gnawing. Examples of rodent gnawing do occur in small numbers in this site and an example is shown in Fig 5. But neither this nor any of the other bones so far found in this site exhibit the marked differential smoothing found on the bone under discussion.

There appears to be no other reasonable explanation than that a hominid used the bone in a manner which polished smooth the surfaces utilized and did not affect the other parts. This is certainly the immediate impression given by the appearance of the specimen. It does not seem likely that it was used for digging, since soil would affect all surfaces of the specimen at the digging end and would also produce a more scratched surface than is the case. The only possibility seems to be that it was used for scraping or rubbing something with a definite and fairly soft surface—for example, the under surface of animal skins. Under a stereo microscope a small amount of very fine scratching is detectable on the polished surfaces. This is much finer than that to be seen on Natufian bone implements from Mount Carmel, which show clear evidence of having been shaped deliberately, some of the shaping having been done with a blade of some sort, some of the other surface marks on these specimens may either have been made with a stone blade with an uneven edge or be the result of use. There is no evidence of cutting on the Sterkfontein specimen.

It seems, therefore, that the characteristics of the Sterkfontein specimen can only be explained as a by-product of intelligent hominid behaviour. As



Fig 4 Enlarged view of a portion of the Sterkfontein specimen showing a shallow oval hollow (near centre) with completely unsmoothed surface partly surrounded by polished surface



Fig. 5 Fragment of fossil bovid mandible, from Sterkfontein extension site, which had been gnawed by rodents

such it is the first clear-cut example of the utilization of bone from the Sterkfontein area and probably the best at present known from the australopithecine era. It certainly appears to be clear evidence of the artificial utilization of bone at that time level. Since this specimen came from the same breccia which has yielded the stone artefacts from this site, it must presumably for the present be attributed to the makers of the latter. In my opinion^{1,2} *Australopithecus* is unlikely to have made the stone artefacts

—it seems more likely that *Telanthropus* was responsible. Probably, therefore, the latter was also responsible for the bone tool. It is not impossible in view of the evidence accumulated by Dart that *Australopithecus* had an 'osteodontokeratic' but not an established stone culture, but that *Telanthropus* did have the latter. If this is the case it is possible that the Sterkfontein bone tool but not the stone industry, was of australopithecine origin. It is in any event, interesting to note that the specimen came from the back portion of the cave as it was at the time of accumulation among a mass of bones. The remainder of the deposit at that level has a much smaller proportion of bone.

I am indebted to the director of the Archaeological Survey and to Dr R. Mason of the same organization for the loan of Natufian bone implements from Mount Carmel for comparative study.

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CHEMISTRY IN THE PRESERVATION OF ANTIQUITIES

AT a joint meeting of Sections B (Chemistry) and H (Anthropology) held during the York meeting of the British Association, Dr A. E. A. Werner and Mr R. M. Organ of the British Museum Research Laboratory discussed the subject of chemistry in the preservation of antiquities.

Dr Werner said that the application of the chemist's specialized knowledge to the problems that arise in the preservation of antiquities may be taken to involve, first, the recognition of the symptoms of deterioration exhibited by antiquities and the realization of the ultimate causes for this deterioration expressed in terms of the physical and chemical structure of the object, and, secondly, the evolution of sound methods of conservation based on theoretical considerations and tested by practical experimentation—preferably, of course, on trial pieces or objects of minor importance specially acquired for the purpose.

In the past, the methods used in the conservation of antiquities were largely of an empirical nature and the materials used were limited to those of natural origin which approximated most closely in their chemical and physical properties, to the needs of the particular work in hand. Typical examples of such materials are waxes such as beeswax and paraffin wax, natural resins and animal and vegetable glues. However, in the past three decades or so, there have been remarkable advances in high polymer chemistry which have led to the introduction of many new synthetic materials, possessing a combination of chemical and physical properties not normally found in materials of natural origin. The assessment of the potential value of these synthetic materials in the elaboration of more reliable methods for the preservation of antiquities was discussed with special reference to specific problems in the preservation of antiquities of an organic nature.

One outstanding problem is the question of the most suitable method for the treatment of wooden objects which are obtained from excavations in a so-called water-logged condition. Old water-logged

wood may have a water content of more than 100 per cent of the dry matter in the wood, and its actual physical state will depend upon the degree of degradation, that is the extent to which the cellulosic cell wall structure has broken down. If this has reached an advanced stage, the wood will be quite soft, almost like cheese and will have a very low mechanical strength. In considering the problem of stabilizing old water-logged wood there are two factors to be considered. The first involves the actual removal of the large excess of water without causing serious deformation of the wood and the second involves the consolidation of the wood to restore sufficient mechanical strength so that it can be handled with ease.

If the water is allowed to escape by ordinary evaporation, surface tension forces exerted on the weakened cell walls will cause them to collapse. Hence special techniques have been evolved. One such technique is the so-called alum process, in which the wood to be treated is immersed in a super-saturated solution of alum at a temperature of about 95°C until complete impregnation is achieved. The idea behind this method is to replace the water by a solid, alum being used because it can be dissolved in a very small amount of water. A more refined method is the use of the well-known biological technique for drying tissues by immersion in successive baths of ethyl alcohol followed by immersion in baths of ethyl ether. If the final ether bath contains a resin such as dammar in solution, the resin will remain after evaporation of the ether to stabilize the wood structure. This is a relatively expensive process and involves a serious fire risk, so that it is confined in practice to the treatment of small objects, where it has been found to give excellent results. The well-known technique of freeze-drying can also be applied. The water is frozen to ice which is evaporated from the wood under vacuum, so that any tendency for the cell wall structure of the wood to collapse due to exertion of surface tension of liquid water is avoided. Experiments

made in the British Museum have shown, however, that the results are unreliable, and the method is very slow and time consuming, since it requires more or less constant supervision unless an expensive automatically controlled refrigerating unit is installed.

Since none of the above techniques may be regarded as being uniformly successful, experiments have been in progress in the British Museum Laboratory based on the use of the synthetic polyethylene glycol waxes. These waxes, although possessing the characteristic physical properties of waxes, have the rather unexpected property of being soluble in water. They are available in a polymeric series ranging from soft waxes rather like 'Vaseline' to hard waxes similar to the typical paraffin waxes. It has been found that the wax of average molecular weight 4,000 (the actual material used is known by the trade name of 'Carbowax 4000' produced by Union Carbide Chemicals Co.) is suitable for the treatment of water-logged wood. The new technique which has been evolved consists in immersing the wooden object in a 12 per cent aqueous solution of the 'Carbowax 4000' at room temperature and slowly increasing the temperature to c. 60° C over a period of many weeks. The water in the wood slowly diffuses out and is replaced by the wax. During the period of treatment, the solution is allowed to evaporate so that at the end the wooden object is lying immersed in molten 'Carbowax'. This technique is particularly suitable for wood which has suffered a considerable degree of degradation while in the water-logged state and is in a spongy condition.

If the structure of the water-logged wood has not suffered too severely, and still retains a certain degree of structural strength, an alternative method of treatment can be adopted. The wooden object is allowed to dry out slowly by being placed under conditions of gradually decreasing humidity. Under these conditions, the wood will dry without suffering distortion apart from a slight flaking of the surface layer. Consolidation is achieved by impregnation with an epoxy resin which is brushed on to the wood as a mobile liquid which readily permeates the wood, where it solidifies *in situ* at room temperature, thus conferring upon the wooden object the necessary mechanical strength. These epoxy resins, which have the highly desirable property of setting to a solid without undergoing appreciable contraction, are of general application as agents for the impregnation of wooden antiquities which are in a fragile state, for example, wooden objects which may have been severely weakened as the result of attack by insects.

In the case of leather objects which may be recovered from excavation in a fragile state as the result of being water-logged, or in a brittle condition due to excessive desiccation, immersion in molten polyethylene glycol wax of grade 1,500 at a temperature of about 45° C affords a simple method of preservation. The hydrophilic wax removes the water and consolidates the water-logged leather, whereas in the case of the brittle leather, the absorption of the polyethylene glycol wax restores to a marked degree the flexibility of the leather so that it can be handled with ease and, if necessary, reshaped without fear of breaking. Two other synthetic waxes which have proved of value in the formulation of a wax mixture for the surface protection of antiquities are the microcrystalline waxes which, owing to their special physical structure, are superior to the conventional paraffin waxes and the hard polyethylene waxes of relatively high melting point.

Another field in which new synthetic materials have found extended use in conservation is that of adhesives. When considering the use of adhesives in the restoration of fragile antiquities, the single factor which is of major importance is the question of the amount of shrinkage which can occur when an adhesive sets; if this is large, strains are set up which may weaken the bond or cause distortion of the bonded complex. In this respect the most suitable adhesives are those based on epoxy resins, these represent a class of adhesive which sets by chemical reaction *without* the loss of any volatile material.

The presence of soluble salts which have been absorbed by porous objects while buried in the earth prior to their excavation—for example, Egyptian ostraka—may be the latent cause of deterioration. When such objects are exposed to atmospheric conditions in which there are large fluctuations in the relative humidity, these salts tend to be transported to the surface where they crystallize out, thus obscuring the surface and, in the course of crystallizing, causing the surface layer to flake away, in the case of ostraka, this would result in the loss of the actual writing. These soluble salts can be removed by the simple process of washing in water, but, before carrying out the washing, it is necessary to consolidate the surface of the object in order to prevent any flaking away of the surface. This consolidation can be readily achieved by the use of a special soluble modified nylon—a material produced by Imperial Chemical Industries, Ltd., under the trade name 'Muranol soluble nylon polymer C 109/P'. This material is soluble in either methyl alcohol or ethyl alcohol, and when a 5 per cent solution in one of these solvents is brushed on to the object prior to washing, it deposits a surface film which is not only permeable to water (thus permitting elution of the soluble salts), but also possesses a marked degree of flexibility so that it does not exert any undue contractile force on the frail surface layers. This material also possesses adhesive properties which render it very suitable for the reattachment of flaking paint on wall paintings. It was used, for example, in the treatment of a fragment of a tempera wall painting from a tomb at Thebes of the XVIIIth Dynasty in which the paint layer was tending to blister badly. A warm 5 per cent solution of soluble nylon was brushed over the areas of flaking paint and gentle pressure applied. The alcoholic solution, having a much lower surface tension than an aqueous solution, readily flows into the minute cracks in the blisters and spreads out underneath the flakes of detached paint, drawing them back into position, in this way a secure bond was formed between the reattached paint and the ground. Furthermore, the surface film has a matt appearance so that it does not leave an aesthetically undesirable sheen on the treatment areas of the painting.

Mr. Organ dealt with the problems that arise in the preservation of bronze antiquities. He first described the causes of corrosion and the build-up of the corrosion layers. Metallographic examination shows that in the majority of bronze alloys the metal consists of a two phase system. Prior to excavation, these contiguous phases have often been in contact with water which had percolated through the soil and contained dissolved salts. An electrolytic system is thus set up in which one of the two phases corrodes to form insoluble salts which are deposited on the surface of the object in the form of minerals which comprise the well-known 'patina' characteristic of

antiquities. Cross sections of a corroded bronze were shown in illustration.

The occurrence of the so-called 'bronze disease' in museums is connected with the presence of cuprous chloride as a component in this mineral structure. This material not only reacts with moisture and oxygen in the air to form basic cupric chloride (which is the light green material that appears as the characteristic spots of bronze disease) but also attacks the underlying bronze with the formation of cuprite. Hence action directed towards preserving a bronze object must be aimed at nullifying the activity of this particular salt.

In those cases where it is desirable to retain the mineral patina on a bronze the reactivity of the cuprous chloride may be overcome by the use of special chemical reagents, namely (a) sodium sesquicarbonate solution or (b) specially prepared solid silver oxide.

In the first method the object is immersed in successive solutions of sodium sesquicarbonate, which has little visible effect on the patina but is sufficiently alkaline to neutralize the hydrochloric acid produced when the cuprous chloride is slowly converted into cuprite: $2\text{CuCl} + \text{H}_2\text{O} \rightleftharpoons \text{Cu}_2\text{O} + 2\text{HCl}$. The second technique involving the use of silver oxide, was specially developed in the British Museum Laboratory for the treatment of objects which for some particular reason cannot be unmursed in an aqueous solution, for example a bronze object inlaid with enamel work. The aim of this procedure is to seal off the corroding areas containing cuprous chloride by applying over them a layer of silver oxide powder which reacts to form an impervious layer of silver chloride.

When it is desirable to remove patina, which may be not only unsightly but also concealing valuable detail on the object, the various layers of mineraliza-

tion can be successively removed by chemical means. First, the green basic carbonate is dissolved by immersing the object in alkaline Rochelle salt, then the cuprite is destroyed using dilute sulphuric acid and, finally, the cuprous chloride layer is removed by cathodic reduction in alkaline solution. When this treatment has been completed, there will still be residual chlorides remaining in the porous metal; these must be removed completely if the object is to remain in a stable state under normal museum conditions. This can only be successfully achieved by a special process of intensive washing in many successive baths of distilled water. The progress of the washing is followed by measuring the electrical conductivity of the successive baths of wash water until it falls to a minimum and the absence of chloride is established. It has recently been found that this process which used to take up to eight months for completion, can be speeded up by a factor of as much as ten by the use of ultra-sonics.

When the mineralized layers are removed the object may sometimes be in such a fragile state that some form of mechanical support is necessary. In the past material such as wood or plaster and adhesives such as shellac and nitrocellulose were pressed into service *à la dent*. An improved technique was recently developed in the British Museum Laboratory using a malleable epoxy resin which can be supplied as a liquid which sets *in situ* to form a reinforcement. This material is ideal for the purpose because it adheres well to the metal, sets without shrinkage so that no contractile stresses are exerted on the fragile object and it is transparent so that no details of design are obscured. This technique was successfully used to strengthen a unique silver hanging bowl excavated at St Ninian's Isle, Shetland which after removal of corrosion products was as thin as an egg shell. A. F. A. WERNER

GENETICS AND THE ORIGIN OF SPECIES

TO assess the magnitude of Darwin's contribution to biology one hundred years after the publication of "The Origin of Species", it is necessary to recognize that Darwin developed his ideas in a very different climate of biological thought from our own. Darwin's recognition of the dynamic nature of species was made not at a time when species were regarded as the static products of natural creation.

Species, as aggregates of individuals subject to variation and constantly being replaced by those of their progeny which escape from the hazards of their environment represent a concept which we owe to Darwin and which still lies behind our knowledge of evolution.

Modern theories of genetics have sprung from Mendel's demonstration of the particulate nature of inheritance and the subsequent discoveries that the hereditary determinants, or genes are located in the chromosomes. The idea that genes are subject to mutation and liable to re-assortment at meiosis represents the crude mechanism of the variation on which natural selection must operate, but behind this lies the more fundamental aspect of gene evolution and the biochemical mechanism of their operation.

If the symposium in Sections D (Zoology) and K (Botany) of the British Association at the recent

York meeting gives an insight into modern evolutionary thought it is clear that geneticists are at present largely concerned with the manner of gene action and the process of modification in genotypic constitution which selection induces. Several speakers pointed out that the precise effect of a gene is modified by the genetic environment of the gene so that successful species come to possess a highly integrated gene assemblage. As Prof K. Mather (Birmingham) emphasized the main features of an organism affected by selection are controlled by swarms of genes acting together. The effects of separate genes are balanced and selection shifts the balance, giving gradual and not jerky evolutionary change. Moreover, it is only in this way that we can understand how an organism can achieve the complex selection advantage we find, for example, in mimicry where a strong degree of visual similarity with the model must be obtained before selection will operate. In the case of the African butterfly, *Papilio dardanus* in which the female mimics several models, Dr P. M. Shoppard (Liverpool) described how the range of variation in mimic characters of the progeny of hybridization of geographical races indicated polygenic control. Dominance of mimic features has been selected so that hybrids between races which naturally meet occur.

mimicry in offspring, in hybridization of races which do not naturally meet, this dominance is lost, but reasserts itself when replaced in its original genotic environment by progressive backcrossing to the race which originally possessed it.

Re-adjustment of the gene-complex under the pressure of selection will account not only for change within a species with the passage of time, but also for divergence of parts of a species. Any tendency for genes not to diffuse throughout all the members of a species will encourage the development of restricted gene complexes. In introducing the symposium, Prof J Heslop-Harrison emphasized that these barriers to gene flow, or isolating mechanisms, are of several types.

Physiological isolation by hybrid failure or sterility is the main genetic criterion by which species status is recognized, and this may be attained at a single evolutionary step in cases of polyploidy.

Dr R Riley (Plant Breeding Institute, Cambridge) directed attention to the high frequency of polyploidy in plants, where successful polyploids usually arise by the combination of genomes, which, even if derived from the same species, are sufficiently different to allow diploid behaviour (chromosome pairing) to be established at meiosis. Dr Riley showed how cytogenetical techniques had allowed the three genomes present in common wheat, which is hexaploid, to be identified as those of *Triticum monococcum*, *Aegilops speltoides* and *A. squarrosa*. By taking advantage of chromosome deficiencies, the mechanism controlling genetic isolation in wheat had been located and the way opened for hybridization with other cereals.

Isolation by breeding preference was discussed by Dr A J Bateman (Christie Hospital and Holt Radium Institute, Manchester). Experiments with

the fly *Drosophila*, where a choice of mating partner is offered, indicate that, for example, body-colour mutants influence preference. Field observations of nesting pairs of birds where a plumage colour variant is present have shown similar preference to operate in natural populations. Constancy of pollinator in plants must play a similar part as, for example, between the two champions, *Silene dioica* and *S. alba*, which are respectively bee- and moth-pollinated.

In both outbreeding plants and animals, however, spatial isolation by ecological or geographical factors is the most widespread external mechanism which allows initial divergence either by chance restriction of genes in limited populations, or because ecological conditions differ between populations or their parts. The nature of soil preference and importance of competition were discussed by Dr C. D Pigott (Sheffield), who described the manner of elimination of *Vaccinium vitis-idaea* from mixed populations with *V. myrtillus* and occasional hybrids, by reduction in grazing pressure after enclosure and exclusion of sheep from upland oak-woods.

That divergence can precede isolation, however, is evident from experiments with *Drosophila* described by Dr J M Thoday (Sheffield). By disruptive selection (elimination of the mean phenotypes and retention of extremes) within a single breeding population over several generations, a steady trend of divergence of the extremes is produced. Furthermore, experiments, in which the most extreme individuals are those used for breeding, demonstrate that this difference can be maintained.

Experimental studies of this type demonstrate very clearly that evolution is no longer a theory propounded by Darwin but an indisputable fact.

C D PIGOTT

OBITUARIES

Dr Louise Pearce

DR LOUISE PEARCE, former associate member of the Rockefeller Institute, who had worked there from 1913 until 1951, died in New York City on August 9 at the age of seventy-four years. Having graduated M.D. at the Johns Hopkins University in 1912, she began in 1913 her chemotherapeutic studies in association with W H Brown of the Institute. A few years previously Ehrlich had had great success in the treatment of disease, including syphilis, with organic arsenicals. In collaboration, these two workers studied experimentally the effect of arsenical compounds on laboratory infections in animals with the parasite causing African sleeping sickness. One compound of this series, namely trypanarsamide, prepared by Jacobs and Heidelberger in 1919, proved very effective against rabbit syphilis and was able to save the lives of animals infected with the pathogenic African trypanosomes. Tests on the response of the human disease to this new substance were now urgently required. Louise Pearce, of resolute character and endowed besides with great physical strength and vigour, was chosen to go out to the Belgian Congo in 1920, where thousands of natives were dying of the disease, and there carried out the tests at great personal risk.

The success of the new drug was soon obvious and, as Peyton Rous has written, "she brought about

one of the most shining and spectacular of the early purposeful achievements of the Institute, the conquest of sleeping sickness." Trypanarsamide owes its importance to the fact that it can reach the cerebrospinal fluid in considerable concentration and has the capacity to affect trypanosomes in the central nervous system. For this work Dr Pearce was awarded in 1953 the King Leopold II prize of 10,000 dollars and made an officer of the Royal Order of the Lion, having previously received the Belgian Order of the Crown. Her colleagues, W A Jacobs, M Heidelberger and W H Brown, were also honoured. With the last-named she discovered a rabbit cancer, known as the Brown-Pearce carcinoma, which could be transplanted to other rabbits and has proved of considerable value experimentally. The virus causing rabbit pox was another of her discoveries.

She was keenly interested in medical education and served during 1946-51 as president of the Women's Medical College of Philadelphia. Besides her successful mission to Africa she served as visiting professor of medicine at Peking Union Medical College during 1931-32. Her interests were wide and embraced many aspects of national and international life. As an officer of a number of organizations concerned with the study of bacteriology, medicine, tropical medicine, cancer and other diseases, she proved a good citizen of the world.

During her life time she was awarded a number of honorary degrees and prizes. Her monograph "The Treatment of Human Trypanosomiasis with Trypanamide", published by the Rockefeller Institute, is a classic.

J D FULTON

Dr E S Duthie

Dr EDWARD STEPHENS DUTHIE died on June 9 at the age of fifty two. He was an experimental and clinical pathologist with an exceptional range of talents. Born in Kilkenny he won a scholarship in mathematics to Trinity College, Dublin, and graduated in arts, medicine and science. He began biological research under Prof J B Gatenby in Dublin and continued under Prof A E Boycott at University College Medical School London where he went as Graham Scholar in 1933. His published work during this period was concerned mainly with the mechanism of glandular secretion. While convalescing from tuberculous pleurisy in Italy he wrote a paper on the origin, development and function of the blood cells in certain marine teleosts.

After a brief interlude as assistant pathologist at the University of Sheffield he joined the staff of the Dunn School of Pathology Oxford and collaborated with Chauin in a study of 'spreading factor' which they identified as hyaluronidase. Duthie was unfit for military service during the War so he worked as hospital pathologist at Northampton until he was recalled to Oxford to help Sir Hugh Cairns. He organized and took charge of all the chemotherapy at the Radcliffe Infirmary and at the Military Hospital for Head Injuries. His development of penicillinase his work with Chauin on the theory of action of penicillin and his demonstration of the influence of pH on the activity of streptomycin have all contributed to the rapid progress of chemotherapy.

Duthie took charge of the Serum Department of the Lister Institute in London in 1940 and worked on serum and bacterial proteases and their inhibitors. In 1948 he was appointed deputy director of pathology

at Southampton becoming director in 1952. During the past ten years he studied various products of the staphylococcus. His crowning achievement was the purification of coagulase—the first blood clotting substance to be purified.

Duthie's integrity, sympathy and kindness were apparent to all who met him. His friends knew his generosity, his concern for refugees and all who were oppressed, his appreciation of art and music and his courage and cheerfulness in the face of prolonged ill health.

CHARLES H. LACK

Mr John Cecil May, CMG OBE

By the death on September 10 of J C May, director of the Empire Cotton Growing Corporation, tropical agriculture has lost one of its wisest and most distinguished administrators of agricultural research. His background of geology and forestry at Oxford and of the administrative service in Nyasaland and Tanganyika was singularly appropriate for the development of his life's work in an independent corporation engaged in research in tropical territories. His judgment and enthusiasm were largely responsible for the high standard of recruitment to the Corporation's service, and his sympathy and understanding for the welfare of his staff in the diverse circumstances in which they work. He understood the needs and difficulties as well as the responsibilities of government departments and his breadth of interest was the foundation of the co-operation between government officials and the research staff of the Corporation that has been so fruitful in the extension of the cotton crop in African territories. His vision and grasp of practical needs and possibilities enabled the Corporation to continue to provide staff for the Sudan when the Republic of the Sudan was established. In planning the British contribution to technical services in the new Africa that is emerging, his counsel will be sorely missed.

J B HUTCHINSON

NEWS and VIEWS

International Red Locust Control Service

THE last plague of the red locust *Nomadus septentrionalis* Scoville, lasted from 1930 until 1944 and affected most of Africa south of the equator. Field investigations by British, South African and Belgian scientists revealed comparatively small outbreak areas in Northern Rhodesia and Tanganyika. In 1941 A. P. G. Mchalemore set up headquarters in Aborcom Northern Rhodesia, and began preventive control of these areas. In 1945 H. J. Brede became director of the International Red Locust Control Service. This Service was established by international treaty in 1940 and the first decade of the treaty was completed on August 5 this year. At first the idea was to watch for any upsurge of locusts in the outbreak areas and then to arrange control measures but it became clear that events moved too quickly and the Service had to be constantly ready to attack. Even so, swarms escaped from the outbreak areas in most years until operational research, mainly by Haydn Lloyd, led to the design of fully effective methods of control using very light aircraft. In 1955 there occurred the largest upsurge ever recorded

it was completely controlled. No swarms have escaped since 1954.

Dr D L Gunn CBE

DURING the period 1952-59 the director of the International Red Locust Control Service was Dr D L Gunn. Educated at the High School and the University College, Cardiff, he was then for seventeen years at the University of Birmingham, first as assistant lecturer and finally senior lecturer in zoology. There he became known for researches on the temperature and humidity relations of insects and he collaborated with Dr Gottfried Fraenkel in "The Orientation of Animals" (Oxf. Univ. Press). Towards the end of the War he was seconded to Kenya to study the behaviour of desert locusts in swarms in relation to aircraft spraying and in 1945 with Douglas Lee and a team from the Chemical Defence Experimental Establishment Porton he carried out the first attacks on adult locusts in Africa that used liquid insecticide sprayed from aircraft. In 1946 he became the first principal scientific officer of the Anti Locust Research Centre then newly separated under Dr B P Urry from the Comman

wealth Institute of Entomology, and was responsible for starting and building up its research programme, both in the Centre laboratory and extra-murally in universities. In 1947 jointly with H A F Lea (now chief locust officer of the Union of South Africa), he was responsible for successful aircraft spraying experiments against the red locust in Tanganyika. In 1950 he did field experiments in Somaliland and the Sudan which resulted in the complete replacement of wet bait by dry bait for controlling the desert locust with great economies in cost. In 1952 he was appointed director of the International Red Locust Control Service. In the following years, this Service was completely reorganized, made effective and cheapened to about half its earlier maximum annual cost. Dr Gunn was appointed CBE in 1958 and he now leaves Africa to become director of the Tea Research Institute of Ceylon.

Mr C du Plessis

THE Council of the International Red Locust Control Service has invited Mr C du Plessis to become director in succession to Dr Gunn. Educated at Oudtshoorn and at Grey University College, Bloemfontein, he lectured in zoology at Grootfontein College of Agriculture for six years and in entomology at Glen for four years before beginning full-time research on stalk-borer at Kroonstad. Soon after the red locust plague reached South Africa, he began research under Prof J C Faure, publishing mainly in the science bulletins of the Department of Agriculture, and becoming increasingly involved in control as well. In 1944, locust research, locust control, and administration, were combined under the newly enlarged post of chief locust officer, to which post Mr du Plessis was appointed. He was responsible for containing within the outbreak areas a prolonged upsurge of the brown locust from 1948 until 1954, during this period, both control methods and administration were completely revolutionized. Representing South Africa on the International Red Locust Control Service Council for many years he was elected president in 1954 in succession to Mr G B Beckett, then Member for Agriculture in the Northern Rhodesia Government. He retired from the post of chief locust officer in December 1958.

Theoretical Mechanics at Southampton

Prof B Thwaites

A THIRD chair of mathematics, with special reference to fluid mechanics, has been created at Southampton. The first holder of the chair will be Dr Bryan Thwaites. Dr Thwaites, after graduating in Cambridge with first-class honours in mathematics, spent three years in the National Physical Laboratory and was then appointed lecturer at the Imperial College of Science and Technology in the Department of Aeronautical Engineering. In 1951 he became assistant master at Winchester College but maintained his contact with university teaching and research as visiting lecturer in fluid mechanics at the Imperial College. Dr Thwaites has been a member of the Performance Sub-Committee of the Aeronautical Research Council and is at present a member of the Fluid Motion, Engine Aerodynamics and Laminar Boundary Layer Panels of that Council. He is chairman of the Aerofoil Theory Panel and editor of "Incompressible Aerodynamics" due to be published this year. His name is familiar in the form of the Thwaites flap and with his engineering interests it is

expected that his appointment will strengthen the already existing ties between mathematics and engineering in the University of Southampton. Dr Thwaites' wide cultural and teaching interests will be particularly welcomed in the rapidly expanding University of Southampton.

Electrical Engineering at Southampton

Prof L G A Sims

DR SIMS, head of the Electrical Engineering Department and senior lecturer in electrical engineering in the University of Southampton, succeeded the late Mr P G Spary in 1952, and he has now been made professor in the University. Dr Sims studied under the late Prof William Cramp at the University of Birmingham, graduating with first class honours and a Bowen Research Scholarship in 1924. He obtained his MSc with an award of a research prize. He joined the Research Laboratories of the General Electric Co., Ltd., under the late Sir Clifford Puterson. Later he joined the lecturing staff of the University of Birmingham, and although primarily concerned with power engineering and founding the first electronics laboratory, he was associated with the first successful television reception in Birmingham received from the original London Baird transmitter. Dr Sims initiated and directed researches at Birmingham upon the incremental properties of magnetic steels. In 1936 he was appointed head of the Electrical Engineering Department of the Northampton Polytechnic in London. On the power utilization and supply side Dr Sims was one of the first engineers in Britain to be interested in energy storage with the a.c. system and initiated research work upon electrothermal storage methods. He has held senior teaching appointments in Government Service both at the Royal Naval College, Greenwich and the Royal Aircraft Establishment, Farnborough. During the session 1957-58 Dr Sims was chairman of the Institution of Electrical Engineers, Southern Centre. His main ambition is that he and his staff shall advance the prestige of the already well known Electrical Engineering Department in the University of Southampton, and liaison work with large industrial concerns in different parts of Britain together with new electrical courses may lead to a system of postgraduate scholarships in electrical engineering by the time of the University centenary in 1962.

Physics at the University College of North Staffs

Prof D J E Ingram

DR D J E INGRAM has been elected to the chair of physics at the University College of North Staffordshire, in succession to Prof F A Vick, who has become deputy director of the Atomic Energy Research Establishment Harwell (*Nature*, 183, 861, 1959). Dr Ingram was reader in electronics at the University of Southampton, where he went in 1952 to work with Prof E E Zepler now president of the British Institution of Radio Engineers. He took a first in physics at Oxford in 1949 and worked for three years under Prof B Bleaney on magnetic resonance. At Southampton he extended his work on microwave spectroscopy, gathering together a team of physicists, chemists and electronic engineers, which has applied the techniques of electron resonance to a variety of problems in physics and chemistry. This work has been particularly fruitful in studies of metallo-organic compounds, such as the haemoglobin molecule, in the investigation of breakdown processes

resulting from ultra violet irradiation and in detection of free radicals in various forms of carbon. Dr Ingram has also been concerned with the study of maser and invar problems, and with the use of electron resonance in applied electronics. He is the author of two books on the applications of microwave spectroscopy to physics and chemistry, and has been one of the instigators of the formation of the Radiofrequency Spectroscopy Group.

Chair of Applied Mathematics at Cardiff

Prof P T Landsberg

Dr P T LANDSBERG, who has been appointed to the newly created chair of applied mathematics at Cardiff, came to Britain from Germany in 1939. He followed his bachelor's degree in the University of London by a master's degree in the field of quantum mechanics and in 1947 he became one of the early members of Dr T E Allibone's staff at the Associated Electrical Industries Research Laboratory, Aldermaston. He participated in the semiconductor interests of the Laboratory, concentrating on the theory of electrical barriers. The generosity of the Laboratory enabled him also to work at the same time for a Ph D degree under Prof H Jones on the effects of electron collisions on the soft X-ray emission bands of sodium; this investigation showed that there were long range correlations among the electrons, resulting in an unexpected screening of the Coulomb interactions. Since 1950 Dr Landsberg has been a lecturer in natural philosophy at Aberdeen, where his teaching interests have ranged from first year practical classes to statistical mechanics at an advanced level. In 1956, together with his pupil, Dr I E Farquhar, he helped to re-open the subject of the quantum statistical ergodic and H theorems, which were thought to have been proved by von Neumann in 1929 and later improved by Pauli and Fierz, by showing that they were based on an erroneous argument. Also in 1956, Dr Landsberg published a notable paper on the foundations of thermodynamics in "Reviews of Modern Physics", and has a book appearing shortly in the same field. He has maintained his interest in semiconductors, where his most recent paper, with his pupil, Dr A R Beattie shows that electron collisions can play the dominant part in limiting the life time of excess carriers in indium antimonide. From the agreement between his theory and the experimental findings, it appears that this substance may be the first semiconductor in which the life time has been made to approach its theoretical maximum.

Festschrift for R E Snodgrass

The whole of Vol 137 of the Smithsonian Miscellaneous Collections (Studies in Invertebrate Morphology Pp v + 410 + 40 plates Washington, D C Smithsonian Institution, 1959) consists of a series of seventeen original articles by well known ontologists from many parts of the world under the general title of "Studies in Invertebrate Morphology", and is published "in honor of Dr Robert Evans Snodgrass on the occasion of his eighty fourth birthday July 5 1959". It is hard to think of R E Snodgrass as having reached this score. He is the tough wiry Mark Twain type of American admirably depicted in a frontispiece made last year. His ready and slightly caustic wit remains unimpaired and he is still turning out first class work on the morphology of insects. The book contains a sympathetic biographical chapter by Dr Ernesto B Thurman

illustrated with some of the highly professional comic drawings that Snodgrass produced in his early days. The scientific articles maintain a high standard throughout and many of them demonstrate the widespread influence exerted by Snodgrass as a morphologist. But Snodgrass has always taught that "morphology must be intimate with function" and it is appropriate that there are several good papers on insect physiology. There is plenty of good material in the volume, but it is fitting that the best paragraphs of all (pp 17-18) should be those in which R E Snodgrass himself resumes his outlook on life in a few well chosen words.

Sir Dorabji Jamsetji Tata (1859-1932)

THE leading architect in the intellectual and industrial renaissance of India, Sir Dorabji Jamsetji Tata was born at Bombay on August 27, 1859 and was educated at Gonville and Caius College, Cambridge and at the University of Bombay, where he graduated in 1882. On his father's death he became head of the company, Tata and Sons the largest industrial concern in India. In 1911 he established the Tata iron and steel works at Jamshedpur and in the same year founded the Indian Institute of Science at Bangalore to prepare young Indians for the direction of modern large scale industries and for industrial research. He was knighted in 1910 and served as president of the Indian Industrial Conference in 1915. A great philanthropist who rendered help without distinction of caste or creed he gave £25,000 to the University of Cambridge in 1920 for the equipment of laboratories in the School of Engineering (he was elected an honorary fellow of his college in 1922). In 1931 he created as a memorial to his wife the Lady Tata Memorial Trust for research in any part of the world into diseases of the blood and for work in India for the alleviation of human suffering. The last of his house he died at Kissingen in Bavaria on June 3 1932 and was buried in the Parsi cemetery at Brookwood Woking. In 1945 the Tata Memorial Hospital was erected in the city of his birth.

National Science Foundation Review of Research and Development

In a statement on Research and Development and Economic Growth (issued as No 13 by the U S National Science Foundation in its Reviews of Data on Research and Development), Dr A T Waterman said that the Foundation's studies indicated that national research and development effort currently stood at more than 10 thousand million dollars compared with less than 500 million dollars before the War, and had doubled since 1954. In terms of performance industry accounted for about 70 per cent, Government about 20 per cent, and universities and other non profit institutions for the rest. In terms of finance Government accounted for rather more and industry for somewhat less than half. Dr Waterman stressed the long term significance of the economic implications of research and development and besides the beneficial results which war expenditure on military research and development might have on the civilian economy research and development could stimulate the under developed economies of other countries. It was the key to the two great challenges of the future: the increasing opportunity to achieve our own potential growth and expansion and the urgent need to co-operate with the great under developed countries of the world. Of the 10 thousand million dollars currently expended

on research and development, only about 6 per cent was on basic research. In making a strong plea for more support of basic research, especially in colleges and universities, Dr Waterman said that this would ultimately reduce development costs by indicating the best fields of research. The Federal Government was supporting research in academic institutions but wished to see industry increasing its support for such research as well as its support of basic research in its own laboratories. Industry was the largest employer of scientific personnel, employing in January 1957 nearly two-thirds of the scientists and engineers in the United States, including 528,000 engineers, 152,000 scientists and 58,000 administrators of such activities about a third of whom were engaged on research and development.

Scientific and Technical Personnel

THE National Science Foundation of the United States has announced that at the request of the Bureau of the Budget it will be responsible for establishing and maintaining a programme of national information on scientific and technical personnel. This will cover their training and utilization, compensation levels, supply and demand, and other related data. The Foundation will organize the register, co-ordinate and analyse all information gained, and ensure that the findings be made public. Much of the information recommended will be produced by extending existing statistical records. Other projects will have to be initiated to meet the objectives of the programme. The decision of the Bureau to ask the Foundation to organize the register arose from recent recommendations of an advisory panel on 'Scientific Manpower Data Requirements'. The panel recommended a programme of fifteen projects, of which the most urgent were considered to be, first, an identification of scientific and technical occupations, secondly, a periodic survey of organizations employing scientific and technical personnel, and finally, a periodic study of the demand outlook for various categories of scientific and technical personnel in each major activity. The last item would include analyses of employment and production growth trends and also the changing roles of particular classes of scientific and technical personnel.

Productivity Measurement in Great Britain

A REPORT by T. E. Easterfield (Department of Scientific and Industrial Research. Productivity Measurement in Great Britain. A Survey of Recent Work. By T. E. Easterfield. Pp. 11+79. London: Department of Scientific and Industrial Research, 1959) attempts to survey recent or current British studies of productivity measurement at the level of the individual factory, together with such other related work as seems particularly illuminating. Studies based on overall statistics of whole industries are included only where they throw light on the problems of more detailed studies. The report first briefly discusses the main purposes of productivity measurement: overall economic analysis and planning, planning, target setting and the forecasting of requirements of industries or firms, the spotlighting of cases that stand out by reason of high (or low) productivity, and investigation of other factors that may affect productivity, and their relative importance. The main sections are the problem of multiple inputs, the problem of multiple outputs, the study of factors affecting productivity and the translation of results for practical application.

Education in the Commonwealth

A PAMPHLET, "Commonwealth Education: The United Kingdom Contribution" (prepared for the Commonwealth Relations Office and the Colonial Office by the Central Office of Information. Text by Duncan Crow. Pp. 68+4 plates. (London: H.M. Stationery Office, 1959). 2s. 6d.), gives an unimpressive picture of what the United Kingdom is already doing in this field, to which, in the twelve years April 1946-March 1958, Britain contributed under the Colonial Development and Welfare Acts £35 million in grants and loans, of which £16 million were for primary and secondary education, £6 million for technical and vocational education and £13 million for higher education. The pamphlet brings together, moreover, facts about an effort which embraces also what is being done through the British Council for the welfare of the 7,000 odd full-time Commonwealth students in the United Kingdom, some of whom are numbered among the 728 training as teachers in the United Kingdom and for the teaching of English in the Commonwealth. There is a section dealing with the Colombo Plan trainees and with the 6,566 Commonwealth students in United Kingdom technical colleges, and another with the remarkable growth of Commonwealth universities between 1938 and 1957, in which period the number of institutions has increased by 50 per cent, their teaching and research staff has trebled and full-time students have nearly quadrupled. No attempt is made to indicate the total cost to Great Britain, and, impressive as it is, the pamphlet shows clearly enough how much more remains to be done and the opportunities which interchange schemes, for example, offer for expansion.

Public Library Statistics in Great Britain

"STATISTICS of Public (Rate Supported) Libraries in Great Britain and Northern Ireland 1957-1958" (Pp. 33. London: Library Association, 1959. 7s. 6d.) gives the number of public library authorities in the United Kingdom on March 31, 1958, as 560, serving an estimated population of 51,597,000 and holding a stock estimated at 68,600,000, approximately 16 per cent being reference stock. Issues for home reading are estimated at about 431,863,000, an increase of 12,435,000 on 1956-57, and total expenditure was £17,522,000 compared with £15,906,000 in the previous year, of which £4,254,000 and £3,863,000 respectively were expenditure on books. Full-time non-manual staff numbered 12,990 compared with 12,760 in 1956-57, and at least 1,870 part-time paid staff were also employed. There are at least 32,755 public library service points in the United Kingdom, including 569 municipal central libraries and county headquarters, 1,333 full-time branches, and 30,853 part-time branches, centres, etc., as well as 200 mobile libraries.

Instrument Construction

THE Russian monthly *Priborostroenie*, which is described as a "scientific, technical and production" journal, is being produced in an English translation under the title *Instrument Construction* (No. 1, 1959. Translated from the Russian. Pp. 38. Published monthly. Subscription £6 yearly post free (17 10 dollars U.S.A. and Canada). Special rate of £3 yearly post paid (8 55 dollars U.S.A. and Canada) available to University and Technical College Libraries. Single copies 15s. each (2 15 dollars U.S.A. and Canada). London: Taylor and Francis, Ltd.,

1959) by the British Scientific Instrument Research Association for the Department of Scientific and Industrial Research. It covers industrial instruments and instrumentation, automatic control and production engineering for precision work and affords a valuable insight into current Russian practices in these fields. The first number of the journal corresponds to the January 1959 issue of *Priboorostroenie* and each issue of the English journal, because of the time needed for translating and printing will be published two and three months later than the corresponding Russian number. The contents of the first number includes five short articles from the twenty first congress of the Communist Party of the Soviet Union. The articles pay tribute to Mr Khrushchev's report "Targets for the Development of National Economy of the USSR for the period 1959-65", and deal mainly with various aspects of the extension of automation in industry in furtherance of the seven year plan. The more technical articles deal with the automatic control of ferro alloy furnaces, a transistorized analogue computer, an electronic phase meter with a range of -180° to 180° and field magnets and magnetic lenses for cathode-ray tubes with cold cathodes. Laboratory notes and reviews and abstracts from the pages of the Czechoslovak journals, make up the remainder of the contents.

French Journal of Science Teaching

THE first edition of *l'Enseignement des Sciences* has made its appearance (1 No 1 May-June 1959). Hermann, Paris, 1,200 francs per annum) it is to be published five times a year. The journal aims to cover a wide field of science instruction and to publish as much original research as possible for the 'amelioration of scientific studies'. The first edition consists of 48 pages with seven plates, bold line graphs and some amusing Lima line cartoons. The main article, the "Known Limits of the Universe" covers eleven pages and is well illustrated. Articles follow on the importance of science in education, a report on the improvements in teaching at the Nancy school of mines and modern mathematics and their teaching. An extensive review of Jean Perrin's *Éléments de la Physique* is included also an interesting article on the philosophy of children which is based on Charles Rollin's *Traité des Études* (1720) in honour of his memory. Inquiring articles also occur on perceptions of geometry etc. The journal concludes with numerous short reviews and a section of general correspondence.

Atomic Energy in Australia

THE contents of the December 1958 issue of *Atomic Energy* (2 No 1) the quarterly published by the Australian Atomic Energy Commission to keep industry and commerce informed of progress in the field of atomic energy, includes an article by J. L. Symonds describing procedures for the commissioning period of the reactor *Hafar*, a review of reports made to the Second International Conference on the Peaceful Uses of Atomic Energy in Geneva during September 1958 on nuclear power developments in the various countries and an authoritative discussion of the power position in South Australia by S. E. Huddleston, assistant general manager of the Electricity Trust of South Australia. He maintains, contrary to the statements of many writers, that South Australia is not in need in the immediate future

of nuclear power largely because of the determined and efficient use being made of the power resources which are at present available. The only economic coalfield in the state is at Leigh Creek, some 350 miles north of Adelaide and in 1958, 694 million kilowatt hours were produced from Leigh Creek coal by the Electricity Trust. This will be stopped up when new plant becomes available and it is expected that Leigh Creek coal will be fully exploited by about 1965. The increase in demands for electricity indicates that it will be necessary for South Australia to introduce nuclear power in 1970, but a decision to build an atomic power station there may not be made for another five or six years. The future of nuclear power in Australia will be governed by the relative cost of generation from nuclear and conventional sources, the relative capital investment involved, and the availability and reliability of nuclear and conventional fuel. Mr Huddleston considers that South Australia will be the first of the States to need nuclear power and his careful review of the relevant factors as they affect South Australia may prove valuable in assessing the value of introducing nuclear power into other parts of Australia.

The Australian Museum

THE annual report of the Trustees of the Australian Museum for the year ending June 1958 (Pp 19 Sydney Government Printer 1959) records with appreciative comment the receipt of increased financial support from the Government. It also states that the clearance of temporary buildings has been carried out and that the site is now ready for the new wing which will form the continuation of the northern frontage of the Museum for which working drawings have been prepared. A generous gift by Sir Edward Hallstrom will enable the lecture theatre to be remodelled and brought up to date and thus make it of more use to the rapidly developing schools service. Much field work has been carried out by members of the staff and it is interesting to note that the appointment of a public relations officer has resulted in good publicity in many media.

Sierra de Tamaulipas, Mexico

BETWEEN 1945 and 1955 Dr MacNeish, now of the National Museum of Canada, led three expeditions to the state of Tamaulipas in north-east Mexico, and in a new publication (*Transactions of the American Philosophical Society*, New Series Vol 48, Part 6, Preliminary Archaeological Investigations in the Sierra de Tamaulipas, Mexico. By Richard S. MacNeish. Pp 210. Philadelphia: American Philosophical Society, 1958. 5 dollars) he gives the results of his work in the Sierra de Tamaulipas, a range of hills in the south of the State. It was not a favourable region for the development of elaborate cultures, although it was occupied for most of the time when the high civilizations of ancient Mexico were flourishing farther south. The importance of this study, which is considerable, lies in the evidence obtained from excavations in a dry cave for the cultivation of maize and squash on a small scale at the very early date of about 2500 B.C. in a mainly gathering and hunting culture. This is the earliest satisfactorily dated example so far known of cultivated maize, and a discussion of its botanical implications was published by P. C. Mingeledorf, the author and W. C. Olin in *Botanical Museum Leaflet* Harvard University 17 (5) 1956.

African Botany

A **VEGETATION** Map of Africa in colour, with accompanying explanatory notes by R W J Keay, and with a French translation by A Aubréville, has been published on behalf of l'Association pour l'Étude Taxonomique de la Flore d'Afrique Tropicale, with the assistance of Unesco (Oxford University Press (1959), price 15s in the United Kingdom only). The vegetation concerned is that which occurs south of the Tropic of Cancer. The author explains that the aim of the map is to show the vegetation as it is to-day and not the presumed climax types. He points out that the boundaries between the zones are seldom precise on the ground although, in the interests of clarity, they are thus represented on the map. The name selected for any particular zone relates to the most widespread natural or semi-natural type of vegetation found within it. Other necessary clarifying observations are also indicated.

'Parsnip' Dermatitis

UNDER this title B J Youngman has given an interesting account of various blisters and rashes caused by certain umbelliferous species, in particular those of *Heracleum* and *Pastinaca* (*Kew Bulletin*, 3, 387, 1958). In one instance, boys who had been playing with the giant species *Heracleum mantegazzianum*, using the stout stems as swords and telescopes, developed such severe red rashes and, later, blisters, as to require hospital treatment. This species of 'cow parsnip', which may grow to a height of 12 ft with hollow stems 4 in in diameter, is a native of the Caucasus. Originally introduced into Britain as a garden plant, it has now become naturalized in waste places, along rivers, etc. The author also discusses the edible, acrid, and vesicant properties of other species of *Heracleum* and of *Pastinaca*, to which the domestic parsnip (*P. sativa*) belongs, and cites evidence of more or less severe dermatitis effects which have been traced to them. She also recalls that some of the Umbelliferae have not merely acrid and scalding juices or ingredients but are virulently poisonous, for example, hemlock. So far the toxic principles present in species of *Heracleum*, *Pastinaca* and other umbelliferous plants have not been isolated or identified.

The Mammals of Banff National Park, Alberta

IN 1885, an area of 10 square miles around the newly discovered hot springs in the Bow Valley of the Alberta Rockies was designated as Rocky Mountain National Park. This was Canada's first national park. Since that date the park boundaries have been altered several times, and the name has been changed to Banff National Park. The present area of the park is 2,585 square miles. It stretches for 210 miles along the eastern flank of the Rocky Mountain from latitude 50° 45' to 52° 45' N. The western boundary is the continental divide. Six main mountain ranges, the axes of which lie north-west-south-east, are contained in the park. A survey of the mammals of the extensive area has been made by A W Banfield, who describes 17 species in the Cordilleran fauna, 11 in the Boreal fauna, 7 in the Prairie fauna, 1 species in the Tundra fauna, and 18 of uncertain affinities (*Nat Mus Canada*, Bull 159, Biol Ser, 57).

The Ophitron

THE GENERAL ELECTRIC Co, LTD, announces that a compact microwave-generator embodying a new

focusing principle has been developed at its research laboratories. The valve is an electrostatically focused backward-wave oscillator which has been named the 'Ophitron', after the Greek *ophis*, a serpent, the word being suggested by the undulating path of the electron stream flowing along the structure. The most striking advantages of the new oscillator are its small size (6 in long and $\frac{3}{4}$ in diameter) and low weight (7 oz), and in addition the 'Ophitron' system has been designed to be simple to construct and to operate. A single stamped-out periodic structure and two flat focusing plates form the propagating path for the radio-frequency wave, and set up the periodic electrostatic field which focuses the electron beam. The system has the fundamental advantage that the crests of the undulating electron beam are brought into the region of maximum radio-frequency field. This feature gives good coupling between beam and wave, and leads to greater bandwidth than is obtained with the equivalent magnetically focused backward-wave oscillator. The present 'Ophitron' tunes electronically over at least a 40 per cent band in the 10,000 Mc/s region. A range of such valves is envisaged, covering most important centimetre wave-length bands. It is expected that the noise performance will be better than that of magnetically focused backward-wave oscillators due to the ion drainage from the electron beam inherent in the focusing method.

Non-Oxide Glasses

ARSENIC trisulphide glass is well known as a useful material in the construction of optical parts transmitting in the infra-red. It suffers from a very low softening temperature compared with the normal type of oxide glass, and so far there is very little promise of harder glasses being prepared with sulphur or selenium as the anion. Some of these glasses are semiconductors of high resistivity, greater than 10^8 ohm/cm/cm². The Bell Telephone Laboratories have just announced an ingenious application of glasses in this family which puts to practical use the low-softening point, the property which is undesired in the other present uses. Glasses composed of varying proportions of sulphur or selenium with arsenic and thallium become very fluid at temperatures between 125° C and 350° C. In this temperature-range the viscosities of the various glasses approximate to that of castor oil at room temperature. These materials have been found to be eminently suitable for coating small electronic devices by dipping into the castor oil-like liquid. At room temperature the materials are typically glass-like solids inert chemically to most reagents except concentrated alkalis. Several compositions are said to resist oxidation in air to above 250° C. Initial experiments in coating semiconductor devices have shown considerable promise.

Joseph P Kennedy, Jr Memorial Foundation

A GIFT of one million dollars has been made by the Joseph P Kennedy, Jr Memorial Foundation for the establishment of the Joseph P Kennedy, Jr Laboratories for research on mental retardation, at the Massachusetts General Hospital. One half of this generous gift will be spent on the construction of these Laboratories and the other half will serve as an endowment to provide continuing operating funds. This is the first of the endowed scientific researchships planned under the 1961 programme in observance of the 150th anniversary of the Massachusetts General Hospital.

Royal Society Research Appointments

DR J S GILLESPIE, of the Department of Physiology, University of Glasgow, has been appointed the first Sophie Fricko Royal Society research fellow in the Rockefeller Institute, where he will work on intracellular recording from innervated smooth muscle. This appointment is a new post which has been established by the Rockefeller Institute from funds left to the Institute by the late Miss Sophie D. Fricko of New York City who died on March 1 1958. The trustees of the Rockefeller Institute have authorized use of the income from the fund for the triple purposes of fostering international understanding, training scientists of exceptional promise and supporting significant research. It is the intention of the Rockefeller Institute to appoint four research fellows each year, from France, Denmark, Sweden and the United Kingdom, the selection being made by the French Academy of Sciences, the Royal Danish Academy of Sciences and Letters, the Swedish Royal Academy of Sciences and the Royal Society.

A Locke research fellowship has been awarded to Dr B G Cragg, of the Department of Anatomy, University College London, to work at University College, London, on the connexion and physiological functions of certain nuclei in the brain. Stohert research fellowships have been awarded to Mr W D Butt of the Department of Biological Chemistry, University of Aberdeen, to work at the Molteno Institute of Biology and Parasitology, University of Cambridge, on intracellular hemoprotein compounds, to Mr R A Webster of the Department of Pharmacology, University College London, to work at University College London, on the pharmacology of tetanus, and to Mr J A. Hunt of Peterhouse, Cambridge, to work on the chemical structure of proteins.

Leopoldina Academy New Members

It is announced that the following with others, have been elected members of the German Leopoldina Academy of Natural Sciences, Halle: Mathematics Section, Profs. Herbert C Grötzsch (Halle) and Hans Schubert (Halle); Physics Section, Prof Otto Kretzky (Graz); Geophysics and Meteorology Section, Prof Erik Herborg Palmén (Helsinki); Chemistry Section, Profs Günther Rindöcker (Berlin) and Wilhelm Treibs (Leipzig); Botany Section, Profs James Bonner (Calif.), William O James (London) and P Maheshwari (Dolui); Zoology Section, Profs A W Ivanow (Leningrad), E N Pawlowski (Leningrad) and Fritz Pous (Berlin); and Geography Section, Profs Rudolf Kähbler (Halle) and Ernst Neef (Leipzig).

University News

London

PROF W R NIBLETT, director of the Institute of Education, University of Leeds, has been appointed dean of the University of London Institute of Education with the title of professor of education in the University.

The following appointments to University readerships have been announced: Dr D J Anderson (physiology in relation to dentistry), tenable at Guy's Hospital Medical School; Dr A Ashmore (experimental physics), tenable at Queen Mary College; Dr F Hobbiger (pharmacology), tenable at Middlesex Hospital Medical School; Dr M B Shapiro (psychology), tenable at the Institute of Psychiatry

J W Stewart (haematology), tenable at Middlesex Hospital Medical School; Dr D F Choceman (biochemistry) in respect of his post at Bedford College; Dr A P Millman (mining geology), in respect of his post at the Imperial College of Science and Technology.

Southampton

THE University has conferred upon Prof P Ford, professor and dean of economics, who is retiring on September 30, the title of professor emeritus. Prof Ford will formally open the newly completed building for the Faculty of Economics and the Ford Collection of Parliamentary Papers on October 14. Mr R G Woods, of the University Library, Cambridge has been appointed deputy librarian. The title of senior lecturer has been conferred upon Dr G W A Fowles (Chemistry), Dr J P Jones (Aeronautical Engineering) and Dr A Pollard (Geography). The following lectureships are also announced: Dr A N Clements (physiology and biochemistry), Dr J Heading (applied mathematics), Mr R W Page (mechanical engineering), Dr J R Rydzewski (civil engineering), Dr R G Seurlock (physics), Dr E V Vernon (electronics).

Announcements

MR J B ADAMS at present director of the Proton Synchrotron Group of the European Council for Nuclear Research near Geneva has been appointed director of a new establishment to deal with controlled thermonuclear research. The work in this field now being done at Harwell, and some of the work now being done at the Atomic Weapons Research Establishment Aldermaston, will be moved to this new establishment when its site has been chosen.

THE Elmer A Sperry Award 'for outstanding achievement in the field of transportation' will be presented in 1959 to the de Havilland Aircraft Co., Ltd the creators of the world's first jet passenger transport, the British built *Comet*. Formal presentation of the award will take place in New York later this year at a joint meeting of the Institute of the Aeronautical Sciences and the Royal Aeronautical Society. The award is sponsored by four engineering societies: the American Society of Mechanical Engineers, the American Institute of Electrical Engineers, the Society of Automotive Engineers and the Society of Naval Architects and Marine Engineers.

AN international symposium on Algalogy will be held at the Indian Agricultural Research Institute, Pusa, New Delhi during December 7-12, under the joint sponsorship of the Indian Council of Agricultural Research and Unesco. Main topics which will be discussed are nitrogen fixing algae, edible algae and their mass culture. Further information can be obtained from the Unesco South Asia Science Co-operation Office, 21 Curzon Road, New Delhi, India.

ERRATUM With reference to the communication entitled 'A New Method for working up Processing Mixtures containing Anhydrous Aluminium Chloride' (*Nature*, July 11 p 117) Dr T Széll states that a mistake was made in preparing the English translation: col 2, line 1 for 20 ml read '25 ml'.

CRYSTAL PHYSICS

THE presentation of the frontier regions of modern physics to an audience with a variable appreciation of scientific and mathematical ideas is, inevitably, a difficult task. None the less, it is one which should not be shunned, unless we are inclined to assume the semantic barrier to be impassable between the pure scientist and the educated public. In the realm of crystal physics with its many facets, the choice of electron-states in crystals as a topic for a discussion by Section A (Physics) of the British Association at the recent meeting in York, did not minimize the difficulties of communication. However, in the first lecture of the session, I attempted to wean the audience from a 'billiard ball' conception of atomic particles and, with little more than de Broglie's hypothesis and the Bragg reflexion law to assist me, to carry them into the mysteries of the energy-band theory of solids. It was not too difficult to begin a discussion of the wave behaviour of electrons in the ordered periodic-field of a crystal lattice, but the going became somewhat harder when the unavoidable introduction of wave vector space occurred. However, the vagaries of the effective electron mass were a little better appreciated by adding the visual aid of a bubble in a spirit-level as an analogy of the positive hole. It was inevitable that such treatment by analogy involved a considerable loss of rigour, but to me it proved to be a valuable exercise in transmitting the important results of the wave mechanical theory of solids without recourse to the mathematical building-materials allowable to the postgraduate seminar room.

The niceties of the band theory for electrons in a perfect crystal were soon disturbed by the reversion to practical situations. The next phase of the lecture dealt with the various crystal imperfections, their effect on electron and hole behaviour and their importance in semiconductor electronics. Again, treating the matter non-rigorously in terms of simple electrostatic forces, brings the problem of donor- and acceptor-levels and types of lattice vacancies into a relatively familiar perspective, and in this instance introduced some of the ideas to be used in the following lecture given by Dr V Hesketh.

Many of the important foundations of both experimental and theoretical solid state physics were laid by the pioneer work of Prof R W Pohl and his research school in Göttingen using the simplest of crystals, the ionic alkali halides. For an audience raised by this stage of the proceedings into the 'thin

but bracing air' of wave mechanics, the appearance in a place of honour among beautifully coloured single-crystals of a familiar packet of common table-salt provided a 'down to earth' relief. The theme of Dr Hesketh's lecture was the alkali halide crystal as a model solid for investigation. Such a claim appears to have been justified by the subsequent discussion. Optical, electrical and other studies provide some of the most certain evidence on the nature of lattice vacancies, single or in aggregation, in solid-state physics to-day. An important feature of this talk was the link which it indicated between such electronic investigations and those concerned with mechanical properties and the role of dislocations in crystals. A connexion with another interest of Section A, magnetism, was in evidence in the paramagnetic-resonance studies of alkali halides. From the general discussion which followed the lecture there was a hint that a 'North eye' was being turned towards dislocations by those, like Prof L F Bates, who follow the motion of magnetic domains. It was a pity that there was no opportunity to demonstrate other links which are rapidly being forged between different branches of solid-state physics and those under examination.

If one might, in conclusion, offer an overall impression of this session in the proceedings of Section A at the York meeting, it is that the conditions of limited time and contact of the meetings have a very stultifying effect on any attempt to make an effective contribution to the communication of new physical concepts to a wider audience of educated people. On this occasion, in spite of the central position occupied by wave-mechanical ideas in the session, it was not a mathematical but a time barrier which blocked the transmission of information. Perhaps this will be borne in mind by the Association in framing a new position for itself as a most important medium for translation as well as transmission of scientific information. From my own limited experience, there is no doubt that courses extended over the year, making use of the facilities offered by extra-mural departments of the universities and similar organizations for further education, would provide a means of digestion for the strong meat of modern physics. As a corollary, the lecturer must bend his rigour of thought to breaking point so that he may admit familiar, though inadequate, analogies as carriers across the semantic obstacles.

G F J GARLICK

SCIENCE BY THE UPPER FORM

AN innovation of Section X (Assembly of Corresponding Societies) of the British Association, whereby a selected panel of young scientists of sixth-form status are able to present short papers on projects with which each has been connected, was continued for the fifth successive year at the York meeting of the Association. This year there were five speakers drawn from Yorkshire schools, each one representing a school team engaged on the acquisition

of scientific knowledge in the field, under competent leadership.

Ampleforth College, York, led the way with a paper by M L M Wright on "Physiography and Scenery of the Isle of Eigg", excellently illustrated by colour slides showing the rugged grandeur of an isolated area along the western Scottish coast of only some twelve square miles in extent. Life is hard for the humans living there, and precarious for plant and

animal life, dictated by Nature over countless years. The object of the expedition was to study the influence of land formation and climatic conditions on the vegetation of the island, even to an investigation of soil salt content, which was found to vary considerably at different levels, the highest percentage of salt being at 500 ft., with diminishing amounts down to sea level. Members of the party collected some 250 species of plant life but no new records were discovered. Further work in the area is to be undertaken.

In a joint effort, the two speakers who followed (A. N. P. Butland and P. A. Crossley, of St. Peter's School, York) dealt with 'Some Scientific Aspects of the River Ouse' the former confining himself to the work of the analytical chemist in connexion with water supply, a work in which he had taken part. Methods adopted in order to detect any possible contamination were described and the results obtained at various points were given, from which it was apparent that the purity of Ouse water is well safeguarded.

P. A. Crossley concerned himself with 'foaming in rivers and canals, a natural phenomenon the reason for which was explained, but in these days very much accentuated by the growing use of detergents'. The River Don was said to foam much more than the Ouse, the Trent slightly less. Excellent slides were shown to illustrate foaming along these rivers, with graphs to present results of investigations made. Each speaker presented an interesting picture of problems involved.

'The Sedges of Askham Bog' formed the subject of Shaun Firth's paper, excellently illustrated by colour slides. The area investigated is well known to naturalists and close to York. It carries a variety of sedges but, so far as the speaker knew, no systematic study of them had been carried out, interest having ranged only around the rarer species, such as the handsome *Carex appropinquata*. In consequence a group of boys from Bootham School, York, including the speaker, undertook to remedy the omission. The aim was to compile a full list of species and, if possible, 'to account for the presence and performance' of the sedges. 'We are aware', remarked the speaker, 'we have come nowhere near an exhaustive treatment of the subject, what made our study of the sedges so enjoyable was the fact that now data came to light with practically every visit to the Bog to upset our rashly formed theories and force us to observe further and think again.' So this, it would seem, is but the introduction to a hitherto neglected subject.

The Bar Convent Grammar School, York, was well represented by Nancy G. Proctor, who, after only

eighteen months residence in the City, has absorbed much of its history, having received an introduction by becoming an assistant to Mr. Wenham, history master of St. John's College, York, who is carrying out an excavation under the eaves of the two local archaeological societies. Thus Miss Proctor has in a short time been able to increase her knowledge of Roman antiquities, and to add this to her main interest in the archaeological field which embraces the works of prehistoric men, in particular the study of promontory forts. Her work in York, even of so short a period, enabled her to trace the City's growth from the time when there was only an insignificant wooden fort founded on the site in 70 A.D., and to describe graphically recent investigations which she and members of her school have undertaken.

Another well known Yorkshire educational establishment supplied both speaker and illustrator for the final paper, 'The Seasonal Rhythm and Behaviour of the Birds of Bampton Cliffs', the former in the person of Eileen Burton, and the latter Joanne Littlefair, pupils of the High School for Girls, Bridlington. A bird watching group visited Bampton at weekly, or twice weekly, intervals during the year, where along an eight hundred feet stretch of the high east cliff, members studied the seasonal variation of population and the behaviour of six species of nesting seabirds—kittiwake and herring gulls, gannet, guillemot, razorbill and fulmar petrel. The date of the arrival of each species was carefully noted together with time of egg laying and hatching, and departure. A count made along 200 ft. of the cliff showed the kittiwake to be the commonest species present during May (915), followed by guillemot (543), razorbill (18), fulmar (15), gannet (13) and herring gull (5). Five gannet chicks were hatched and reared in 1959 and as a pair of this species nested on a new ledge there would appear to be hope for an extension of the nesting area which is the solitary British mainland station all others being found on islands. A study was made of bird display at various times, methods adopted during time of incubation, and of the feeding of young which gave Miss Littlefair an opportunity of producing drawings of remarkable quality which were used to illustrate the talk in wall-chart form.

The Countess of Albemarle, president of Section X, occupied the chair throughout the meeting and in her closing remarks complimented the sixth formers on their powers of observation, method of presentation and keenness in the respective tasks undertaken, a tribute not only to the young people but to their teachers and leaders as well.

J. A. S. STENDALL

THE MUSEUMS ASSOCIATION

THE sixty fifth annual conference of the Museums Association was held at Worthing during June 15-19. The proceedings opened with an informal reception in the entirely re-organized Museum and Art Gallery and members were particularly interested in the additional accommodation provided by a new gallery, laboratory, workshop and storage space.

The Conference continued on the following day with an official welcome from the Mayor or Councillor Horace W. Bradley. This meeting, as the others was

held in the spacious and attractive rooms of the Assembly Hall placed at the disposal of the Conference by the Corporation of Worthing.

Dr. W. E. Swinton, British Museum (Natural History), in his presidential address, after outlining the early struggles of the Association, emphasized the value of television and urged both museums and art galleries to use it extensively. It was his belief that acceptable medium of today may have but direct There was abundant evidence that already it had

attracted people to visit museums and see the actual objects. Dr Swinton emphasized the close relation between science and the arts and stated that whereas thirty years ago they were pleading for more science in museums, which were then chiefly artistic, in this scientific age there was some need for a reversal of the process.

The main subject of the Conference was museums and finance, introduced by Lord Rosso, chairman of the Standing Commission on Museums and Art Galleries. After recalling the increase of grants from the government which had recently taken place, he emphasized particularly the need for more staff in museums. The present shortage of staff was both absolute, because there were not enough qualified people, and comparative, because museum rates of pay were not competitive with comparable professions. He felt that museums should not depend too much on the Exchequer but that local authorities and others should do their share. Dr Barnett Stross hoped that curators would use the increased grant of £15,000 made available through the Victoria and Albert Museum. He felt that the chief needs of the museum movement were for staff of high status with adequate pay, a high standard of conservation and for more realistic purchase grants. Sir Hamilton Kerr thought that two stages were necessary, an immediate first aid operation and secondly an expert committee to consider all the problems confronting museums in Britain. Sir George Dyson outlined the help that the Carnegie United Kingdom Trust had given to museums over the past thirty years, and Sir Philip Hendy gave some striking facts of the magnitude of the loss suffered by the decay of private patronage since 1914. Sir John Hobhouse outlined the initial steps taken by the newly formed South-West Regional Council, and Mr E M Hutclinson, National Institute of Adult Education, was anxious that local authorities should use to the fullest extent the power to raise money that has already been vested in them.

At the close of the discussion resolutions were passed endorsing the recommendations of the Standing Commission relating to tax reliefs on gifts and bequests which should be made applicable to all museums, urging the Standing Commission to form a joint committee with the Museums Association to advise on all professional matters and requesting the Joint Committee on Government Assistance to make a survey of existing conditions in museums and art galleries.

In a discussion on the country house and the museum, Mr R Romilly Fadden, secretary of the Historic Buildings Committee of the National Trust, emphasized that the great country house with its contents formed a living organism, and stated that the trust had close relations for expert advice and so on with museums. Lord Methuen suggested that the Government might take over some of the empty great houses not too far from London and use them for showing secondary pictures from the National Gallery. He also advocated the co-operation of persons with specialized knowledge on local authority committees. Mr Philip James, director of Waddesdon Manor, stated that the crux of the problem for using furnished country houses as museums was how to get as many people as possible round the house without destroying its atmosphere as a home.

At the annual general meeting Dr. W E Swinton was re-elected president, Mr G L Conran was elected secretary and Sir John Rothenstein, editor. Mr Charles Carter (Aberdeen), Mr R R Clarke (Norwich), Dr D Dilwyn John (Cardiff) and Dr Mary Woodall (Birmingham) were the newly elected professional councillors and Sir Hamilton Kerr, the Institutional councillor. The Earl of Rosse and Dr D B Hadden were appointed as additional vice-presidents. It was decided to hold the 1960 Conference at Stoke-on-Trent during July 4-9.

The concluding day was devoted to field meetings to inspect the historic and archaeological wealth of Sussex.

THE INTERNATIONAL VETERINARY CONGRESS

THE sixteenth International Veterinary Congress, held in Madrid during May 21-27, was attended by nearly 2,000 members of the veterinary profession from all continents, including official delegates from fifty-two countries and more than one hundred from the United Kingdom. The Congress, under the patronage of the members of the Spanish Government, enjoyed the hospitality of the University of Madrid. The inaugural general assembly and plenary session meetings took place in the large hall of the new and magnificent building of the Faculty of Law. The variety of the papers—about 400 in all—presented during the Congress was very great. They were concerned with physiology, nutrition, pathology, public health aspects of animal diseases, food products and veterinary education. A balanced review is not practicable here, but a few papers of greater general interest and a few more interesting papers presented by British delegations can be mentioned.

As a result of the extensive public interest and concern there has been considerable research and investigation into contamination of the Earth's surface with radioactivity, and its subsequent effect

on farm animals, as well as on man and human food of animal origin. It has been found that an extremely heavy environmental contamination with fission products would be necessary to produce any significant damage as a result of external exposure of farm animals to β - or γ -rays. The radiation exposure of farm animals from grazing in contaminated areas presents no significant hazard to the animals, except perhaps in localities very close to test sites. Cows contaminated with radionuclides may become a potential hazard to man through milk, in which they are secreted in more significant quantities than in any other animal food product. Papers on this problem were presented by American, German, Dutch and Swedish workers. It was generally agreed that in order to be able to appraise continually the effects of fall out from atomic-weapon tests, and of the discharge into air and water of waste from all plants where nuclear energy is produced and applied, it is necessary to make regular measurements of the radio-

activity present in soil, air and food, and the contamination which has not been taken into account concerning public

health, and particularly the problem of diseases which are transmissible from animals to man. Nearly one hundred diseases are known to be so transmissible, and additional ones are still being found. Some of these diseases are transmitted by direct contact of man with live animals, others are transmitted indirectly to people through the consumption of milk, eggs or meat. Diseases transmitted from animals to man are defined as 'zoonoses'. At present there are many international groups or agencies that are concerned with the control of the zoonotic diseases but still closer collaboration is necessary between the medical and the veterinary professions in protecting man from zoonoses.

One subject which has not before been discussed was that of blood groups of domestic animals. In dogs, six distinct blood group factors are recognized.

As is the case with newly born babies, it is possible for newly born foals and pigs to die from haemolytic disease, which is a pathological condition resulting from the union of maternal antibodies with blood group factors of the red cells of the fetus.

There were several interesting contributions from Great Britain. Workers at the Research Institute for Animal Virus Diseases (Pirbright) reported new knowledge on living attenuated vaccines which gives hope of a method of combating foot-and-mouth disease in countries where it is widely spread. Foot and mouth disease is one of the most serious viral diseases affecting cattle in nearly every country of the world.

Workers of the Glasgow Veterinary School have reported successful trials with a vaccine produced against lung worm infection which causes great losses in cattle and sheep. Immunological basic work concerning parasites was reported by workers from Cam-

bridge. They also demonstrated a correlation between immunity and chemotherapy. From the Cambridge Veterinary School there also came an important paper classifying respiratory diseases in poultry.

A paper on the international standardization of veterinary biological products was delivered by the director of the Veterinary Laboratory of the Ministry of Agriculture and Fisheries.

At a charming ceremony during the Congress the president of the Royal College of Veterinary Surgeons presented honorary associateships awards usually made during the Congress to five eminent foreign veterinary scientists.

The Spanish people were the most hospitable hosts and, in addition to the well-organized scientific side of the Congress they had prepared a very full programme of evening receptions and other social functions that were greatly enjoyed and appreciated by the members of the Congress. At the closing general session of the Congress an invitation conveyed by the German delegation to hold the seventeenth International Congress in Hanover, in order to celebrate there the centenary of the Congress which first started in Germany, was received with acclamation. The first International Congress on animal diseases was held in Hamburg in 1893. It was initiated by an English veterinary surgeon, Prof. John Gamgee. The principal subjects of discussion during the first congress were rinderpest also called cattle plague, contagious pleuropneumonia of cattle and sheep pox. All these diseases ceased to exist in Britain many years ago.

The veterinary profession combating many devastating diseases of animals plays an important part not only in the improvement of the health of animals but also the health of man.

M. A. SOLZG

PLANT GROWTH REGULATION

THE fourth International Conference on Plant Growth Regulation was held at the Boyce Thompson Institute for Plant Research, Yonkers New York, during August 10-14. The Conference was sponsored jointly by the Institute and by the New York Botanical Garden and the Brooklyn Botanical Garden. The programme was co-ordinated with the ninth International Botanical Congress held in Montreal Canada during August 10-28.

The Conference was attended by many invited participants from seventeen countries. The United Kingdom was represented by sixteen participants. The last conference was held at Wye College (England) in 1955 and before that conferences were held at the University of Wisconsin in 1949 and in Paris under the auspices of the League of Nations in 1937.

The first day of the Conference was devoted to naturally occurring growth substances the second to the gibberellins, the third to the synthetic auxins, and the fourth to other plant growth substances. Chairmen of the various sessions included, Prof. K. V. Thimann (Cambridge Mass.), Dr. H. Burström (Lund, Sweden), Dr. P. W. Brian (Welwyn, England), Prof. F. Lona (Parma, Italy), Prof. R. L. Wain (Wye College), Dr. J. Henderson (Tuskegee Alabama), Dr. P. E. Pilot (Lausanne, Switzerland) and Dr. J. van Overbeek (Modesto, California). Major evening addresses were given by Dr. William J. Robbins

director emeritus of the New York Botanical Garden, on the "Expanding Concepts of Plant Growth Regulation", and by Dr. James Bonner (California Institute of Technology) on the 'Probable Future of 'Auxinology'."

In addition to the scheduled papers ample time was provided for discussion. The papers presented and the discussion remarks will be published in book form by the Iowa State College Press in May 1960. Copies will be sent to each participant and will be available to others at nominal cost.

Among the new advances reported at the Conference was the isolation of a new class of auxins from Maryland Mammoth tobacco by Dr. D. G. Crosby (Union Carbide Chemicals, South Charleston West Virginia) and Dr. A. J. Vitis (Caroni, Ltd., Trinidad formerly at the Boyce Thompson Institute). About 10 mgm. of active chemicals were obtained from a ton of tobacco leaves and growing tips. One of the chemicals was identified as 1-decanol and the other as a long-chain fatty acid not yet fully characterized. Bruce Stowe (Harvard) also presented results showing the growth promoting activity of long-chain aliphatic compounds.

Prof. T. A. Bonnet Clark (University of London) reported on the effect of gravity on the distribution of auxins. The metabolism of indole auxins in plants was discussed by C. H. Fawcett. R. J. Wain and

F R Wightman of Wye College The isolation of a new acid from coconut milk which gives about half the stimulation produced by whole milk was reported by L H Weinstein, L G Nickell and W J Tulee (Boyce Thompson Institute and Chas Pfizer)

New concepts on the relation between structure and auxin activity with special reference to the requirements for reactions with necessary binding sites were discussed in separate papers by Prof K V Thimann and Dr J van Overbeek Some physical chemical aspects of synthetic auxins with respect to their mode of action were presented by Prof V Freed (Oregon)

This was the first international conference in which the gibberellins were discussed The Japanese scientists who carried out some of the early work with the gibberellins, T Hayashi, J Kato and Yusuke Sumiki, were on hand to present their most recent results Dr P W Brian (Imperial Chemical Industries, Welwyn), who was a pioneer in directing the attention of the Western world to the Japanese discoveries and who has been very active in this field, reported on new developments from his laboratory Evidence showing the probable widespread

occurrence of gibberellin-like substances in higher plants was presented by C A West (University of California)

A feature of the Conference was a memorial dinner to the late P W Zimmerman (Boyce Thompson Institute), who with his associate A E Hitchcock first tested 2,4-D for its effect on plant growth and development Other chemicals first tested in his laboratory include indolebutyric acid and 1-naphthaleneacetic acid as well as a variety of substituted derivatives of benzoic acid and various substituted aryloxyacetic acids P W Zimmerman was originally a member of the organizing committee for this Conference but became ill while on a business trip and died in August 1958 at the age of seventy-four

Financial support for the Conference was given by the Rockefeller Foundation, the National Science Foundation, and fifteen industrial companies interested in agricultural chemicals George L McNew, managing director of the Boyce Thompson Institute, was chairman of the Organizing Committee for the Conference A J Vitos was secretary of the Organizing Committee and chairman of the Programme Committee

LAWRENCE P MILLER

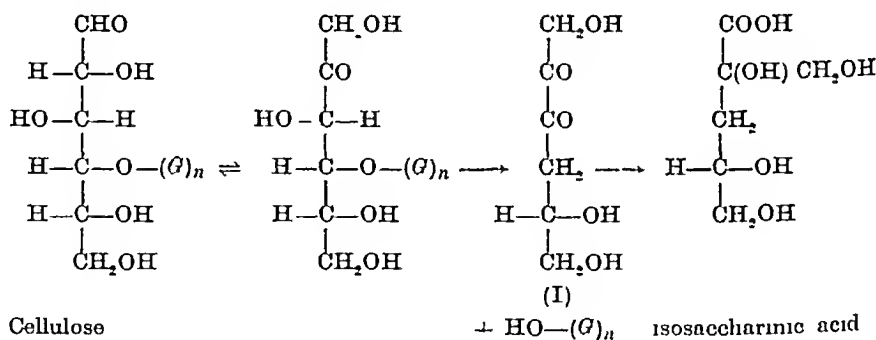
THE BRITISH RAYON RESEARCH ASSOCIATION

OPEN DAYS

THE British Rayon Research Association held the fourth of its annual open days during May 6-8 The total attendance was 900-1,000, a marked increase on the two previous years Encouraged by the favourable reception last year, the senior chemist and senior physicist again gave short lectures, after lunch on each day, illustrating the relevance of the basic research to current problems in the textile industry Instead of endeavouring to demonstrate all the work of the Association, a limited number of current researches on topical problems were illustrated rather more fully than usual, and it is believed that this approach may have been, in part at least, responsible for the very high attendance Two aspects of the work, namely, that on 'fluid beds' and that on vibration problems in spinning machinery, were not exhibited because of the desire not to interrupt this work at a critical stage of evaluation

During the past year the research programme of the Association has been critically reviewed particularly in view of the improvements required in the finishing of fabrics constructed from continuous filament viscose and acetate yarns to enable them to compete with resin-treated cotton fabrics The emphasis on this work has led to a reduction in work on dyeing and on the photo-sensitized oxidation of cellulose and to the termination of the work on the alkaline degradation of cellulose Concurrently with this, more attention is being given to research on the mechanical properties of textile fibres and to the study of the fine structure of crystalline polymers with the object of defining parameters which will characterize these polymers

The recent work on the alkaline degradation of cellulose has considerably strengthened the conclusions on the mechanism put forward previously This mechanism can be summarized in the following reaction sequence



The intermediate (I) has now been isolated and its structure proved The alkaline rearrangement of (I) is specifically catalysed by calcium and in lime water an almost theoretical yield of the isosaccharinic acid is obtained The complex mixture of acids obtained with sodium hydroxide from this intermediate under the hot alkali-refining conditions used in purification of wood pulp is very similar, qualitatively and quantitatively, to that obtained from cellulose under the same conditions

A considerable part of the resources of the Association are now directed to obtaining an understanding of the structure of textile fibres and attempting to correlate these with their physical, and particularly their mechanical, properties On the chemical side a systematic study of the effect of known numbers of specific cross-links in cellulose and of substituents in specific regions, namely, crystalline or amorphous, of the cellulose on the mechanical properties has been

in progress during the past year. The study of the formation of structure in solution precipitated polymers is still in progress, but the first system examined, cellulose triacetate in chloroform, has been rejected. Polydecamethylene terephthalate in benzophenone appears to be a more suitable system. Further work on the fine structure of cellulose has established that the microfibrillar structures observed in Tenasco and 'Fortisan' materials are not artefacts but are structural features of these materials. Their significance with regard to the physical properties of these materials has not, however, been established.

The determination of the amount of crystalline material in any crystalline polymer requires special consideration for each case. In the case of the determination of crystallinity in cellulose by X-ray methods the problem is to obtain the shape of the scattering of the amorphous component in which there is considerable orientation, as there is always considerable overlap with the crystalline reflexions. An independent assessment of the shape of the amorphous scattering curve is being made by comparing the information which can be extracted from the X-ray diagrams of highly oriented rayon fibres with the entirely 'amorphous' scattering of freeze-dried cellostetraose and of ball milled viscose and native cellulose fibres. (It is well established that ball milling will completely destroy the crystalline structure.) A study, by narrow beam X-ray and other techniques, of the nature of spherulites in nylon and of their effect on the mechanical properties of this material has been started.

It is difficult to find a new approach to understanding the mechanical behaviour of textile fibres

A textile fibre is essentially a uniaxial solid and most measurements on stress/strain relations are referred to this axis. In many applications, for example the evaluation of the stress system in a yarn, the behaviour of the fibre in a direction perpendicular to this axis may be of equal importance. The mechanical behaviour of an elastic solid with axial symmetry should be completely characterized, within the region of small strains by five constants. An attempt is being made to measure these constants on polymer films which are more amenable to such measurements than fibres, and to study their dependence on orientation.

The main emphasis in the Technological Department has been, and will continue to be, on quality. In continuous filament yarns, periodic overstraining caused by inadequate control of tension in winding processes can cause a variety of faults in cloth which often appear markedly only after dyeing. Instruments have been developed for measuring processing tensions and the properties of filament yarns and these are now being marketed. This type of work has absorbed a large amount of technological effort. Certain worsted types of cloth fault which occur as 'shirring' in continuous filament acetate fabrics and as 'cloudiness' in low construction nylon and 'Terylene' fabrics appear to be due to frictional effects between warp and weft yarns, and consequently in the weaving research, more emphasis is being placed on these frictional effects.

The number of staff is 266. This total is made up as follows: research staff 90, laboratory and technical assistants, 77, engineering drawing office and maintenance staff, 59, library and administrative staff, 31, canteen staff, 9. L. A. WISEMAN

NEW RESEARCH AND PRODUCTION FACILITIES OF CIBA (A R L), LIMITED

NEW research laboratories, a new production plant and sales office extensions of Ciba (A R L) Limited at Duxford, Cambridge were formally opened by Dr R. Kappell of Ciba Limited on May 21 during the celebration of the twenty fifth anniversary of the establishment of the Company.

The new laboratories are housed in an L-shaped, two storied building of concrete and brick construction with large plate glass windows giving the maximum internal illumination in conformity with modern concepts in laboratory construction. The new building together with the existing research blocks enclose three sides of lawn and shrub garden. Internally, the use of teak, exposed facing brick and white painted surfaces accentuates the functional character of the design of the building.

The upper floor of the new building houses the research and development department, and the space thus vacated in the original buildings is being used for application and technical service work on wood adhesives. With the additional laboratory space now available in the upper floor of the new block, the group of graduate chemists and their technical assistants in the research and development department are able to explore more thoroughly the current resins marketed by the Company, resins of the epoxy, resorcinol, phenol, urea and melamine types. The work is concerned with the development of resins

and hardeners for casting and laminating purposes for chip board and wood glue manufacture, as well as with specialized applications such as adhesives for metal bonding, printed circuits, high temperature performance and a host of other uses. The extreme variety of the applications to which these classes of resins may be put, and the differing conditions under which they are employed, necessitate a continued and intense search for modified and improved chemical properties and physical forms. An integral part of the investigations undertaken by this unit is the testing of these new and modified materials, and the upper floor of the new building contains a test room well equipped with the necessary machines. This department maintains a close co-ordination with the other departments in the organization concerned with the application of existing products. There is, in addition, a lecture room where frequent colloquia and lectures are given by scientists from the plastics and related industries and by scientists from the academic world.

The ground floor of the new building contains the laboratories of the newly formed fundamental research department which is devoted to the study of the synthesis of new plastic substances with improved mechanical and electrical properties and with high temperature and chemical stability. The scope of the work is not restricted to adhesives but embraces the

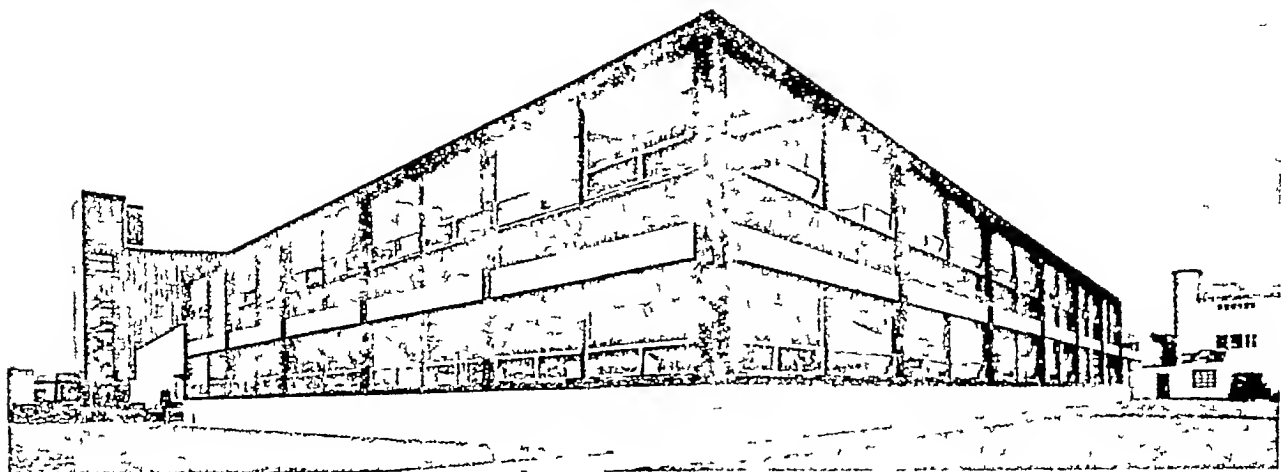


Fig 1 The new Cliba (A R L) research laboratories

possible uses of plastics in many fields. The new group is divided into seven teams, each of which is investigating some distinct aspect of the problem, including the synthesis of new raw materials and the pursuit of new condensation and polymerization processes. In addition to the usual equipment required for this type of work, the department has an analytical section where particular emphasis is given to infra-red and ultra-violet spectrophotometric and vapour-phase chromatographic analysis. The ground floor also contains a central chemical and glassware store and a glass-blowing room, and there is easy access to the library, which has also been expanded to meet the increased requirements.

The addition to the research staff at Duxford brings the proportion of those employed in laboratories on research, application, formulation and quality control to twenty per cent of the total staff employed. It is clear that the laboratory work can be greatly assisted by the use of modern and automatic equipment and wherever possible this is done, but the quality and quantity of these investigations are still dependent upon the individual skill, knowledge and efforts of the scientist and technician, and every new field entered necessitates an increase in the laboratory staff. In contrast to this, the factory has repeatedly

been able to increase the volume of production without proportional increases in the labour force employed, and this has been possible only by the continuous introduction of fully automatic processes. An outstanding example of this is provided by the new plant, which is now in production, for the manufacture of epoxy resins—resins based upon the condensation of diphenylol propane with epichlorohydrin. This plant—although it has a working area of more than 16,000 square feet, several types of reaction vessel and ancillary distillation units with miles of pipe work and more than 500 valves—is maintained by only three men per shift and has more than five times the capacity of the plant it replaces. In the new plant the equipment has been designed with the view of minimizing fire hazards, the building itself is of concrete and glass with dished floors to contain spillages, is well ventilated and sited away from the tank farm for the inflammable solvents used in the process, and also from the accompanying control laboratory and switch-house.

These new facilities, continuing the programme of expansion of both research and production, demonstrate the rapid growth of the industry and the faith of those who have determined this growth from the modest beginnings of the early 1930's. R F WEBB

THE ATOMIC ENERGY AUTHORITY

REPORT FOR 1958-59

THE fifth annual report (pp vii+68+4 plates London: H M Stationery Office, 1959 5s net) of the Atomic Energy Authority and the last to be issued over Sir Edwin Plowden's signature, who is being succeeded as chairman by Sir Roger Makins on January 1, 1960, covers the year ended March 31, 1959. In that year work started on construction at Windscale of the advanced gas cooled reactor prototype, the last of the four Calder Hall reactors became critical on December 8, 1958, the first reactor at Chapelcross came into use for generating electricity on February 25, 1959, and the Authority's staff increased from 30,341 to 35,260. No final decision has been reached regarding the transfer from Harwell to Winfrith Heath of the whole of controlled thermonuclear project. The terms of the first contract for

the supply of fuel for a nuclear power station overseas—the Latina station of Agip Nucleare—were negotiated during the year. The Industrial Group has been divided into two groups: development and engineering, under Sir William Cook, and production, under Sir Leonard Owen, executive, as well as functional, responsibility has now been restored to the technical members of the Board.

The report reviews briefly progress made during the past five years in the application of nuclear energy, during which the first five large-scale nuclear power stations came into operation: besides Calder Hall and Chapelcross, the United States 60 MW pressurized water reactor power station at Shippingport, the French 30 MW gas-cooled, graphite moderated reactor power station at Marcoule and the U.S.S.R.

100 MW graphite moderated, water cooled reactor power station in Siberia. In the United Kingdom gas cooled graphite moderated reactors developing towards exit gas temperatures of 550°C and 750°C promise to lead to higher efficiency and ratings and a 30 per cent fall in capital costs of nuclear power stations is predicted with the development of the present main types. The application of radioactive isotopes continues to grow, including the use in industry of control instruments based on radioactive isotopes, such as thickness gauges. Total sales of radioisotopes and related products rose from £650,000 to £800,000 the proportion exported remaining at about 60 per cent to 55 countries. Plans for the extraction of radiocaesium from radioactive waste are being considered in the United Kingdom and the potential output amounts to tens of millions of curies per annum. In raw materials, developments during the year confirmed that the present over-supply of uranium is likely to persist at least until the late 1960's, and the uranium requirements of the free world's current military and civil programmes can now be met by mines already in production, and it seems likely that the forward price of uranium may fall below 8 dollars per pound.

Apart from its first aim of ensuring the successful construction and operation of the nuclear power stations now under construction for the electricity boards, the Authority's reactor development programme comprises extensive work on the development of more advanced types of reactor, the aim of which is to provide progressively cheaper sources of nuclear power, and here the achievement of lower capital costs is a major objective. Efforts are being made to develop ways of using as fuel the plutonium that will gradually become available from the burning of uranium in the early stations. Beyond the natural uranium reactors two stages of development are envisaged. First, the advanced gas cooled reactor and the water moderated reactors seek to attain lower capital costs by using slightly enriched fuel. Secondly, the high temperature gas-cooled reactor being developed at Winfrith Heath as a joint project with other member countries of the European Nuclear Energy Agency, and the fast breeder reactor at Dounreay are characterized by both low capital costs and negligible net fissile fuel consumption. While the present type of gas-cooled, graphite moderated reactor may command a market overseas where large stations are required the report points out that considerable advances in nuclear technology will be required before smaller reactors (20-100 MW) become competitive in normal circumstances. The study of plutonium utilization in reactors continued

as well as reactor physics studies in several zero energy reactors.

The report summarizes further research on controlled thermonuclear reactions. The main object of the present experimental programme on *Zeta* and *Sceptre III* is to discover the reason for the excessive loss of energy to the torus walls during the current failure. Work on smaller scale gas discharge devices was considerably expanded and some of the formidable technological problems involved in building a thermonuclear reactor are being studied. An Advisory Committee under the chairmanship of the Board Member for Scientific Research was set up in December 1958 to examine and keep under review all aspects of the Authority's research programme on controlled thermonuclear reactions, to advise the Member responsible for research policy on the merits of proposals for new work and to make recommendations on changes in policy which seem necessary. Other research and development work being carried out by the Research Group, the Industrial Group and the Weapons Group is also briefly summarized. The first ranges from metallurgy, the physics of the solid state to work on particle accelerators. That of the Industrial Group extends far beyond the Group's laboratories, and extramural agreements between the Group and universities, research associations and industry now accounts for about a tenth of the Group's annual expenditure on research and development. That of the Weapons Group is illustrated by its examination of soluble chelate complexes of the alkaline earth metal ions and by its measurements of particle size including use of a centrifugal system to increase the rate of sedimentation with the photo-sedimentometer.

Since its establishment in 1958 under the chairmanship of Sir Douglas Veale the committee advising the Authority on the supply of specialized health and safety staff has had detailed consultations with many Government departments, hospitals, universities and industry. An interim report to the Authority recommended the initiation of courses in radiobiology and radiological physics at selected universities and provision of studentships if possible for the 1959-60 academic year. This recommendation has been accepted in principle by the Authority and details of the scheme are being worked out in collaboration with the University Grants Committee and the Department of Scientific and Industrial Research. The amount of research and development work contracted out by the Authority continues to increase and more than three hundred professional staff and technical staff from industry have worked with Authority staff during the year.

THE INSTITUTE OF PHYSICS

THE main sections of the thirty ninth annual report of the Board of the Institute of Physics for 1958 (pp 18 London: Institute of Physics, 1959) which was presented to the annual general meeting of the Institute on July 7, deal with membership, examinations, education and publications. During the year 851 applications for election or transfer to the various grades of membership were received. The total membership increased by 415 to 6,300, with a slight decrease in the number of subscribers (430 compared with 453 in 1957) but

with fairly large increases in the associate and student membership grades. Seven technical colleges which had applied for recognition as institutions possessing courses of study approved for the purpose of the membership regulations were visited by representatives of the membership and examinations committee and six of the applications were approved. In addition the application by the Borough Polytechnic London, for recognition of courses on which the Diploma of Technology in physics is awarded was granted. Twenty six of the eighty candidates

who presented themselves for the examination for the graduateship grade of membership were successful, twelve were university graduates and fourteen held the Higher National Certificate in applied physics. Forty-one colleges presented 637 candidates for the Ordinary National Certificate in applied physics and twenty colleges 246 candidates for the Higher National Certificate.

A joint committee of the Institute and the Physical Society has been set up to inquire into the post-graduate training of physicists and has held discussions with university and industrial physicists. The report on "The Teaching of Mathematics to Physicists", which was prepared by a joint committee of the Institute and the Mathematical Association and published originally in 1943, is now being revised. The Institute was invited to give its views on the subject of grants to students, and the text of the memorandum submitted by the Board to the governmental committee under the chairmanship of Sir Colin Andersen was published in the January issue of the Institute's *Bulletin*.

Satisfaction is expressed in the annual report at the standard and increased circulation of the Institute's older monthly, the *Journal of Scientific Instruments*. There was no significant change in the circulation of the other monthly, the *British Journal of Applied Physics*, but both journals suffered a further decline in advertisement revenue. New arrangements for selling advertising space to become effective during 1959 and for widening the scope and content of the *British Journal of Applied Physics* have been decided upon. A new feature in the 1958 *British Journal of Applied Physics* was the introduction, in the June and October issues, of a 'New Books' section which together contained reviews of 87 books. The type size of the *Bulletin* was reduced for the 1958 volume. This resulted in a considerable saving in paper, but the 366 text pages, comprising twenty-five articles and fifty-two book reviews, etc., contained more material than the 404 pages of the previous volume.

The first annual dinner of the Institute was held on March 26, 1958, at the Savoy Hotel, London, when 267 members and guests were present.

The Institute maintains nine branches and seven specialist groups in Great Britain, and two branches overseas, in Australia and Malaya respectively. The activities of these sections are briefly described in the annual report, together with extracts from the reports of the Board's representatives and nominees on joint and other committees and organizations. The South Australian Division held the sixth Australian instrument exhibition in Adelaide during August 19-22, at the same time as the Adelaide meeting of the Australia and New Zealand Association for the Advancement of Science. The second Einstein Memorial Lecture was delivered in October in Adelaide by Prof. B. J. Bok, who took as his subject "Stellar Evolution". The London and Home Counties Branch held a joint meeting in March with the London Section of the Royal Institute of Chemistry on the subject of science and society, and the South-Western Branch joined with the Education Group in a three-day conference in April at the University of Bristol on "Physics in Schools". The Electronics Group and the Midland Branch collaborated in a one-day symposium during April on some applications of solid-state physics in computers and automation, and in September the Group held a two-day conference on "Solid-State Memory and Switching Devices" at University College, London. The Non-Destructive Testing Group held its summer meeting in Paris jointly with the Société Française de Métallurgie, when the subject of discussion was "The Utilization of Physical Properties for Studying Relationships between the Constitution Structure and Service Behaviour of Metals".

At the general meeting of the Institute, the following were elected to take office on October 1: *President*, Sir George Thomson, *Vice-President*, Dr. J. M. A. Lenihan, *Hon. Treasurer*, Dr. J. Taylor, *Hon. Secretary*, Prof. F. A. Vick, and *New Ordinary Members of Council*, Dr. V. E. Cosslett and Mr. L. Rotherham.

SOME INTERNATIONAL GEOPHYSICAL YEAR ACHIEVEMENTS

THE Royal Society has issued under the above title a small pamphlet constituting an interim statement at the end of the observational phase of the International Geophysical Year. The pamphlet contains short notes, arranged under the fifteen subject fields, of statistical details of the work done and of important new deductions so far made from the International Geophysical Year observations. Some features of special interest are as follows.

Meteorology Ozone observations at the Royal Society base, Halley Bay, Antarctica, show an annual variation in total ozone content with a sharp increase in early summer markedly different from the variation over the Arctic where there are smooth rises and falls about an autumn minimum.

Geomagnetism Halley Bay is found to have been most advantageously sited for recording geomagnetic disturbances as it is the only antarctic station just outside the zone of greatest concentration of ionospheric currents. In one magnetic storm the range of the fluctuations in horizontal force reached the

enormous value of one sixth the average value of horizontal force.

Ionosphere Halley Bay has recorded remarkable features in the diurnal variation of ionospheric electron density in winter. The noon value in winter exceeds that at noon in summer and is ten times that at midnight. In summer the diurnal range is small with a minimum at midnight. These variation types change over suddenly near the equinoxes.

Solar activity United States ionospheric observations made by rocket reveal the existence of a powerful flux of solar X-rays at the time of a solar flare. This X-ray flux produces the increase in D-level ionization which in turn affects long-range radio communications.

Cosmic radiation Cosmic ray measurements made by Van Allen with the United States artificial satellites have, as is now well known, revealed the existence of an intense belt of cosmic radiation surrounding the Earth.

Oceanography British ships have observed directly the deep ocean currents of the North Atlantic using the 'Swallow' acoustic signalling float which can be set to drift at the required depth. One of the currents measured was a southward one below the Gulf Stream.

Nuclear radiation The existence of the International Geophysical Year network of nuclear sampling stations in Europe permitted a detailed study to be made of the diffusion of radioactive material released by the Windscale nuclear reactor accident in November 1957.

The full prescribed observational work ceased with 1958 and the main task of the present and future is the study of the observations made during the

year. It is, however, planned to continue some observations apart from those which are part of regular meteorological etc. services, during 1959 under the title "International Geophysical Co-operation 1959".

The International Council of Scientific Unions has formed special committees to co-ordinate further international work in antarctic research, oceanic research and space research.

A further possibility is the making of a magnetic survey on a world wide scale during the next sunspot minimum for comparison with the magnetic observations made during the maximum period with which the International Geophysical Year was timed to coincide.

RADIO FIELD-STRENGTHS IN THE TROPICS

IT is well known that radio communications conducted by waves which are propagated by reflexion from the ionosphere are critically dependent on the properties of the layers of ionized gas which transmit and attenuate the signals. The regular observation of the characteristics of the ionosphere at stations distributed widely over the Earth's surface has made it possible to understand and explain many phenomena which were obscure even ten years ago. The International Radio Consultative Committee has among its other studies been investigating many technical problems involving the propagation of radio waves by way of the ionosphere, and of these a most important one is that of tropical broadcasting for which high frequency waves are much more effective than medium waves on account of the very high atmospheric noise-level present in most tropical regions. Unfortunately the attenuation of the signals in the higher frequency bands is much greater during the day than is usual at higher latitudes and the reflecting layers are also less stable. Thus the problem of providing an adequate signal to noise ratio is considerably more difficult in the tropics.

The past studies of the International Radio Consultative Committee have shown that the standard methods of computing the field strength of sky wave signals were considerably in error at low latitudes

but it also became clear that the additional basic data obtained in recent years provided an explanation of many of the discrepancies disclosed. In a report* by W. R. Piggott, recently published by the Department of Scientific and Industrial Research Radio Research Station, this subject is reviewed with the aid of an analysis of the problem of identifying the most effective type of ionospheric reflexion for particular circumstances. This report shows that some of the difficulties in interpreting the results of field strength measurements at low latitudes have been due to changes in the dominant mode of ionospheric propagation, and the consequent variations in the attenuation of the waves and the angle of elevation at which they arrive at the receiver. The rate of advance of knowledge of this subject depends on the continual interplay of practical observations with theory and it is hoped that the publication of this report, together with its presentation at the Plenary Assembly of the International Radio Consultative Committee recently held in Los Angeles, will encourage radio research workers in low latitudes to investigate their wave propagation phenomena in more detail.

* Department of Scientific and Industrial Research, Radio Research, Special Report No. 27, 'The Calculation of the Median Sky Wave Field Strength in Tropical Regions', by W. R. Piggott, pp. 38. (London: H.M.S. Stationery Office, 1959.) 2s. 6d. net.

BRITISH BOOKS AND FOREIGN MARKETS

IN reply to a series of questions in the House of Commons on June 23 regarding the supply of British books and periodicals overseas, Dr O. Hill, the Chancellor of the Duchy of Lancaster, made a long statement which was circulated in Hansard. The study of ways and means of increasing the flow of British books and periodicals overseas has now been completed. Recognizing that British books can do much to help other peoples to understand our way of life and that they make a very real contribution to the life and thought of other nations, the statement points out that there is an ever increasing demand for reading matter in English and we must do more to promote the flow of British reading matter overseas. Other countries are already producing large amounts of well produced attractive literature which

is easy to read and inexpensive and is aimed particularly at Asian and African countries. Although in 1958 exports totalled nearly £24 million, or almost two fifths of the turnover of the United Kingdom book trade, several countries impose, for currency reasons, substantial restrictions on imports of British books and periodicals and our exporters cannot make further headway in these markets. Low individual incomes in many countries and the lack of effective library and other distribution systems are also major difficulties.

Accordingly, the Government has decided to take five steps to promote the export of British books and periodicals:

(1) To enter into negotiations with various countries with the aim of establishing schemes operating

broadly on the lines of the British book export schemes which were established during the War and in the immediate post-War period

(ii) To promote the production of low-priced editions of a range of British books for sale in certain countries where there is a large unsatisfied demand for such books. This will call for substantial Government expenditure

(iii) To authorize a further expansion of the British Council's library services in several centres and of the Council's resources for presentations of books and periodicals abroad on which the Council this year expects to spend in all about £650,000

(iv) To assist, through the British Council, in the development of library systems in some Colonial territories, including the establishment of central libraries, regional branches, book vans and book boxes

(v) To co-operate with publishers in measures to enable them to increase their circulations in some of the more difficult markets overseas

Parliamentary approval for the expenditure involved will be sought at the earliest convenient

opportunity and it will be necessary to proceed in consultation with the Governments of the Commonwealth and foreign countries concerned, and Dr Hill promised to inform Parliament as soon as agreements had been concluded. In reply to a further question Dr Hill said that the increase in the British Council's resources would be concentrated on scientific and technical books, but the schemes to be negotiated with countries where import restrictions prevent the flow would cover a wide range of books. He hoped that in the next year it would be possible to reach up to 2 million copies of low-priced books. This would be done in association with the publishers who own the copyright of the books concerned and would involve Government aid to narrow the gap between the economic price and what could be paid in the countries of reception. Replying to specific questions, Dr Hill said that British book exports in 1958 to India were recorded in the Trade and Navigation Accounts as £424,427, to Pakistan £30,950, to Ceylon £15,732 and to Israel £9,473. Dr Hill estimated the increased expenditure as about £500,000 next year.

FORESTRY IN NEW ZEALAND

THE annual report of the director of forestry of New Zealand for the year ending March 31, 1958, is of more than usual interest in that it includes a general historical review of both departmental activities and general land use and administration, covering the past forty years. The need for such a review had been particularly stressed by the Minister of Forests (Mr Tirikatene) and was prompted also by the meeting of the British Commonwealth Forestry Conference which had been held in the country during September–October 1957. The Minister himself (a Maori) contributes a prologue recognizing that the great forestry effort involved in creating a very large acreage of exotic softwood plantations, mainly of *Pinus radiata* from California, by the quick production of an alternative supply of essential timber, has saved a large remnant of the native forest. At the same time he calls for much greater attention to the maintenance of this forest, especially for its value in protecting soil and conserving water. The disastrous consequences of the denudation of the hill-sides in the form of soil erosion and then extensive floods are all too widespread and serious to be ignored any longer. Quoting two specific examples, he suggests that the Urewera indigenous forests in North Island, largely in Maori ownership, might in the national interest have to be managed primarily for soil stabilization and water retention, not timber, while in the hills behind Canterbury, all land more than 3,000 ft high might have to be taken out of pastoral use, even the city itself is now threatened by flood devastation. It must be encouraging to the Forest Service to have this official backing, which is combined with full recognition of the essential need of stable finance for the necessary research work and for remedial measures.

The visit of the Commonwealth Conference stimulated the preparation of a number of research papers covering many of the lines of activity which have called for special attention of recent years. Some of the topics dealt with are also currently prominent elsewhere, especially where softwood plantations play an important part, such are problems in genetics, and the relation between silvicultural treat-

ment and market requirements in respect of both dimensions and quality (whether for timber or pulp). There are also problems of the later management and regeneration of the plantations, as in the United Kingdom. During recent years, a good deal of thought has been given to the management and regeneration of the native forests, both those with important softwoods, notably kauri (*Agathis australis*) and the various species of *Podocarpus*, and the 'beech' forests (*Nothofagus* spp.). Encouraging progress is being made but rates of development are, of course, very slow compared with those of the introduced conifers, and, as already noted, these forests have other functions to fill as well as timber production.

The Commonwealth Conference appointed a special committee to report on New Zealand forestry. In the report, as Resolution 6 of the Conference, alarm is expressed at the poor condition of the remaining indigenous forest as a result of past exploitation, and expansion of research programmes is urged, the publication of Volume 1 of the "National Forest Survey of New Zealand" for these forests in 1953 is commended as is also the extension of the survey to protection forests.

It may be noted that damage to the native forests by introduced animals, above all red deer and opossums but also wild goats and pigs, is still a really serious problem, so much so that there is a special division to deal with 'noxious animals'. To reinforce shooting operations in the natural forests, bounties are paid for animals killed outside. The numbers killed in the year in what do not claim to be more than 'holding' operations are striking, namely, 55,000 deer, 28,000 goats, 4,000 pigs and 4,000 chamois by the State alone. The opossums are mostly killed outside the reserves, 900,000 in the year (after more than a million in 1956).

The control of noxious animals was only taken over by the Forest Service two years ago and there is a strong case for a similar taking over of soil conservation and river control, so that the troubles can be dealt with at their source instead of trying to remedy them after the damage has already been done, as is currently happening.

There is still a big exotic planting programme, 8,744 acres having been added in the past year. The major features are the clearing and replanting of former failures, notably those with *Pinus scopulorum*, a mistaken choice, and the extension of the work on to the coastal sands of the North Island which are unsuitable for agriculture, where the plantations will not only be productive in themselves but will also protect the fields from sand encroachment.

The annual report of the New Zealand Forest Research Institute for the same year ending March 31

(Pp 100 Wellington Government Printers, 1958) amplifies many of the points referred to above, and it also looks back over its first decade of work, expressing the feeling that it is now well established as a fully co-ordinated research centre, with an advisory committee representing both industry and all related research organizations. The graduate staff now numbers nearly fifty with a comparable number of technicians but the Commonwealth Conference thought that there is still need for an increase on both the forestry and forest products sides.

H G CHAMPTON

UBIQUINONE AND VITAMIN E

By DR. THOMAS MOORE

Dunn Nutritional Laboratory University of Cambridge and Medical Research Council

SOME time ago we noticed¹ the presence in the livers of rats of an alkali labile substance with a sharp absorption band at 275 m μ . For the purpose of studying the distribution of vitamin E in the body the rats had been given diets which were only barely sufficient in vitamin A. This restriction was intended to eliminate the strong spectroscopic absorption of vitamin A at 328 m μ , and so allow the measurement of vitamin E by its weaker absorption² at 294 m μ . In the body fat of rats given wheat germ rich in vitamin E, the presence of this vitamin was readily detected. In the liver, however, the detection of vitamin E was made difficult by the absorption at 275 m μ which has already been mentioned.

We were reminded³ of these early observations by reports by Lowe, Morton and Harrison⁴ of fractions from the livers of rats deficient in vitamin A which adsorbed at 275 m μ , with other maxima at 233, 283 and 333 m μ . Those workers thought, at the time, that abnormal steroid products had been formed as the result of the avitaminosis. We confirmed the presence of a band near 275 m μ in liver extracts of rats deficient in vitamin A. Saponification of the liver fat with hot alcoholic potash caused the band to disappear but it survived the same treatment when applied to the liver tissues. Presumably the tissues protected an unstable substance against oxidation. The band disappeared from solutions which were treated with 85 per cent sulphuric acid, were aerated or stored for 37 days at -10°C. It survived treatment with digitonin. Sterol free extracts of unsaponifiable matter made by the direct saponification of the tissues were neither fluorescent under ultra violet irradiation nor chromogenic in the antimony trichloride test. By paper chromatography evidence was obtained of the presence of two substances with absorption maxima at 275 m μ . One had a single sharp band at this position but the other had also an inflexion at 330 m μ . Both substances were faintly yellow, but had no selective absorption in the visible. Bands at 272-275 m μ were also found in liver extracts from rats which had been cured of avitaminosis A from normal sexually immature rats, and from a normal pig and guinea pig.

The existence of two substances, with their main absorption maxima at the positions observed by us,¹ was also reported by Henton, Lowe and Morton⁵. The names substance A and substance C were given. Both had their absorption maxima at 275 m μ , but C differed from A in having a sharper inflexion at

330 m μ , both substances A and C were found in the livers of normal animals although the concentration of substance C in the liver of normal rats was much lower than in the livers of rats suffering from vitamin A deficiency. A and C were also found in various tissues other than liver, and in different species^{6,7}.

Further extensive investigations by the Liverpool school, reviewed by Morton⁷ have led to the isolation of substance A. It is not a sterol product as first expected, but a derivative of 1-methyl-5,8-dimethoxy-p-benzoquinone. In view of its wide distribution the name ubiquinone was given. The striking feature of its structure is a long unsaturated side-chain, comprising 50 carbon atoms, attached at the 2 position. Similar conclusions as to the constitution of ubiquinone, otherwise known as Q 75⁸ or mitochinone⁹, have been reached in America¹⁰. According to Lester, Crane and Hatoff¹¹, ubiquinone is only one of a whole new series of quinones, which vary in the nature of the side chain.

Some workers¹² consider that ubiquinone plays an important part in tissue oxidations. Others¹³ have ascribed a similar role to vitamin E. The roles of both vitamin E and ubiquinone in heart muscle preparations have been reviewed by Slater¹⁴, who has suggested that the question whether there is a chemical or functional relationship between the two substances deserves investigation.

Vitamin E and ubiquinone have common properties in being soluble in fats in being capable of undergoing reversible oxidation or reduction and in being unstable to alkaline saponification in the presence of oxygen. They differ in vitamin E being found in animal tissues mainly in the reduced state whereas ubiquinone is mainly in the oxidized state. Regarding their distribution, ubiquinone has been found mainly in mitochondria whereas vitamin E can be stored in the body fat¹. Since vitamin E is a potent antioxidant it might possibly intervene in the metabolism of ubiquinone by protecting it against irreversible and destructive oxidation.

It was of interest therefore, to inquire into the effect of vitamin E deficiency on the concentration of ubiquinone in the tissues. The preliminary evidence on this point¹ may now be re-examined on the basis of pure ubiquinone having E (1 per cent 1 cm)¹⁵ at 272 m μ = 107. A rough estimate of the concentration of ubiquinone without allowance for the possible presence of substantial amounts of substance C, may be calculated from the difference

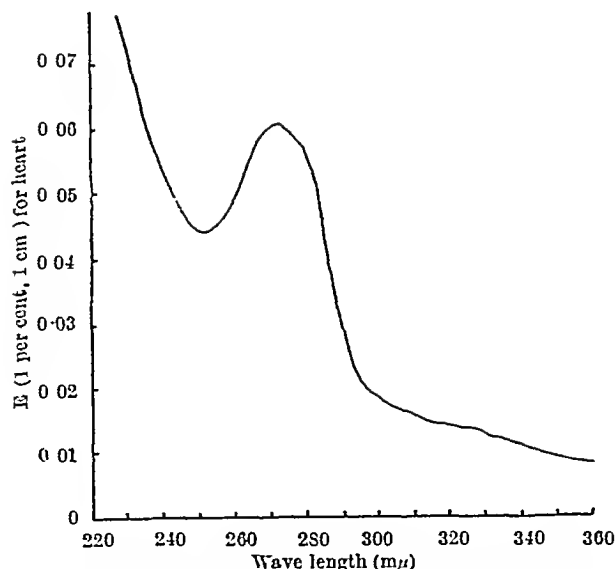


Fig. 1 Absorption spectrum of an extract of the heart of a rat, deficient in vitamin E. The presence of ubiquinone is indicated by the maximum at 275 mμ.

between the absorption of the extracts at 275 mμ before and after saponification. On this basis the liver of a rat which had been kept for four months on a diet deficient in vitamin E contained about 320 μgm of ubiquinone per gm. The liver of a rat which had been kept for two or four months on a diet containing 60 per cent of wheat germ, and therefore rich in vitamin E, showed little difference from that of the deficient animal with 270 and 290 μgm per gm of ubiquinone, respectively.

These early values for liver have now been supplemented by results, obtained by the co-operation of Dr I. M. Sharman and Miss Margaret Smith, on rat's hearts. The hearts were taken from piebald males, which had received a diet deficient in vitamin E for eight months. The severity of the deficiency was demonstrated in all the animals by the degeneration of their testes. Since vitamin A does not accumulate in the heart in more than traces, it was unnecessary to restrict the intake of this vitamin, as is advisable when the liver is to be examined for ubiquinone. The hearts were digested in alcoholic potash in the presence of pyrogallol as an additional protective agent¹⁶, and the fraction containing

ubiquinone was extracted with ether. In spectrophotometric examination the maximum at 275 mμ seemed sharp enough to provide a rough indication of ubiquinone contents without further refinement of the extract. A typical curve is shown in Fig. 1, from which it will be seen that there was no inflexion at 330 mμ, the position indicative of substance C. For four deficient rats, ubiquinone concentrations of 277–365, mean 338 μgm per gm of heart, were found. Four similar rats, which had been given the same diet but with adequate doses of *dl*-α-tocopheryl acetate, had ubiquinone concentrations of 303–371, mean 331 μgm per gm of heart. No evidence of an absorption maximum at 294 mμ, indicative of vitamin E, could be seen in heart extracts from either the rats deficient or adequate in vitamin E. This was in line with our early experience¹ that the detection of vitamin E in liver extracts is prevented by ubiquinone even when vitamin A is absent.

In these investigations therefore, there was no indication of any relationship between the ubiquinone contents of the tissues and the vitamin E status. Morton⁷ has reached the same conclusion, but his evidence has not yet been published.

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MECHANISMS OF RESISTANCE OF ADULT HOUSEFLIES TO THE INSECTICIDE DIELDRIN

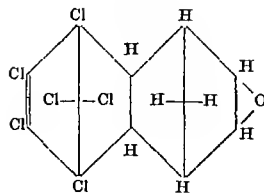
By F. P. W. WINTERINGHAM and A. HARRISON

Pest Infestation Laboratory, Slough, Bucks

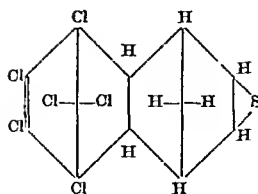
PENDING the successful syntheses¹ at this Laboratory of the insecticides labelled with carbon-14, the absorption, metabolism and excretion of the sulphur analogue labelled with sulphur-35 (II) of dieldrin (I) by dieldrin-resistant (*R*) and susceptible (*S*) adult houseflies (*Musca domestica*) have been studied. Adults of the *S*-strain were from the normal laboratory stock. Pupae of the *R*-strain were obtained through the kindness of Dr J. R. Busvine and originally collected at Omdurman (Sudan)². The first generation of *R*-adults at this Laboratory (March 1957) displayed little resistance to topically applied I but after breeding through 6 generations

on larval food containing I at a final concentration of 150 p.p.m. the adults were highly resistant to either I or II when applied topically in acetone. There was evidence of only a slight initial loss in resistance in adult *R*-flies after breeding through a further 19 generations in the absence of I.

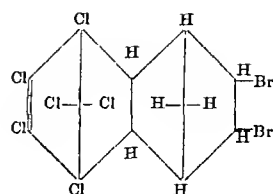
The radioactive insecticide (II) was applied topically to the dorsal thorax in 2 μl acetone to individual *R*- and *S*-adult flies while under mild cyclopropane anaesthesia and the flies kept in fresh air at 25°C without food or water for 3 hr. Signs of poisoning appeared in *S*-flies alone towards the end of this period. The flies were confined in groups of 10 or 20 to 1-in strips



(I)



(II)



(III)

of Whatman No. 1 paper by means of shallow glass-covered cages so that almost all the excreta and vomit were collected on the paper. Control groups were similarly set up in which the ani had been sealed to prevent excretion. The difference between the radioactivities recovered on the normal and control papers thus represented net excretion, radioactivity of the control paper represented contamination by mechanical contact with the flies vomit etc. After 3 hr the insects were anaesthetized and rinsed in acetone to remove unabsorbed insecticide. Heads, thoraxes and abdomens were separately homogenized and extracted with acetone. Acetone-insoluble metabolites were assayed in the extracted tissues. Unchanged insecticide and metabolites were determined by radio paper chromatographic techniques. Only unchanged insecticide was recovered from flies which had been killed by heat before the experiment except for a small fraction present in all extracts which behaved as the sulphone of II under the conditions of paper chromatography used and is believed to arise largely through atmospheric oxidation. The results of experiments in which 2 μ gm of labelled II was applied to adult flies (50 males + 50 females) are collected in Table 1. This dose was lethal to all *S* flies but innocuous with respect to *R* flies. The results were determined as 35 S radio activity, corrected for decay, self absorption, etc., and expressed as a percentage of the dose applied.

After 3 hr all the *S* flies became prostrate and ceased to excrete but metabolism of the absorbed insecticide continued for several hours, the metabolites

accumulating mainly in the abdomen. Resistant flies on the other hand continued to excrete their metabolites. Thus sealing of the anus had little effect on the accumulation of metabolites in the abdomen of the *S* fly but a marked effect on that of the *R* fly as shown graphically in Fig. 1.

Some experiments were made with a non-insecticidal compound labelled with bromine 82 (III) so that metabolism and excretion of a related compound by *S* and *R* flies could be compared in the absence of toxic effects. These experiments indicated that over a 24 hr period both strains excreted similar proportions of the unchanged compound together with small similar proportions of water soluble metabolites.

These experiments strongly suggest that resistance of the *R* flies to dieldrin is not due to lack of cuticular penetration, or to a gross difference in the rates of excretion or metabolism of the insecticide by the *S* and *R* insects. An efficient defensive mechanism is certainly operating in the *R* insect during the first 3 hr because towards the end of this period the *S* insect rapidly succumbed and there were signs of an irreversible lesion such as an exhaustive burst of respiration and fall of tissue α -glycerophosphate. Other experiments at different dosages (0.37–5 μ gm insecticide/insect), or of different duration (0.3–24 hr),

Table 1. PATH OF (35 S) SULPHUR ANALOGUE OF DIELDRIN 3 HR. AFTER TOPICAL APPLICATION TO DIELDRIN RESISTANT (*R*) AND SUSCEPTIBLE (*S*) ADULT HOUSEFLIES AT A DOSE OF 2 μ GM. PER INSECT

| | <i>S</i> -strain Per cent applied dose | <i>R</i> -strain Per cent applied dose |
|---|--|--|
| Lost by volatility of insecticide* during treatment, manipulation etc. | 34.3 | 27.2 |
| Unabsorbed from cuticle | 37.6 | 45.0 |
| Unchanged insecticide in head | 1.6 | 2.0 |
| Unchanged insecticide in thorax | 7.2 | 7.9 |
| Unchanged insecticide in abdomen | 0.6 | 6.5 |
| Acetone-insoluble metabolites in head | 0.2 | 0.1 |
| Acetone-insoluble metabolites in thorax | 1.0 | 0.7 |
| Acetone-insoluble metabolites in abdomen | 5.2 | 4.3 |
| Unchanged insecticide excreted | 3.4 | 2.7 |
| Water-soluble metabolites excreted† | 0.3 | 0.8 |
| Water-insoluble metabolites excreted | 0.5 | 0.9 |
| Unchanged insecticide lost by mechanical contact and vomit | 2.1 | 2.2 |
| Total effective detoxication: stored metabolites + excreted metabolites and insecticide as per cent dose absorbed | 100 | 100 |
| | 33 | 35 |

* Determined by difference but in one experiment a loss to the air of the insect chamber was demonstrated radiometrically.
† Not sulphate.

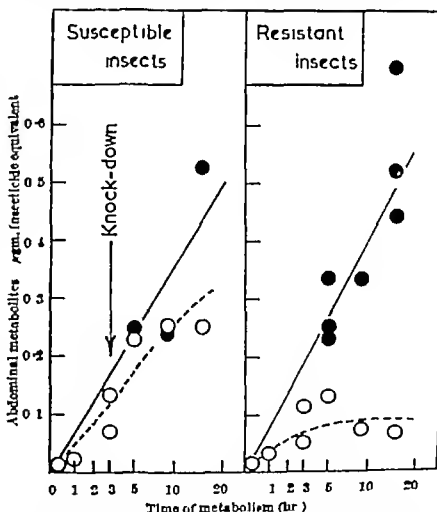


Fig. 1. Accumulation of sulphur-35 metabolites in the abdomens of adult houseflies exposed to 2 μ gm dieldrin- 35 S analogue. \circ excretion possible; \bullet excretion not possible.

or with an independent pair of *S*- and *R*-strains have led to the same conclusions

By chemical assay March, Metcalf and Baich (Metcalf, R. L., personal communication) were unable to find any difference in cuticular penetration or in the apparent disappearance of absorbed dieldrin from their susceptible and resistant houseflies

The protective mechanism may be confined to particular sites, which involve only a small fraction of the absorbed insecticide. For example, Yamasaki and Narahashi² found some evidence of a lowered

sensitivity to dieldrin of the exposed thoracic ganglion of resistant houseflies which did not involve detoxication in other tissues

These experiments are part of an investigation into the mechanisms of dieldrin resistance in Diptera, supported in part by a research grant from the World Health Organization. Full details will be published elsewhere

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MOLECULAR SHAPE AND THE PHYSICAL PROPERTIES OF MUCIN

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EPITHELIAL mucin is an important secretion having somewhat unusual physical properties, and it has been shown, in two instances, that the materials responsible for these physical properties are so-called 'neutral' mucoids of the blood group substance type¹. Little is known at present of the molecular form of this class of compound, but evidence has been obtained, mainly from flow-birefringence measurements, indicating that these particular mucoids are molecules of the 'random-coil' type¹. It is of interest to re-examine some earlier work on mucoids of this type in the light of this result. In particular, the physico-chemical data on the human blood group mucoids of Morgan and co-workers² may be re-considered. These specimens were isolated from the same source and carefully purified using similar mild techniques; they differ in molecular weight over the range 2.6×10^5 to 1.8×10^6 , but the chemical differences between them are, from the physico-chemical point of view, minor. They may thus be taken to represent a homologous polymer series, something difficult to find elsewhere in the field of mucoid chemistry.

Of the relationships known to exist between members of a homologous polymer series of random coils, two may be tested using published physico-chemical data. The relationship between sedimentation coefficient at infinite dilution, s_0 , and M , the molecular weight, should be of the form $s_0 = A + B\sqrt{M}$, where A and B are constants³. Further,

$$\left[\frac{d(1/s)}{dc} \right]_{c \rightarrow 0} \quad (c = \text{concentration}) \text{ should be independent of } M \text{ as the following considerations will show.}$$

Burger's equation for the variation of sedimentation rate of suspension of spheres with dilution has been found applicable to a number of polymers at low concentrations⁴, as is reasonable in that the random coil molecule in translation approximates well to an impermeable sphere⁵, due to the large amount of solvent it entrains within it.

Taking $s = \frac{s_0}{1 + \Lambda nv}$, where Λ is a constant⁴, n is the number of molecules per unit volume, and writing $\frac{Nc}{M}$ for n , where N is Avogadro's number, we have

$$\frac{1}{s} = \frac{1}{s_0} + \frac{\Lambda Ncv}{s_0 M}, \text{ so that } \frac{d(1/s)}{dc} = \frac{\Lambda Nv}{s_0 M} \text{ Remembering}$$

that $s_0 = \frac{M(1 - \bar{v}\rho)}{N\bar{v}\pi\eta_0 a}$, and $v = \frac{4}{3}\pi a^3$, [where a is the effective radius of the molecule and the other symbols have their usual significance, we may write the differential $\frac{8\Lambda N^2\pi^2\eta_0 a^4}{M^2(1 - \bar{v}\rho)}$. For a homologous polymer

series in the same solvent, M is proportional to the square of any linear dimension of the molecule⁶.

Hence $\frac{a^4}{M^2}$ is constant in these conditions.

The values of $s_{0,20,w}$ and $\frac{d(1/s)}{dc}$ given in Table 1 were obtained by extrapolation of the graph of $\frac{1}{s}$ against c to $c = 0$. A linear extrapolation was made although in the case of the first and third specimens quoted linearity is not good. The values of $\frac{d(1/s)}{dc}$ given in Table 1 are thus averages between $c = 0$ and $c = 1$ per cent, furthermore, different degrees of polydispersity in the samples will cause some variation in the slopes observed, so that there is reasonable agreement with theory. Linearity between s_0 and \sqrt{M} is good. The conclusion that these mucoids are of the random-coil form may be drawn with some confidence.

It is interesting to note that the physical properties of mucin may be reasonably interpreted on the basis

Table 1 SEDIMENTATION COEFFICIENTS AND MOLECULAR WEIGHTS OF MUCOIDS

| $s_{0,20,w} \times 10^{13}$ | M | \sqrt{M} | $\frac{d(1/s)}{dc} \times 10^{-13}$ |
|-----------------------------|-------------------|------------|-------------------------------------|
| 8.9 | 2.6×10^5 | 509.9 | 0.72 |
| 9.1 | 2.7×10^5 | 519.6 | 0.75 |
| 10.0 | 3.2×10^5 | 565.6 | 0.91 |
| 12.3 | 4.6×10^5 | 678.2 | 0.80 |
| 25.0 | 1.8×10^6 | 1341.6 | 0.95 |

* c in gm/100 ml

Data from Kekwick (ref. 2) and Caspary (ref. 2)

of what is already known of the properties of random coil molecules. Epithelial mucin frequently gives rise to two phases in water, a rather dilute swollen gel phase and an aqueous phase which is almost pure water. The gel phase displays visco-elastic or pseudo-elastic rheological properties and may also show the Voissenberg effect. These properties are entirely consistent with those of a random coil polymer below its θ point. The gel phase may be dispersed to give a viscous solution by raising the pH, or the temperature, or by adding to the solvent a third component (for example, urea, calcium ions). Again, this behaviour is to be expected of a random-coil polymer if it contains potentially negatively charged groups, and if the solute solvent interaction parameter² is increased by the addition of the third component.

The physical properties of solutions of random-coil polymers have been extensively studied, and a good deal of the theoretical thermodynamic background is available, a full exposition is given by Flory³. A consideration of this work may be of some value in the interpretation of the biochemistry and biophysics of mucous secretions, and attention is invited to three points. (1) The molecular weights of mucoids may be determined from sedimentation coefficients and intrinsic viscosities, the latter being a more readily

and more precisely determinable parameter than the more usual diffusion constant. Moreover, axial ratio as usually evaluated from the frictional ratio is not meaningful with respect to this type of molecule. (2) Where mucoids are modified by chemical treatment or by enzymes and a fall in viscosity is observed, this has usually been interpreted as a depolymerization. Some caution is required here, since the change in viscosity may be largely due to chemical changes which alter the thermodynamic interaction parameter, or the related molecular expansion factor, and not necessarily to depolymerization. (3) The degree to which the molecule is coiled up (that is, the molecular expansion factor) may effect the availability of antigenic sites on a mucoid molecule to antibody and may be a factor concerned in its immunological reactivity.

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AN ASSOCIATION BETWEEN ABO BLOOD GROUPS AND FERTILITY IN A NORMAL AMERICAN POPULATION

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THE possibility of fertility differences associated with ABO blood group phenotype has been investigated in married couples in two populations^{1,2}, using couples unselected with respect to their fertility. In 161 white American couples who had completed their families, fertility differences associated with blood groups could not be demonstrated¹. Such differences were found, however, in 1,429 Japanese couples of varying ages². A study of the fertility of 1,290 married English men and 1,310 married English women age fifty years or more, failed to demonstrate an association between individual fertility and ABO blood group³. We wish to record here observations on 558 white American couples in which fertility differences associated with blood groups do appear to be present.

The present data were obtained from an investigation carried out for other purposes. In the winter of 1950-51 a mass blood grouping (ABO and Rh) programme was carried out in Jackson County, Michigan, on 48,662 individuals by the Michigan Civil Defense⁴. 72 per cent of the inhabitants of the city of Jackson (pop. 51,088 in 1950) were included in this programme. Blood from venopuncture was used and the ABO phenotypes were determined both by cell typing and back typing of isoagglutinins. In addition to ABO and Rh status, the name, address and religion were recorded for each individual. For 64 per cent of the individuals, the date of birth was also noted, about 50 per cent of these persons were less than 15 years

of age. Family relationship was not recorded. Afterwards, for the present analysis, the information on each individual was transferred to an IBM punch card and these cards were sorted by exact street address. Whenever two or more persons having the same surname, street number, and street name in the city of Jackson were found, the city directory was consulted to determine if two of the persons were husband and wife. If this was the case and there were other individuals of the same surname at this address, age relationships were examined to see whether these individuals could reasonably be children of the husband and wife. Unless there was some definite indication, such as appropriate dates of birth, that this was so, the individual was not counted as a child of the couple. Three thousand six hundred and twenty eight families⁵ were found. Home interviews of 90 randomly chosen couples were made in the spring of 1958 to test whether these families had been 'constructed' successfully. The true number of children born by the time of the blood grouping to 53 couples in which the wife was born in 1910 or later was 79, the number in our 'families' was 66 of whom 62 were correctly assigned. 1 was adopted, and 3 (all in one Negro family) were born out of wedlock but probably were the biological children of the couple. For couples whose wives are in this age range it is therefore probable that about 80 per cent of the actual children are correctly recorded.

measured under optimal conditions for growth. This is true also for the high-temperature strain at 25° C. It is noticed that at 25° C the rates of growth, respiration and photosynthesis are close or slightly higher for *Chlorella* 7-11-05 than for the Emerson strain. However, if compared at a temperature optimal for their growth, the Emerson strain has about 3 doublings and *Chlorella* 7-11-05 more than 9 doublings of cell material per 24-hr period. With further refining of the technique, 10 doublings per day are readily obtainable. This gives an 8-fold increase of cell material for a 24-hr period for the Emerson strains and 1,000-fold increase for *Chlorella* 7-11-05. The rate of photosynthesis in the high-temperature algae is 4 times higher at light saturation than in low-temperature algae and 3.6 times higher at half-saturation. For growth the corresponding figures are 3 and 2.9.

The greater productivity of higher-temperature algae in comparison with low-temperature strains is due to the ability of the high-temperature algae to use higher temperature and illuminance levels. This is indicated by much higher positions of light-saturating points for growth and photosynthesis in the higher-temperature algae. The suggestion, that for the low-temperature strain the saturating light intensity for growth is slightly higher than that for photosynthesis and for the high-temperature strain the relationship is reverse, is probably of no significance since the determination of light-saturating intensity involves some degree of approximation.

A most general characteristic of the high-temperature algae is their higher responsiveness to the increase (within limits) in temperature and in incident light energy. In this respect they actually are higher-efficiency algae. The term 'efficiency' here is an expression of two processes—the absorption of the incident energy and conversion of the absorbed energy into the product which is used for measuring the rate of the process. Its pragmatic usefulness is based on the fact that it describes the performance of the organism at high levels of temperature and light energy. The highest levels of the incident energy are of utmost importance for the organism of high productivity capable of using temperatures and light intensities which are of no use if not harmful for the low-efficiency (low-temperature) strains.

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PHOTOCHEMICAL AND STEREOCHEMICAL PROPERTIES OF CAROTENOIDS AT LOW TEMPERATURES

By STAFF OF THE BIOLOGICAL LABORATORIES OF HARVARD UNIVERSITY, CAMBRIDGE, MASS

IN this series of articles we report the results of measurements carried on in this laboratory over the past six years. They involve the absorption spectra of carotenoids and haplo-carotenoids (vitamin A, retinene) at temperatures between 25° and -196° C. The most important single result of these measurements is to demonstrate that cooling such molecules relieves certain instances of steric hindrance ('intramolecular overcrowding')¹, with large effects upon the absorption spectrum and other properties.

The first communication records three observations which, though all made with retinene, have some general interest: (1) the abnormally large changes exhibited by the absorption spectrum of a sterically hindered *cis* carotenoid on cooling, (2) the capacity of a carotenoid to undergo *cis-trans* isomerization at low temperatures in a rigid solvent, and (3) a more specific observation, a new instance of reversible photobleaching.

In the second communication we examine further the first of these phenomena, and show that the absorption spectra of all-*trans* and unhindered-*cis* configurations of retinene, vitamin A, vitamin A₂, lycopene and β-carotene exhibit parallel changes on cooling, whereas those of sterically hindered con-

figurations of these molecules display the abnormally large changes first observed with retinene alone. The third communication discusses the significance of these observations.

(1) Photochemical Behaviour of Retinene

By DR LAWRENCE JURKOWITZ

In these experiments retinene (vitamin A aldehyde, C₂₀H₂₈CHO, Fig. 1) was dissolved in the mixtures of ether, isopentane or isohexane (3-methyl pentane) and alcohol (5:5:2) called EPA and EHA². Such solutions were brought to temperatures close to that of liquid nitrogen (-196° C), at which EPA and EHA become so highly viscous as to form what are essentially clear glasses.

The measurements were made in a Dewar flask designed by Dr R. C. C. St. George, mounted in a special housing which could be substituted for the standard cell compartment of a Beckman DU spectrophotometer. The Dewar flask was silvered throughout except for a clear band at the level of the light path, serving as window. It was made of

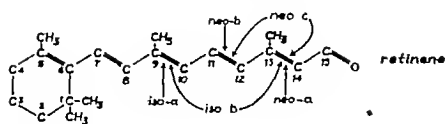


Fig. 1 Structural formula of all-*trans* retinene. Above and below the formula are indicated the positions of the *cis* linkages in known geometrical isomers. Unhindered isomers below: iso-a (9-*cis*), neo-a (13-*cis*) and iso-b (9-13-*cis*). Sterically hindered isomers above: neo-b (11-*cis*) and neo-c (11-13-*cis*).

'Pyrex' glass, and had a high transmission only for wave lengths longer than about 320 mμ. The Dowar was blown in the form of an H, with two vertical chambers connected by a horizontal section. One of the chambers held the absorption cell. Liquid nitrogen could be added from time to time through the other chamber without disturbing the absorption vessel, and thus also provided an additional store of the coolant, which for this reason needed to be replenished less often. The absorption cell could be lowered and raised, into and out of the light path of the spectrophotometer, and all measurements were made with the cell alternately in these positions. That is, all absorptions were measured relative to the absorption of the Dowar flask without the absorption cell in position. The level of liquid nitrogen was at all times below the absorption cell, and hence out of the path of light. A blank correction was obtained by measuring separately the absorption spectrum of the cell containing solvent alone under the same conditions. A further correction involves the contraction of the solvent at low temperatures. EPA and EHA were observed to contract fairly regularly on cooling. Their volume at -100° is about 0.77 of that at room temperature. The temperature of the solution in the absorption cell was followed continuously with an iron-constantan thermocouple immersed in it.

All irradiations were performed with a high pressure mercury arc lamp (General Electric AH6, 250 watts) mounted so that its radiation, having passed through a Luovite cell containing a layer of water 2.5 in. thick, could be focused with a glass lens directly upon the solution in the absorption cell. The full radiation of the arc was employed but enough glass lay between the lamp and the absorption cell to exclude wave-lengths shorter than about 320 mμ.

(1) *Relief of steric hindrance at low temperatures*
Retinene owes its absorption spectrum to the possession of five double bonds—four in the side-chain and one in the attached ring—all in some degree of conjugation with one another and with the terminal carbonyl group (Fig. 1). The molecule exists in a variety of geometric configurations—*cis-trans* isomers—the most prevalent of which have been isolated, and their configurations established by synthesis.⁸ These include the all-*trans* isomer, the relatively unhindered 0 and 13 *monocis* and 0, 13-*dicis* isomers and the sterically hindered 11-*cis* and 11, 13-*dicis* isomers (Fig. 1).⁴ The hindered 11-*cis* isomer (called also neo b) has a special interest, since this configuration of retinene and retinone, serves as the chromophore of all the known visual pigments.⁸

The absorption spectrum of all *trans* retinene at room temperature consists of a single broad band, maximal in EPA at about 373 mμ (λ_{\max}), and with a molar extinction coefficient ϵ_{\max} of 47 600 (Fig. 2). Brought to about -185° the absorption spectrum

still displays no fine structure but λ_{\max} moves about 14 mμ toward longer wave lengths and ϵ_{\max} rises about 10 per cent. Also the long wave-length toe or tail of the band is drawn in toward shorter wave lengths. Such changes are characteristic of polyenes brought to low temperatures (of ref. 6) also following communication).

The same experiment performed with the sterically hindered 11-*cis* isomer yields a very different result (Fig. 2 right). A primary consideration that governs the behaviour of such molecules is the degree to which they achieve coplanarity, that is, to which they succeed in lying flat. Only when coplanar can their systems of alternate single and double bonds come into full conjugation, the condition in which the absorption spectrum lies at longest wave lengths displays the most detailed fine structure and has the largest maximal and integrated extinction. Any loss of coplanarity—any twisting of the system—results in a loss of conjugation, with corresponding losses of extinction and fine structure and usually also a shift of spectrum toward shorter wave lengths.

A *cis* linkage at position 11, since it brings into conflict the H atom on carbon 10 and the $-\text{CH}_3$ group on carbon 13, prevents coplanarity causing a twist in the molecule at this level. The result (Fig. 2) is a considerable degradation of spectrum at room temperature evident mainly in the depression of ϵ_{\max} to 26,400—only 0.55 the ϵ_{\max} of the all *trans* isomer. λ_{\max} also lies at slightly shorter wave lengths than in the all *trans* isomer (at 360 mμ) a remarkably small change compared with other hindered *cis* polyenes.⁹

On cooling to temperatures near that of liquid nitrogen both λ_{\max} and ϵ_{\max} change so greatly as to approach the values observed in all *trans* retinene at these temperatures. λ_{\max} shifts to about 385 mμ and ϵ_{\max} increases to about 43 000 (Fig. 2, right). That is whereas cooling to -185° raises the ϵ_{\max} of all *trans* retinene about 10 per cent, it raises that of 11-*cis* retinene 62 per cent. These changes are entirely reversed on warming. It should be noted that the temperature to which we have brought these solutions is arbitrary further cooling presumably would result in a further approximation of the 11-*cis* to the all *trans* spectrum.

It is as though cooling to about -185° had largely relieved the steric hindrance associated with a *cis* linkage in position 11. This interpretation of

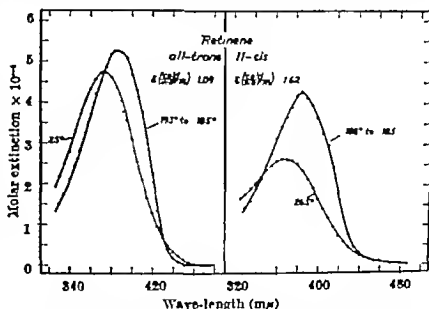


Fig. 2 Absorption spectra of all-*trans* and 11-*cis* retinene, at room temperature and at that of liquid nitrogen. Cooling raises the ϵ_{\max} of the all-*trans* isomer 9 per cent and that of the hindered 11-*cis* isomer 62 per cent.

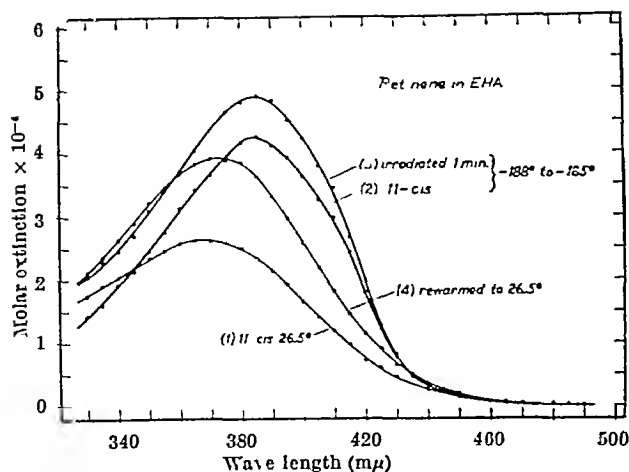


Fig 3 Geometrical isomerization of retinene by light at a low temperature in a rigid solvent (1) Absorption spectrum of 11 *cis* retinene in *EHA* at room temperature (2) Same at the temperature of liquid nitrogen, the solvent is vitrified (3) Irradiated 1 min in the cold (4) Returned to room temperature, in the dark. The rise of ϵ_{\max} in the cold, accentuated in the warm, is associated with the isomerization of the hindered 11-*cis* isomer to a steady state mixture of all possible isomers, primarily all-*trans*

the observations is pursued further in the communication which follows

(2) *Cis-trans* isomerization Retinene is isomerized by simple exposure to light. Beginning with any single geometric isomer, this process ends with the production of a steady-state mixture of all possible isomers, the proportions of which vary with solvent and other conditions, but the major component of which is usually all-*trans*⁸

It occurred to us to ask whether this process would be inhibited by low temperatures, perhaps because it includes a thermal component⁹, or by being carried out in a rigid solvent, which might restrict the necessary rotation about double bonds. It should be noted that geometric isomers of retinene in the crystalline state are not isomerized, even by long exposure to bright sunlight. (It must be conceded that our experiments to date leave it undecided whether this is owing to the crystalline state itself, or to failure of light to penetrate the crystal. The specific extinction of retinene is so high that at λ_{\max} the intensity of light is cut to 1 per cent after penetrating only about 0.12 μ of the pure substance, so that the interior of even a small crystal might scarcely be affected by even a long and intense irradiation.)

In the present experiment we used 11-*cis* retinene, which, being a hindered isomer and relatively unstable, isomerizes almost completely and with a particularly large change of extinction^{8,10}. A solution of 11-*cis* retinene in *EHA* was brought to about -187° , and irradiated for 1 min (Fig 3). The extinction rose about 16 per cent, λ_{\max} remaining almost unchanged. On warming the product to room temperature, these changes were magnified compared with the spectrum before irradiation, the extinction had risen 1.5 times, and λ_{\max} had shifted about 5 μ toward longer wave-lengths, arriving close to the λ_{\max} of all-*trans* retinene. These are the changes that characteristically accompany the isomerization of neo-b retinene to the steady state mixture of isomers, primarily all-*trans*.

All-*trans* retinene behaves very differently under these conditions. On irradiation in *EHA* for 1 min at about -185° , the extinction of this isomer falls about 2 per cent, and on re-warming to room tem-

perature, the spectrum compared with that before irradiation had fallen 1.3 per cent in extinction, with no appreciable change in λ_{\max} . Once again, this behaviour is characteristic of the isomerization of the all-*trans* isomer to a mixture containing small amounts of *cis* isomers, all lower in extinction.

It may be concluded that neither the low temperature nor a rigid solvent inhibits the geometric isomerization of this molecule. The process appears to go about as well in these circumstances as at 100m temperature. Apparently the rigid solvent leaves the molecule sufficient 'elbow room' to allow free play for the rotations involved in geometric isomerization.

(3) *Reversible photo-bleaching* In this experiment, all-*trans* retinene in *EPA* was brought to the temperature of liquid nitrogen, and exposed to the full radiation of the mercury arc. As stated earlier, however, only wave-lengths longer than 320 μ penetrated to the sample. It should be noted that no particular precautions were taken to exclude oxygen or water vapour.

The effects of the irradiation are shown in Fig 4. In 30 min the maximum extinction, at 387 μ , had fallen to about 60 per cent, and in another 30 min to about 20 per cent of its initial value. Small new maxima had appeared at about 350 and 412 μ .

On re-warming this solution to room temperature, the absorption rose again, not indeed to its original height at room temperature, yet to 87 per cent of it, and λ_{\max} returned approximately to its original position. Some of the fall in final extinction is caused by isomerization, owing to the irradiation, from the all-*trans* configuration to the steady state mixture of isomers already described, the remainder probably involves some destruction of pigment.

The major change in this experiment, however, was the photo bleaching at low temperature, reversed (except for the concomitant isomerization) on re-warming to room temperature. The same phenomenon has been observed also with all-*trans* retinene dissolved in *EH* amine (other, isohexane, triethylamine, 5:5:2). On irradiation at about -187° , the extinction falls, and a new maximum develops at about 350 μ and a minimum at about 368 μ . Again, on warming, these changes are largely

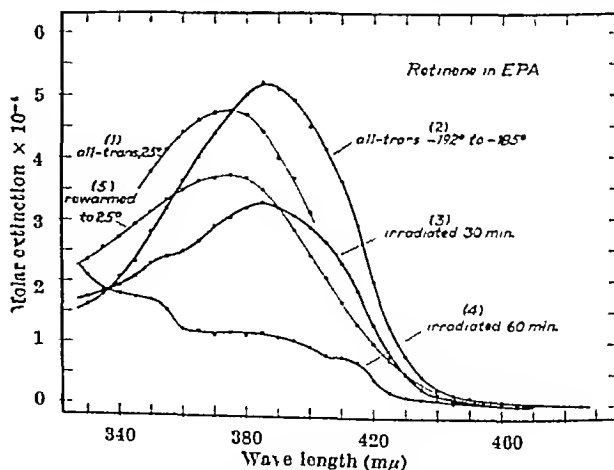


Fig 4 Reversible photobleaching of retinene at low temperature in a rigid solvent (1) All-*trans* retinene in *EPA* at room temperature (2) Same brought to liquid nitrogen temperature (3) Irradiated 30 min in the cold, ϵ_{\max} falls 40 per cent (4) Irradiated 30 min longer, ϵ_{\max} has fallen 80 per cent (5) Re-warmed to room temperature in the dark. Most of the original extinction is regained, what has been lost is due mainly to the light having isomerized the all-*trans* retinene to a steady state mixture of *cis* and *trans* forms

reversed, the band at 350 m μ disappearing and the retinene band rising to nearly its original height. On the other hand, similar experiments with retinene, dissolved in *EPA* and *EH* amino have not displayed photo bleaching.

This photo-bleaching of retinene resembles some what, in the character of the spectral change, the production of a metastable (triplet T) state in chlorophyll by exposure to a brief, very intense flash of light¹¹. The present product, however, appears to be too long lived to represent a triplet state. It may correspond rather to the formation of a pair of free radicals or ions trapped in the rigid solvent but able to recombine on warming to reconstitute normal retinene. In this regard the reversible photo bleaching of retinene may resemble another mode of photo bleaching of chlorophyll discovered some years ago by Porret and Rahinowitch¹², yet which demanded a degree of exclusion of oxygen probably not achieved in the present experiments.

(2) *Cis-trans* Isomerism and Steric Hindrance

By JOHN N. LOEB, PAUL K. BROWN
and PROF. GEORGE WALD

HAVING observed one instance in which cooling to the temperature of liquid nitrogen largely abolished the degradation of spectrum associated with a sterically hindered *cis* linkage we wished to learn how general this phenomenon may be, and how related to other aspects of molecular geometry. With this object in view, we have examined the spectra of geometrical isomers of retinene, vitamin A and A₂, lycopene and β -carotene at room temperature and at that of liquid nitrogen. The procedures were as already described, except that for the measurement of vitamin A we used a quartz Dewar flask and quartz absorption cell in place of the 'Pyrex' vessels used otherwise.

(1) *Retinene*. The most extensive set of geometrical isomers of known constitution now available is offered by the stereoisomeric retinenes. We have already described the changes of spectrum on cooling the all *trans* and the hindered 11 *cis* isomer. In the present experiments these measurements were extended and similar measurements performed with the relatively unhindered 9 *cis*, 13-*cis* and 9,13-*di-cis*

isomers (Fig. 1)*. These measurements are summarized in Table 1 and the changes of extinction with temperature are shown in Fig. 5.

As already noted the all *trans* isomer on cooling to about -185° C exhibits a displacement of λ_{max} of about 14 m μ toward longer wave lengths, and a rise of ϵ_{max} of about 10 per cent. Very nearly the same changes are displayed by all the unhindered *cis* isomers, so that they, together with the all *trans* isomer, show on this degree of cooling an average displacement of λ_{max} of 13 m μ , and an average rise of ϵ_{max} of 11 per cent. This correspondence in behaviour is evident in Fig. 5 in the close parallelism of the lines describing the change of ϵ_{max} with temperature for these isomers.

The extraordinary behaviour of the 11-*cis* isomer is especially evident in this context. To examine this more closely we have measured the spectra of all *trans* and 11 *cis* retinene at intermediate temperatures between 25° and -185° C, the variations of ϵ_{max} over this temperature range are included in Fig. 6.

On cooling all *trans* retinene, ϵ_{max} rises linearly over the entire range of temperatures. The 11 *cis* isomer exhibits altogether different behaviour. Having begun at room temperature far below that of any of the other *cis* isomers, the ϵ_{max} of 11 *cis* retinene rises so rapidly on cooling that by the temperature of liquid nitrogen it has become higher than that of the unhindered 9,13-*di-cis* isomer, and as high as those of the unhindered 9 and 13-*mono-cis* isomers. One would expect that having achieved this position ϵ_{max} should continue to rise at still lower temperatures in parallel with the rise of the unhindered *cis* isomers yet this would demand a considerable decrease in slope, of which there is no hint in the data of Fig. 5. Indeed, the rise of ϵ_{max} in the 11-*cis* isomer proceeds in two stages each linear with temperature a relatively slow change from room temperature to about -100°, and a considerably more rapid further change to about -185°. The significance of the break in the curve and change of slope is not yet clear, but it makes all the more problematical the course of this function at still colder temperatures.

Inidentally, these measurements show that the effects of cooling are regular and continuous. They go primarily, therefore, with the change of tem-

Table 1 EFFECTS OF COOLING UPON CAROTENOID SPECTRA

| Geometric isomer | Room temperature | | -185 to -105 | | Ratio of ϵ_{max} (cold/warm) | Shift of λ_{max} (cold-warm) (m μ) |
|---|--|-------------------------------|--|-------------------------------|--|---|
| | ϵ_{max} ($\times 10^{-4}$) | λ_{max} (m μ) | ϵ_{max} ($\times 10^{-4}$) | λ_{max} (m μ) | | |
| <i>Retinene</i> | | | | | | |
| All- <i>trans</i> * | 47.6 | 373 | 51.7 | 337 | 1.09 | 14 |
| 9- <i>cis</i> | 39.7 | 366 | 41.1 | 339 | 1.11 | 13 |
| 13- <i>cis</i> | 38.8 | 366 | 43.5 | 330 | 1.12 | 14 |
| 9,13- <i>di-cis</i> | 35.0 | 360 | 39.0 | 371 | 1.11 | 11 |
| (Retinene, all- <i>trans</i>) | 42.0 | 362 | 46.5 | 409 | 1.09 | 17 |
| 11- <i>cis</i> (hindered)† | 26.4 | 369 | 43.0 | 334.5 | 1.03 | 16.5 |
| β Carotene | | | | | | |
| All- <i>trans</i> ‡ | 13.5‡ | 451.5 | 184 | 409 | 1.34 | 17.5 |
| 16- <i>mono-cis</i> | 9.3‡ | 441 | 130 | 465 | 1.42 | 18 |
| (Lycopene, all- <i>trans</i>)† | 18.0 | 470 | 272 | 454 | 1.46 | 12 |
| 11-11- <i>di-cis</i> | 46.2 | 403 | 154 | 432.5 | 2.90 | 40.5 |
| Vitamin A | | | | | | |
| All- <i>trans</i> | 52.1 | 324 | 51.2 | 333.5 | 1.04 | 9.5 |
| (Vitamin A ₂ acetate all- <i>trans</i>) | 39.5 | 310 | 45.0 | 360 | 1.14 | 11 |
| 11- <i>cis</i> | 34.5 | 318 | 48.7 | 332.5 | 1.42 | 14.5 |

* Averages from three sets of measurements

† Averages from four

‡ Averages from two

§ For carotene and lycopene ϵ_{max} and λ_{max} are of the middle maximum that of next-to-longest wave-length

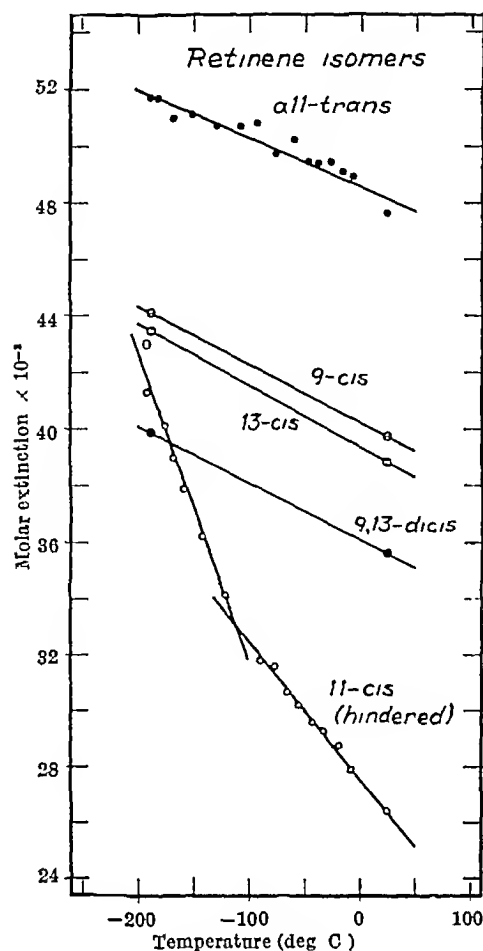


Fig 5 Rise of maximum extinction (ϵ_{\max}) of geometric isomers of retinene on cooling to liquid nitrogen temperature. The all-*trans* and unhindered *cis* isomers exhibit parallel changes, ϵ_{\max} rising on the average 11 per cent. In the hindered 11-*cis* isomer, ϵ_{\max} rises in two linear stages, a total of 62 per cent. The significance of the break in the latter function is not known.

perature and not with vitrification of the solvent, which becomes apparent only at very low temperatures, below -160° .

It is a striking characteristic of the 11-*cis* isomer that though its sterically hindered configuration greatly depresses ϵ_{\max} , it has little effect on λ_{\max} , which is displaced from the all-*trans* position no more than in other *monocis* configurations. By the same token, cooling has no greater effect on the λ_{\max} of the 11-*cis* isomer than on the others. Furthermore, the change of λ_{\max} with temperature for this as for the other isomers is simple and linear, with no evidence of such a break as appears in the function for ϵ_{\max} .

(2) β -Carotene. The spectrum of all-*trans* β -carotene ($C_{40}H_{56}$, Fig 6) exhibits three absorption maxima in the visible region, the central one of which has the highest extinction (Fig 7). These maxima constitute vibrational fine structure superimposed upon a broad absorption band which represents a single electronic transition from the ground to the first electronically excited state. On cooling to the temperature of liquid nitrogen, the spectrum

as a whole is displaced toward longer wave-lengths, and the fine structure is greatly accentuated, five maxima now being distinguishable. Now also the absorption maximum of longest wave-length has the highest extinction. Ordinarily in carotenoid spectra the band of next-to-longest wave-length is highest, and this maximum also can most readily be compared with cases in which no vibrational fine structure appears, the entire absorption taking the form of a single, broad band. For these reasons our measurements are summarized in Table 1 and Fig 8 in terms of the central maximum. A more significant index is the area under the entire absorption band. A comparison on this basis is shown in Table 2 (below).

On cooling to about -185° , the central maximum in all-*trans* β -carotene is displaced about 17 $m\mu$ toward longer wave-lengths, and rises 32 per cent in extinction. Similar measurements were made upon all-*trans* lycopene, $C_{40}H_{56}$, the straight-chain isomer of β -carotene (Fig 6) with similar results (Table 1). On cooling, its central maximum was transposed about 12 $m\mu$ toward longer wave-lengths, and the extinction rose 46 per cent.

As an example of an unhindered *monocis* β -carotene, we have examined the 15,15'-*monocis* isomer (hereafter called 15-*cis*), prepared synthetically¹³. Such a centrally placed *cis*-linkage causes a maximum bending of the molecule, and is associated with a particularly tall '*cis*-peak'¹⁴ in the near ultra-violet at about 340 $m\mu$. The ϵ_{\max} of 15-*cis* β -carotene is only 71 per cent as high as that of the all-*trans* isomer, but on cooling to about -185° , this spectrum undergoes parallel changes (Fig 8). Once again λ_{\max} is displaced 16 $m\mu$ toward longer wave-lengths, and ϵ_{\max} rises 42 per cent. As in the retinones, cooling has about the same effect on the unhindered *cis* isomer as on the all-*trans* configuration.

15 *monocis* β -carotene offers a particularly good opportunity to examine the effects of cooling upon a *cis*-peak. At room temperature the *cis*-peak of this molecule consists of a single band, maximal at about 335 $m\mu$ in EPA, and with ϵ_{\max} 58,500, almost 60 per cent as high as the main absorption band. On cooling to about -185° , the maximum moves to about 349 $m\mu$ —a shift of about 14 $m\mu$, slightly less than in the main band—and ϵ_{\max} rises about 9 per cent—very much less than in the main band. This difference in the effect of cooling on ϵ_{\max} is probably

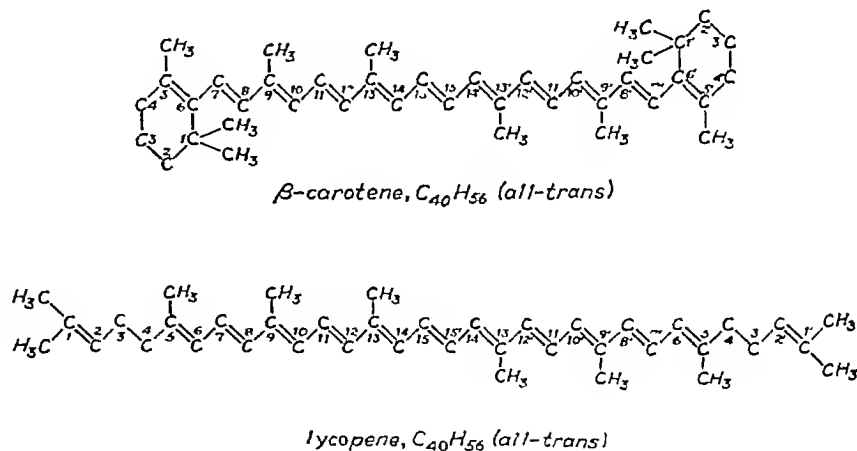


Fig 6 Structures of all-*trans* β -carotene and lycopene. These isomeric carotenoid hydrocarbons differ mainly in that lycopene is straight-chain, whereas β -carotene possesses terminal β -ionone rings. The latter are twisted out of coplanarity with the side-chain, owing to steric hindrance between the methyl groups at 1, 1' and the H atoms at 8, 8', so causing a large loss of conjugation of the ring double bonds with the straight-chain portion of the molecule.

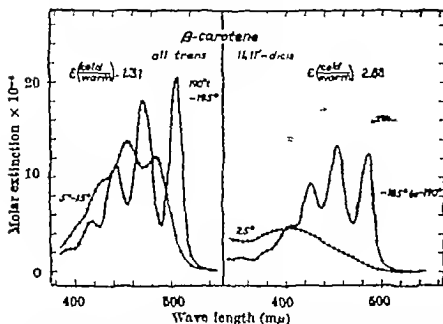


Fig. 7 Absorption spectra of all-trans and 11,11'-di-cis β -carotene in EPA at room temperature and at that of liquid nitrogen. On cooling the maximal extinction of the middle band (that of next-to-longest wave length) rises 31 per cent in the all-trans isomer and 188 per cent in the hindered *cis* isomer. The spectra measured in the cold display five distinct maxima representing transitions from the 0 vibrational level of the ground electronic state to five vibrational levels of the first electronically excited state.

not very significant, in both cases the area of the band remains practically unaltered (cf Table 2). On the whole, it may be concluded that the effect of cooling is much the same on the *cis* peak as on the long wave-length absorption.

As in the retinenes, however, a hindered *cis* isomer behaves very differently. As example of such a form we have examined 11,11'-di-cis β -carotene, prepared synthetically¹⁸. This molecule contains, symmetrically placed two hindered *cis* linkages like that of 11 *cis* retinene. The absorption spectrum in the visible region is greatly degraded at room temperature, consisting of a single broad band displaying no fine structure with ϵ_{\max} only 33.0 per cent as high as that of all-trans β -carotene, and λ_{\max} .

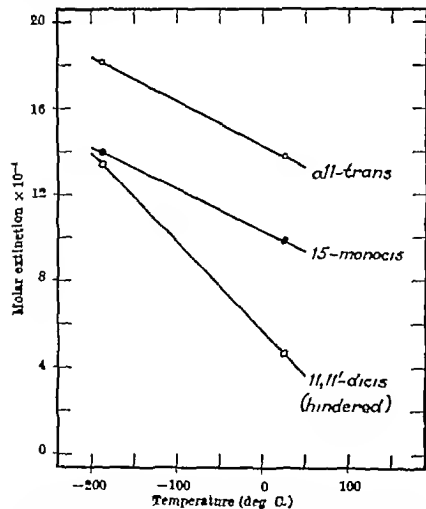


Fig. 8 Effect of cooling on the maximal extinction of geometric isomers of β -carotene. The ϵ_{\max} recorded is that of the middle (next-to-longest wave-length) band. The changes in the all-trans and unhindered 15-*cis* isomers are nearly parallel. The hindered *cis* isomer exhibits a much larger change.

displaced about 50 m μ toward shorter wave-lengths (Fig. 7). On cooling to about -185° , this spectrum changes out of all proportion with the all-trans and 15-*cis* isomers. ϵ_{\max} rises 290 times, approaching close to the ϵ_{\max} of 15 monocis carotene (Table 1, Fig. 8) and λ_{\max} is displaced 49.5 m μ towards longer wave lengths. In addition, the spectrum in the cold exhibits all the fine structure characteristic of unhindered isomers of β -carotene. As with 11-*cis* retinene, there is every appearance that cooling to this degree has almost wholly relieved the steric hindrance.

(3) **Vitamin A** The attempt to perform similar measurements with vitamin A ($C_{20}H_{30}CH_2OH$) on counters special difficulties. These measurements must extend further into the ultra violet than with the other polyenes, hence we transferred to a quartz Dewar flask and quartz absorption cell. Unfortunately also a large solvent 'blank', and consequent impairment of the accuracy of measurement, develop below 330 m μ .

What is more troublesome is that vitamin A fluoresces strongly at room temperature and brilliantly at the temperature of liquid nitrogen. In the Beckman spectrophotometer as ordinarily employed much of the fluoresced light is picked up by the photocell, and recorded as if it were a decrease of extinction. The error so introduced is negligible at room temperature, but considerable in the cold, both because of the increased fluorescence, and because the need to open the slit of the spectrophotometer widely at short wave-lengths greatly increases the radiation incident on the solution. In our first measurements, having done nothing to temper this effect, we were surprised to find that, unlike all the other polyenes measured, vitamin A appeared not to rise in extinction on cooling. In the later measurements to be described we inserted a Jena UG 1 filter, which transmits light only between about 320 and 400 m μ between the Dewar flask containing the absorption cell and the photocell, so removing at least the visible fluorescence. This helped somewhat to bring the measurements on vitamin A into line with those on other polyenes, but was not wholly adequate since fluorescence in the near ultra violet still reached the photocell.

The absorption spectra of all-trans and 11 *cis* vitamin A, measured in EPA at room temperature and in the cold, are shown in Fig. 9. The changes in λ_{\max} and extinction which occur on cooling are summarized in Table 1 and Fig. 10.

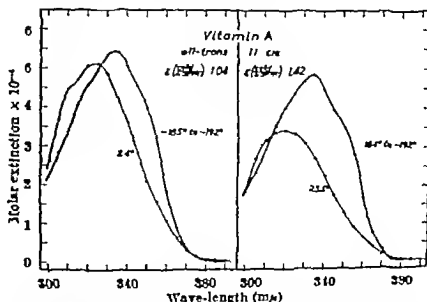


Fig. 9 Absorption spectra of all-trans and 11-*cis* vitamin A at room temperature and at that of liquid nitrogen. Cooling raises ϵ_{\max} of the all-trans isomer 4 per cent and that of the hindered *cis* isomer 42 per cent.

(3) Discussion

By PROF GEORGE WALD

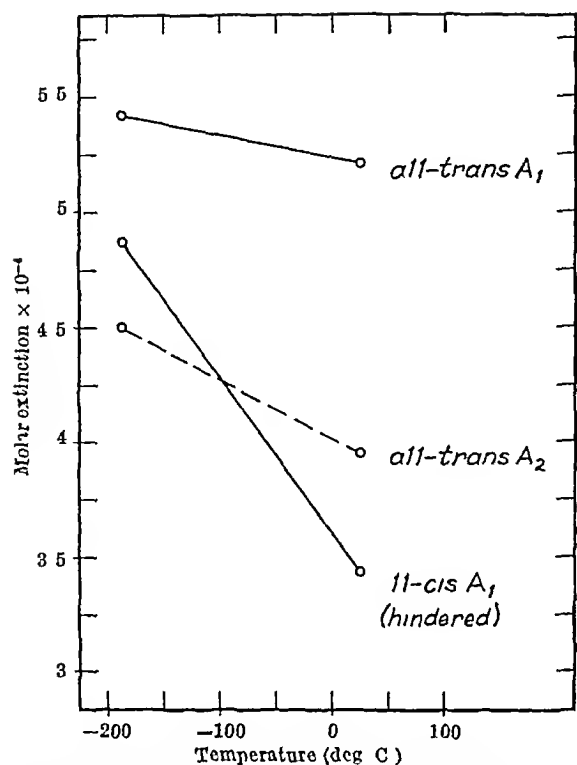


Fig 10 Effects of cooling on ϵ_{\max} of all-*trans* and 11-*cis* vitamin A and all *trans* vitamin A₁. Vitamin A₁ fluoresces so intensely in the cold that it appears to absorb less than is actually the case. The change in ϵ_{\max} exhibited by vitamin A₁ is probably more nearly correct for both all-*trans* molecules. The hindered *cis* vitamin A₁ exhibits a much larger change, though here again the change is under estimated because of strong fluorescence in the cold.

When the all-*trans* isomer is cooled, λ_{\max} is displaced about 9.5 m μ toward longer wave-lengths. The absorption band acquires also a degree of symmetry that is lacking at room temperature, shoulders appearing on each side of the maximum, reminiscent of the three-banded structure of the polyene hydrocarbons. The extinction meanwhile rises only about 4 per cent, perhaps owing to the under correction for fluoresced light already noted. From this point of view some special interest is attached to the behaviour of all *trans* vitamin A₂, which does not fluoresce strongly, on cooling, its extinction rises 14 per cent (Table 1, Fig 10).

As with the other polyenes examined, the hindered 11-*cis* isomer of vitamin A exhibits special behaviour. Cooling this isomer shifts λ_{\max} only slightly more than in all-*trans* vitamin A₁ or A₂, as was the case with the retinene isomers, but ϵ_{\max} rises 42 per cent, and would probably have risen more if the fluorescence had been adequately controlled. Whereas the extinction of 11-*cis* vitamin A is only 66 per cent of that of the all-*trans* isomer at room temperature, in the cold its extinction rises to 90 per cent of that of the all-*trans* isomer, with simultaneous development of comparable evidences of fine structure, in the form of inflexions lying at both sides of the maximum.

Conclusion This examination of the absorption spectra of all-*trans* and *cis* isomers of retinene, β -carotene, lycopene and vitamins A and A₂ shows that whereas all-*trans* and unhindered *cis* isomers exhibit parallel behaviour on cooling, sterically hindered *cis* isomers exhibit abnormally large changes of spectrum, including very large increases of extinction, as though cooling had largely or completely relieved the hindrance.

THE unique feature of the carotenoids is that they possess conjugated systems of alternate single and double bonds in linear array. This arrangement not only lends them colour—a property of all extensive conjugated systems—but also the capacity to undergo large changes in shape through *cis-trans* isomerization¹⁴. In other types of pigment, natural and synthetic, the conjugated systems are mainly bound in rings, and hence held rigidly in position. Exposure to light is one of the most general means for causing *cis-trans* isomerization, and the relatively unrestricted capacity of carotenoids to change their shape in the light is probably the main reason for their special position in animal and plant photo-reception¹⁵.

The absorption of light goes with the possession of particularly mobile electrons, associated not with single atoms or bonds, but with the conjugated system as a whole¹⁷. In valence bond theory this special electronic mobility is embodied in the concept of resonance or mesomerism: the molecule is regarded as a hybrid of all the possible electronic configurations that can be associated with a given constellation of atoms. In molecular orbital theory, the same effect is achieved with the concept of overlapping π -orbitals, occupied by π -electrons which move more or less freely through the entire conjugated system.

Resonance, or the presence of π -electrons (which, ever so many one prefers), lowers the energy required to raise an electron from the ground state to the first excited state, hence posing the absorption at relatively long wave-lengths, and also greatly increases the probability of such transitions, with a consequent intensification of absorption. These are the properties that characterize a pigment.

The spectra considered in the present experiments, except for a passing reference to the *cis* peak of β -carotene, represent such transitions from the ground to the first electronically excited state. Fine structure, when evident, is caused by superimposed changes of vibrational state (Fig 12).

The most significant aspects of these spectra are (1) Their wave length range, a measure of the energies involved in the electronic transition (Fig 12), through the relation $\Delta E = Nh\nu = Nhc/\lambda = 2.854 \times 10^7/\lambda$, in which ΔE , the energy of the transition, is expressed in gram calories per mole of quanta, and λ in m μ . (2) The width of spectrum and detail of fine structure. In general, a narrow spectrum and sharp fine structure are signs of the simplification of vibrational changes. Any increase in the variety of such changes, through the overlapping of bands, tends to broaden the spectrum and to wash out detail. (3) The area under the absorption band, when it is plotted on a frequency scale ($\int \epsilon \cdot d\nu$). This is a measure of the probability of the electronic transition¹⁸. If the absorption band is reasonably symmetrical and lacks fine structure, the product of ϵ_{\max} and the half-width of the band ($\epsilon_{\max} \Delta\nu_{1/2}$) does nearly as well, but these conditions are not usually fulfilled by carotenoid spectra. ϵ_{\max} itself, though frequently involved in theoretical discussions, has little physical meaning, and offers only a rough hint of whether the band area has changed.

For conjugation to be strong, the atoms which compose the conjugated system must lie approx-

mutely in a plane. It is only then that π -orbitals can overlap or resonance occur¹⁰. Any departure from coplanarity—any twisting of the system—interferes with conjugation to a degree depending upon the angle of twist¹¹. The result is to depress the probability and usually to increase the energy of the lowest order of electronic transitions, so decreasing the area of the longest wave length band and usually shifting it toward shorter wave lengths.

Simple bending of the conjugated chain even though in a plane, also affects the absorption spectrum. Polyenes absorb most strongly when the electric vector of the light is parallel with the long axis of the conjugated chain. A polyene in the all *trans* configuration is linear (except for the regular zigzagging between carbon atoms) and is at its longest extension (Fig. 11a). In this state its absorption is concentrated in a single electronic transition, and has at relatively long wave lengths. Any bending of this structure such as is caused by a *cis* linkage shortens it, and at the same time opens a new axis of absorption at right angles to the main axis (Fig. 11b). The result is a decrease in the area, and usually the height, of the main absorption band, and the appearance of a new absorption band (the *cis* peak) associated with the new absorption vector lying at shorter wave lengths and polarized at right angles to the main band¹¹.

Mulliken^{12,13} has derived the approximate expression $\epsilon_{\max} \propto l^2$, in which l is the length from tip to tip of the conjugated system. The greatest shortening is caused by a central *cis* linkage which bends the whole system at an angle of about 120° , shortening it to about 87 per cent (that is $\cos 30^\circ$) of its all *trans* length (Fig. 11b). By Mulliken's formula this should diminish ϵ_{\max} to 76 per cent of the all *trans* value. The available measurements tend to show somewhat larger decreases of ϵ_{\max} (compare all *trans* and 15-*cis* β -carotene in Table 1). Furthermore, a *cis* linkage anywhere in the chain effects λ_{\max} 4–6 m μ toward shorter wave lengths¹⁴, an effect that is not a necessary consequence of simple bending in a plane. Perhaps both departures from expectation are caused

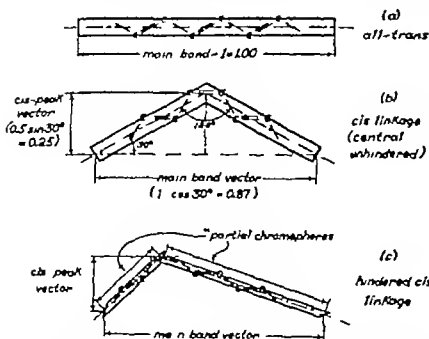


Fig. 11. Diagram to show the absorption vectors of such conjugated systems as are present in the carotenoids. The conjugated system of an all-*trans* carotenoid is coplanar throughout and at its longest extension. An unhindered *cis* linkage bends the molecule, shortening the fundamental vector and opening a new absorption vector polarized at right angles to the main axis for the *cis* peak. A hindered *cis* linkage both bends and twists the molecule, resulting in absorptions corresponding not only to the main and *cis* peak vectors, but to the 'partial chromophores' into which the conjugated system is divided by the break in coplanarity.

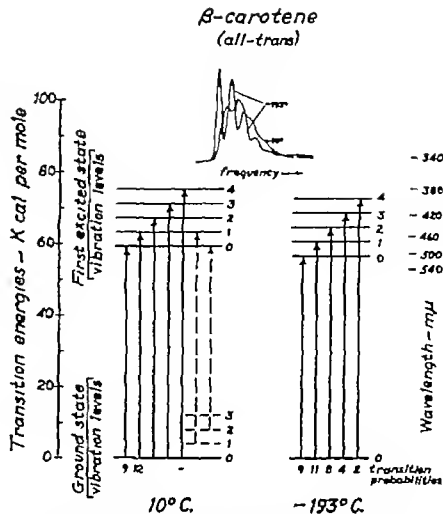


Fig. 12. Energy diagram of all-*trans* β -carotene constructed from the data of Fig. 7 (left). These results are re-plotted on a frequency scale at the top of the present figure. The five maxima that appear in the cold represent transitions from the 0 vibrational level of the ground electronic state to five equally spaced vibrational levels (about 4 kcal apart) of the first electronically excited state. The energy of the 0-0 transition is 50.1 kcal per mole in the warm, and 66.6 kcal in the cold. In the warm a few transitions go from higher vibrational levels of the ground state, particularly short transitions of this type shown here with broken lines, are responsible for a long wave-length tail on the absorption band which is lost in the cold. (This difference does not emerge in the present spectra though apparent in general.) The areas under the successive maxima are an index of the transition probabilities. In both warm and cold the 0-1 transition is most probable. Similar energy diagrams differing only in numerical detail can be drawn for 15-*cis* and (cold) 11-*cis* β -carotene and for lycopene.

by the small twisting that may also be associated with 'unhindered' *cis* linkages (see below). On the other hand as already noted, such theoretical arguments are properly pursued on the basis not of ϵ_{\max} , but of the area of the absorption band.

In a sterically hindered *cis* linkage, the overlap of projecting groups causes a large departure from coplanarity. At such a point, as already said, the conjugated system is both bent and twisted (Fig. 11c). The bend as always is associated with a decrease in the fundamental absorption, and the appearance of a *cis* peak. In addition, the twist causes a partial break in conjugation, which to some degree divides the whole system into two shorter segments—'partial chromophores'. Associated with the latter are subsidiary bands, lying at shorter wave lengths than the fundamental band, and overlapping with the *cis* peak, the main band, or both, depending on the lengths of the segments.

It can be concluded that the absorption spectrum offers a variety of indices of molecular structure: the linear co-ordinates of the conjugated system, its complexity of vibrational states, whether it lies bent or straight, whether twisted or in a plane. With these notes as background, we may discuss the effects of cooling on the absorption spectrum.

General effects of cooling. Cooling resulted in the same general pattern of changes in all our all-*trans* and unhindered *cis* carotenoids. Many of these

Table 2 EFFECTS OF COOLING ON THE AREAS OF ABSORPTION BANDS

| Carotenoid | Relative area | | Ratio of areas (cold/warm) |
|------------------------------------|------------------|----------------|----------------------------|
| | Room temperature | -185° to -195° | |
| <i>Unhindered species</i> | | | |
| Retinene, all-trans | 320 | 317 | 0.99 |
| 9-cis | 306 | 313 | 1.02 |
| β Carotene, all trans | 695 | 654 | 0.94 |
| 15 monocis | 494 | 484 | 0.98 |
| cis peak | 236 | 274 | 0.86 |
| Lycopene, all trans | 835 | 834 | 1.00 |
| Vitamin A, all trans | 293 | 310 | 1.06 |
| Vitamin A ₁ , all trans | 324 | 315 | 0.97 |
| <i>Hindered species</i> | | | |
| Retinene, 11-cis | 171 | 241 | 1.44 |
| Vitamin A, 11-cis | 193 | 264 | 1.37 |
| β -Carotene, 11, 11'-dicis | 292 | 529 | 1.81 |

Relative areas, in arbitrary units, of the fundamental absorption bands plotted on a scale of molar extinction versus frequency, that is, ϵ/ν , $\text{cm}^2/\text{cm}^{-1}$.

changes had been noted earlier in studies of diphenylpolyenes⁶. They include (1) displacement of the spectrum toward longer wave-lengths, (2) ϵ_{max} rises, and the absorption band narrows, its area does not change (Table 2), (3) fine structure may appear, or be accentuated, (4) the long-wave length tail of the absorption band is abbreviated, so that usually it cuts off at shorter wave-lengths than in the warm.

These changes have a common basis, which can most readily be understood with reference to such a typical example as all-trans β -carotene, the energy diagram of which is shown in Fig 12. Above the energy diagram are the absorption spectra from which it was derived, the curves of Fig 7 (left) redrawn on a frequency scale.

The fundamental absorption band of β -carotene, as is apparent in the spectrum measured in the cold, possesses five maxima, representing transitions from the zero vibrational level of the ground electronic state to five vibrational levels of the first electronically excited state. The five absorption maxima are equally spaced, $1,430 \text{ cm}^{-1}$ apart, corresponding to differences in the vibrational energy levels averaging $4.08 \text{ kcal per mole}$. The three peaks that appear in the warm clearly correspond to the first three peaks in the cold spectrum, and have almost the same spacing. That is, in both cold and warm, the first five vibrational levels of the first excited state are equally spaced about 4 kcal apart.

The absorption peak of lowest frequency measures the energy change corresponding to the 0-0 transition. At room temperature this peak occurs at $20,700 \text{ cm}^{-1}$ ($\Delta E = 59.1 \text{ kcal}$), in the cold it has shifted to $19,780 \text{ cm}^{-1}$ ($\Delta E = 56.5 \text{ kcal}$). That is, cooling the molecule has lowered the energy of the first electronic excitation by 2.6 kcal , accounting for the displacement of the spectrum towards the red.

Though in the cold the highest extinction appears in the first band (0-0 transition), if the areas under the vibration bands are measured, these are seen to be largest in both the cold and warm in the second ('middle') band (0-1 transition). Such areas are an index of the relative probabilities of the various transitions, indicated in Fig 12 below the energy diagram. The 0-1 transition is most probable at all temperatures.

All these features of the energy diagram, except for small numerical differences, are shared by 15-cis and 11,11'-dicis β carotene (cold) and by lycopene.

At room temperature a small fraction of molecules is at higher vibrational levels of the ground state,

from which transitions to the upper state involve smaller increments of energy, and hence longer wave-lengths of absorption. A few such transitions are shown in Fig 12 with broken lines. A scattering of particularly short transitions of this kind accounts for the long wave-length tail on the absorption band in the warm. In the cold, virtually all transitions go from the zero vibrational level of the ground state, and this tail is lost. (Our measurements on β -carotene do not show this difference, though I think that more detailed measurements would have revealed it. It is apparent in many of our other spectra.)

Why do all polyene spectra that have been examined rise in extinction, that is, sharpen in structure, and shift toward the red on cooling? The shift towards the red, as just said, is an expression of the lowering of the transition energy between the ground and first excited state. It may be supposed that in the warm, molecular motions, in part the result of collisions, bend and twist the conjugated system from moment to moment so as to produce effects that resemble statistically those of cis linkages, hindered and unhindered. In the cold and in a rigid solvent, the molecule is subjected to less deformation, and can maintain relatively undisturbed its most extended and planar conformation. Such a view raises no serious energetic difficulties, for the mean thermal kinetic energy at room temperature is about $0.9 \text{ kcal per mole}$ ($3/2 RT$), which is of about the right magnitude to produce the minor bendings and interruptions of conjugation that would account for the displacement of spectrum toward shorter wave-lengths and the fall of extinction and broadening that we observe in the warm. The effects of warming can mimic those of a cis linkage only qualitatively, for an actual cis linkage is fixed in position in all molecules of one species, whereas warming causes transient and fluctuating effects, different in all members of the molecular population.

It seems to me that this hypothesis involves several theoretical consequences that should be mentioned, though they do not emerge in the present measurements. If it is true that the molecule achieves more perfect conjugation in the cold than in the warm, this should result in an increased resonance energy, and a consequent lowering of the ground state as well as the first excited state. Furthermore, one should expect the area of the absorption band to be larger in the cold than in the warm, just as it is larger in the all-trans than in cis configurations, as Table 2 shows, within the accuracy of the present measurements, the areas are the same at room temperature and in the cold. Finally, I think one should expect to find higher absorption in the warm in the ultra-violet, owing to contributions from new absorption vectors and partial chromophores. Perhaps more detailed investigation will uncover all these effects.

Cooling and steric hindrance. It was shown above that sterically hindered cis carotenoids exhibit abnormally large changes of spectrum on cooling, as though lowering the temperature had relieved the hindrance. ϵ_{max} rises, and λ_{max} shifts toward the red, so as to approach the properties of an unhindered cis molecule.

More significant than either of these effects is the behaviour of the area of the absorption band. As shown in Table 2, though the areas of the main absorption bands of all-trans and unhindered cis carotenoids are approximately the same in the warm and cold, those of 11-cis retinene and vitamin A

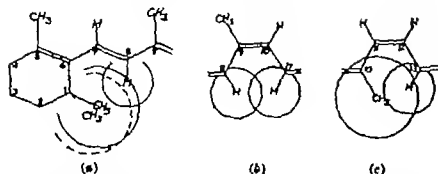


Fig. 13. Three sources of intramolecular steric hindrance encountered in carotenoids: (a) Hindrance between methyl groups on a β -ionone ring and a hydrogen atom on the side-chain. What is believed to be the prevalent *a-trans* orientation is shown here. (b) Hindrance between H atoms at an 'unhindered' *cis* linkage. It is only when H is given a van der Waals radius of 1.2 Å. that the overlap shown here occurs. At a radius of 0.65 Å. or less, there would be no hindrance. (c) Hindrance between a methyl group and H at a hindered *cis* linkage. Only this last type of hindrance appears to be appreciably relieved by cooling.

increase about 40 per cent and that of 11,11-*di*- β carotene increases just twice as much, about 80 per cent, on cooling to liquid nitrogen temperature.

Such molecules present three sources of steric hindrance (Fig. 13) (a) overlap between the methyl groups on C₁ of the ring and the H atom on C₂ causing a twist between the ring and side chain²², (b) overlap between H atoms at an 'unhindered' *cis* linkage. This is small, if it exists at all, yet is some times held responsible for the small shifts of spectrum toward shorter wave-lengths and some of the decrease of extinction that characterize such linkages¹⁴, (c) overlap of an H atom with a methyl group at such linkages as 11-*cis*.

Of these three types of hindrance, only one appears to be relieved by cooling. (a) Cooling does not change appreciably the hindrance between ring and side chain, as shown by the fact that it has parallel effects on β carotene which possesses two ionone rings, and lycopene, which has none (Tables 1 and 2). (b) Cooling does not relieve whatever overlap of H atoms may exist at 'unhindered' *cis* linkages, as shown by the fact that it has parallel effects on unhindered *cis* and all *trans* carotenoids. (c) It can be concluded that cooling relieves specifically the steric hindrance at such linkages as 11-*cis*.

What is the mechanism of this effect? The geometry of molecules involves two kinds of dimension: the distances between bonded atoms, expressed in the bond radii, and the distances at which non bonded atoms and groups begin to repel one another, expressed in the van der Waals radii. Instances of intramolecular steric hindrance seem as though they should involve van der Waals radii. These are generally estimated to be about 0.8 Å. larger than the bond radii¹⁰. Yet estimates of intramolecular over crowding made on this basis tend to predict larger effects than are observed, and values smaller than the van der Waals radii, perhaps at times approaching the bond radii, may be more applicable (cf. ref. 24).

I would suppose that the repulsion radius is made up not only of the space occupied by atomic structures, but includes also to a degree the space swept out by atoms and groups in their thermal stretching, bending and twisting motions. In this sense the close approach of such groups must give rise to a soft rather than a hard hindrance. It is equivalent, not to the contact between rigid surfaces, but rather to a fluctuating interpenetration of 'Lebensräume' that involves considerable give.

I would suppose that lowering the temperature, by quelling down the thermal stretching, bending

and twisting motions of attached groups, effectively contracts their van der Waals radii. This is the same type of effect that we have already invoked with regard to the conjugated chain. It is this effect that I think is primarily responsible for the relief of steric hindrance on cooling.

Why are hindrances of types (a) and (b) in Fig. 13 not relieved by cooling?

The hindrance between the ring and side-chain is probably considerably 'harder' than at an 11-*cis* linkage, because, in the *trans* configuration shown in Fig. 13, two methyl groups are in conflict with an H atom, and the ring holds these methyl groups more rigidly than would a straight chain¹⁴.

The assumed hindrance between H atoms at an 'unhindered' *cis* linkage requires further consideration. Such hindrance exists if hydrogen is assigned the full van der Waals radius of 1.2 Å. but this value is probably too large to be applicable in the present instance. Brude has suggested that the onset of spectrally detectable effects owing to steric hindrance coincides better with a van der Waals radius of about 0.6 Å. for hydrogen¹⁴, even if one expanded this to 0.8-0.9 Å. no conflict would exist at an unhindered *cis* linkage and the problem of relieving it by cold or otherwise would not arise. On the other hand, if this is a source of hindrance one would not expect it to be relieved appreciably by cooling, for the stretching and bending energies of bonded hydrogen atoms are so large as scarcely to be activated even at room temperature²⁵.

For this reason also the relief of hindrance on cooling at such a linkage as 11-*cis* cannot appreciably involve the H atom, and must be ascribed almost entirely to the contraction of the effective van der Waals radius of the methyl group.

Implications and consequences. The assumption that the effective van der Waals radii contract considerably at low temperatures can be tested further and made quantitative with the help of these and other kinds of measurement. In particular, X-ray crystallography at low temperatures should yield valuable information concerning the variation of van der Waals radii with temperature, and whatever molecular distortions accompany such changes. (I understand that such measurements have been made by W. N. Lipscomb at Minnesota and by Fankuchen at Brooklyn Polytechnic Institute both of whom inform me in personal communications that cooling seems to have only very small effects on bond radii, and should have its principal effects on the distances of intermolecular and intramolecular contact.)

One interesting result of our observations is that in the two instances in which measurements were made at intermediate temperatures (Fig. 5) ϵ_{\max} rose linearly as the temperature was lowered, though in the case of 11-*cis* retinene an abrupt change in slope occurred at about -100° , the reason for which is not known. The solvent is still highly fluid at this temperature and continues so until below -150° .

The temperature at which our measurements stopped was arbitrarily that of liquid nitrogen. At this temperature as already noted 11-*cis* retinene has achieved as high an ϵ_{\max} as an unhindered *mono-cis* isomer. That is, it behaves as though its steric hindrance were entirely relieved, and judging from Figs. 8 and 10 this must be nearly the case also with 11,11-*di*- β -carotene and 11-*cis* vitamin A. Once the hindrance is gone one should expect any further rise of ϵ_{\max} with lowering of the temperature to have the same slope in all these molecules.

The only data adequate to bear upon this point are those involving 11-*cis* retinene in Fig 5, and here there is no indication that this expectation will be realized. The slope of the function would have to break very sharply to a lower value at temperatures just below that of liquid nitrogen, for ϵ_{\max} of the hindered *cis* molecule not to rise rapidly above that of unhindered *cis* forms, a phenomenon we would be hard put to explain.

From this point of view the band areas shown in Table 2 are more reassuring. At -190° , 11-*cis* retinene has a band area still only 0.77 as great as that of 9-*cis* retinene. 11,11'-*di-cis* β -carotene has a band area higher than that of 15-*monocis* carotene, as it should, since two *cis* linkages tend to compensate each other, bending the molecule less, and usually for this reason depressing the extinction less than one central *cis* linkage¹⁴. Perhaps, therefore, as in other aspects of this problem, the argument encounters difficulties in terms of ϵ_{\max} that are avoided when one considers instead the band area.

The observation that steric hindrance is partly or wholly relieved at low temperatures has a curious consequence. The twisting of the molecule occasioned by steric hindrance may, if sufficiently large, cause observable optical activity, depending upon whether the twist is to the right or the left. In all but highly hindered molecules, since, as noted, such hindrances are 'soft', racemization occurs rapidly at room temperature, and ordinarily the single optical isomers cannot be isolated. In several instances of large hindrance, however, racemates have been resolved, and the enantiomorphs are relatively stable^{25, 27}. Our observations suggest that cooling such a single optical isomer, by decreasing the hindrance, might remove the barrier to racemization. We should then observe the strange phenomenon of a chemical reaction, a racemization, activated by lowering the temperature. This possibility should certainly be examined.

Changes of absorption spectrum similar to those we have observed on cooling carotenoids in solution are observed in the warm when these and other pigments are embedded in solid or quasicrystalline structures. So, for example, spectra of the visual pigments—all of which are retinene-proteins—exhibit a displacement of λ_{\max} several m μ toward the red, and rise of extinction, when measured in the retina or in suspensions of whole or fragmented outer segments of rods²⁸. The latter are quasi-crystalline structures, in the sense that many of their molecules, including the visual pigments themselves, are oriented relative to one another²⁹. The same relations involve the spectra of the chlorophylls, measured in cells or chloroplast suspensions, compared with their spectra in solution³⁰. In all these cases the spectrum in cell particles appears to differ from that measured in solution in much the same way that spectra at low temperatures in rigid solvents differ from those at room temperature. Perhaps in solid structures, as in the cold, the quieting of thermal motions and relief from collision permit these pigments to maintain a less disturbed condition of linearity and coplanarity, with the consequent increase of target length and improvement of conjugation that yield the observed spectral changes.

These investigations were supported in part by grants from the Rockefeller Foundation and the U.S. Office of Naval Research. We are indebted to Dr. H. H. Inhoffen for a gift of 15,15'-*cis* β -carotene, to Dr. O. Isler for gifts of 11,11'-*di-cis* β -carotene and

vitamin A₂ acetate, to Prof. L. Zechmeister for lycopene, to Dr. W. Orosnik for 11-*cis* vitamin A and retinene, and to the Organic Research Laboratory of Distillation Products Industries, Rochester, New York, for supplies of 9-*cis*, 13-*cis* and 9,13-*di-cis* retinene.

(Dr. Jurkowitz—now at the University of Chicago Clinics—performed these experiments in the summer of 1955, following his first year at medical school. Mr. Loeb, now a third-year student at Harvard Medical School, was an undergraduate at the time of these experiments (1956–57).)

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FORTHCOMING EVENTS

(Meetings marked with an asterisk * are open to the public)

Monday October 19

ILLUMINATING ENGINEERING SOCIETY (at Caxton Hall, Caxton Street, London, S.W.1) at 6 p.m.—Mr L. J. Davies: "The Generation of Light" (Golden Jubilee Lecture)

UNIVERSITY OF LONDON (at Birkbeck College, Malet Street, London W.O.1) at 8 p.m.—Prof. E. G. Boring (Harvard University): "The Psychology of the History of Science" (First of three lectures on "The Pattern of Modern Psychology")

BRITISH ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE in association with GRANADA TV NETWORK (at the Guildhall, London E.C.2) at 8.30 p.m.—Dr Edward R. Murrow: Second of the Inaugural Series of the Granada Lectures on the theme of "Communication in the Modern World"

ROYAL GEOGRAPHICAL SOCIETY (at 1 Kensington Gore, London S.W.7) at 8.30 p.m.—Sir Charles Darwin F.R.S. "Darwin the Traveller"

Tuesday October 20

UNIVERSITY COLLEGE (in the Anatomy Theatre, Gower Street, London W.C.1) at 1.15 p.m.—Dr A. W. Stonier: "The Differences between English and American Universities"

ROYAL INSTITUTE OF CHEMISTRY (Joint meeting with the South East Essex Technical College Scientific Society at the South East Technical College, Longbridge Road, Dagenham, Essex) at 7 p.m.—Mr D. G. Chisham: "The Education and Training of Chemists"

Wednesday October 21

INSTITUTION OF CHEMICAL ENGINEERS (at the Geological Society Burlington House, Piccadilly, London, W.1) at 5.30 p.m.—Mr K. P. Larnhou: "Gas-liquids Contacting in Distilled Beds"

INSTITUTION OF MECHANICAL ENGINEERS STEAM GROUP (at 1 Birdcage Walk, Westminster, London S.W.1) at 5 p.m.—Mr P. Hamer: "Present-day Feed water Treatment for High Pressure Boilers"

ROYAL INSTITUTE OF CHEMISTRY LONDON SECTION (at King's College Strand, London W.C.2) at 6.30 p.m.—Dr D. D. Davies: "Recent Advances in Plant Biochemistry"

Thursday October 22

UNIVERSITY COLLEGE (in the Anatomy Theatre, Gower Street, London W.C.1) at 1.15 p.m.—Prof. L. S. Penrose F.R.S. "Human Chromosomes"

PHYSICAL SOCIETY OPTICAL GROUP (in the Science Museum Lecture Theatre, South Kensington, London S.W.7) at 2 p.m.—Discussion on the Stockholm Conference

UNIVERSITY COLLEGE (in the Englefield Theatre, Gower Street, London W.C.1) at 5 p.m.—Dr B. Cheng: "Some Aspects of Space Law"

ROYAL SOCIETY OF MEDICINE EXPERIMENTAL MEDICINE AND THERAPEUTICS SECTION (at 1 Wimpole Street, London W.1) at 5.30 p.m.—Prof. Sir Hans Krebs: "Biochemical Aspects of Retoxia (W. E. Dixon Memorial Lecture)"

ILLUMINATING ENGINEERING SOCIETY (at the Institution of Civil Engineers, Great George Street, London E.C.4) at 6 p.m.—Dr W. H. Glanville F.R.S. "Light and Road Safety" (Golden Jubilee Lecture)

INSTITUTION OF MECHANICAL ENGINEERS HYDRAULICS GROUP (at 1 Birdcage Walk, Westminster, London S.W.1) at 5 p.m.—Discussion on "Effect of Cavitation in Hydraulic Machinery"

UNIVERSITY OF LONDON (at Birkbeck College, Malet Street, London W.C.1) at 8 p.m.—Prof. E. G. Boring (Harvard University): "The Pattern of Modern Psychology" (Second of three lectures on "The Pattern of Modern Psychology")

SOCIETY OF CHEMICAL INDUSTRY (at the Royal Institution, 21 Albemarle Street, London W.1) at 8 p.m.—Prof. H. Mark (U.S.A.): "Recent Progress in Polymer Chemistry" (Backland Memorial Lecture)

GILKIN COLOUR CHEMISTS' ASSOCIATION, LONDON SECTION (Joint meeting with the Oils and Fats Group of the Society of Chemical Industry at the Royal Society of Tropical Medicine and Hygiene, 36 Portland Place, London W.1) at 7 p.m.—Dr W. C. Ault (Iliad, Delphi): "Polymers and Elastomers Derived from Fats"

Friday October 23

ROYAL INSTITUTION (at 21 Albemarle Street, London W.1) at 6 p.m.—Sir Norman Kipping: "How Can We Help Underdeveloped Countries?"

Saturday, October 24

BRITISH PSYCHOLOGICAL SOCIETY (in the Garter Tuck Theatre, University College, Gower Street, London W.C.1) at 2.35 p.m.—Prof. E. G. Boring: "The Role of the Zeitgeist in the History of Perception"

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned

RESEARCH ASSISTANT (with a special interest in electronics or fluid mechanics) for work in the Hydraulics Laboratory—The Professor of Civil Engineering, The Queen's University Belfast (October 31)

RESEARCH FELLOW in PHYSICAL CHEMISTRY for work involving the study of solids by physical methods including mass spectroscopy and positive ion bombardment—The Deputy Registrar, The University of Edinburgh, Edinburgh 15 (October 31)

SENIOR LECTURER IN ELECTRICAL ENGINEERING at the University of Tasmania, Australia—The Secretary, Association of Universities of the British Commonwealth, 30 Gordon Square, London W.C.1 (Australia, October 31)

SENIOR LECTURER (with a special interest in ecology, plant physiology or genetics) in AGRICULTURAL BOTANY in the Department of Plant Science, Canterbury Agricultural College, University of New Zealand—The Secretary, Association of Universities of the British Commonwealth, 30 Gordon Square, London W.C.1 (New Zealand, October 31)

ANALYST (with a good honours degree in chemistry or its equivalent and prepared to specialise in the analysis of rocks and minerals) in the GEOLOGY DEPARTMENT—The Professor of Geology, King's College, University of London Strand, London W.C.2 (November 1)

LECTURER OR ASSISTANT LECTURER in the DEPARTMENT OF PHYSICO-COLOGY—The Registrar, The University, Leeds 2 (November 4)

LECTURER IN PHYSICS to undertake research in the field of metal physics or solid state physics (low temperature facilities are available)—Prof. P. M. S. Blackett, F.R.S. Physics Department, Imperial College of Science and Technology, London W.7 (November 7)

LECTURERS in the DEPARTMENT OF PATHOLOGY in the Faculty of Medicine, University College, Ibadan, Nigeria—The Secretary, Senate Committee on Colleges Overseas in Special Relation, University of London, Senate House, London W.C.1 (November 9)

CHAIR of GEOLOGY in the University College of Rhodesia and Nyasaland—The Secretary, Inter-University Council, Higher Education Overseas, 29 Woburn Square, London W.C.1 (November 10)

LECTURER in PSYCHOLOGY at the University of New England, Australia—The Secretary, Association of Universities of the British Commonwealth, 30 Gordon Square, London W.C.1 (Australia, November 14)

CHAIR of PHILOSOPHY and HEADSHIP OF THE DEPARTMENT—The Registrar, The University, Nottingham (November 30)

CHAIR of GEOGRAPHY in the University of Guelph, Guelph, New Zealand—The Secretary, Association of Universities of the British Commonwealth, 30 Gordon Square, London W.C.1 (New Zealand, December 15)

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

International Wool Secretariat: British Sheep Breeds Wall Sheets Set of 12 sheets, 64 (post free) (Size 18 in x 13 in) (London, Inter-Industry Wool, 1959) 14s. 6d.

Educational Productions Ltd. Filmstrip No. 5260: Insects in the Garden 28 frames. Notes for use with Filmstrip No. 5260. Pp. 10 (East Ardsley, Wakefield, Educational Productions Ltd., 1959) 16s. 6d.

Gine (A.R.L.) Limited: Technical Notes No. 103 (June 1959) Bonding in the Fairchild F-27. Pp. 6. (Duxford, Cambs (A.R.L.), Ltd., 1959) 14s.

Educational Productions Ltd. Filmstrip No. OX 6290: Seed Germination 23 frames. 27s. 6d. Notes for use with Filmstrip No. OX 6290. Pp. 6. Filmstrip No. OX 6335: Grasses 22 frames. 27s. 6d. Notes for use with Filmstrip No. OX 6335. Pp. 13 (East Ardsley, Wakefield, Educational Productions Ltd., 1959) 14s.

Colonial Office: Fishery Publications No. 12: The Hydrography of the British East African Coastal Waters, Part 2. By J. B. Newell. Pp. vi+113. (London, H.M. Stationery Office, 1959) 6s. 6d. net. 1147

National Institute of Agricultural Botany: Hicote 82 and Grovers Loesche No. 4: Harvesting and Threshing Grass and Clover Seed. Pp. 17. (Cambridge, National Institute of Agricultural Botany, 1959) 12s.

British Steel Castings Research Association: Sixth Annual Report 1959. Pp. 25. (Sheffield: British Steel Castings Research Association, 1959) 12s.

Education for the Age of Science: Statement by President Eisenhower's Science Advisory Committee 24 May 1959. Pp. 47. (London, United States Information Service, 1959) 12s.

Department of Scientific and Industrial Research and Fire Offices Committee: Fire Research 1958: Report of the Fire Research Board with the Report of the Director of Fire Research. Pp. vi+54+8 plates. (London, H.M. Stationery Office, 1959) 6s. net. 1257

United Kingdom Atomic Energy Authority: Fifth Annual Report for the period 1st April, 1958—31st March, 1959. Pp. vii+63+4 plates. (London, H.M. Stationery Office, 1959) 12s. 6d. net. 1257

Anglo-American Catalogue of the Stars in the Second Edition of the General Catalogue of Variable Stars. Pt. 4. (Hertsmere, International Astronomical Union, Royal Greenwich Observatory, 1959) 12s.

Other Countries

The Indian Engineer and a Technical Almanac for the year 1959. Pp. xxviii+444. (Delhi: Manager of Publications, 1959) 12s. 14s. 6d.

- United States Department of the Interior Fish and Wildlife Service Fishery Bulletin No 146 Decline of the Yellowtail Flounder (*Limanda ferruginea*) Off New England By William F Royce, Raymond J Buller and Ernest D Prometz Pp iv+169-267 (Washington, D C Government Printing Office, 1959) 55 cents [107]
- Pennsylvania State University Mass Transfer Between Phases By Prof Thomas K Sherwood (Thirty-third Annual Priestley Lectures) Pp xi+86 (University Park, Pennsylvania Pennsylvania State University, 1959) [107]
- Continuity and Number By B Goussinsky Pp 31 (Tel Aviv B Goussinsky, 5 Rosenbaum Street, 1959) 0 50 dollars [107]
- Annals of the New York Academy of Sciences Vol 72, Article 14 The Influence of Hormones on Lipid Metabolism in Relation to Arteriosclerosis By Abraham Dury, Carleton R Treadwell and 35 other authors Pp 787-1054 (New York New York Academy of Sciences, 1959) 4 dollars [107]
- Report of the FAO/UNICEF Regional School Feeding Seminar for Asia and the Far East, Tokyo, Japan, 10-19 November 1958 (FAO Nutrition Meetings Reports Series, No 22) Pp v+52 (Rome Food and Agriculture Organization of the United Nations, London H M Stationery Office, 1959) 2s 6d [107]
- International Council of Scientific Unions Financial Statement for the period from 1 November 1957 to 31 December 1958 Pp 12 (The Hague International Council of Scientific Unions 1940) [107]
- British Honduras Annual Report of the Forest Department for the year 1957 Pp 24 (Belize Forest Department, 1959) [107]
- Arbeitsgemeinschaft für Forschung des Landes Nordrhein-Westfalen, Heft 82 Periodisch Wiederholte Zündungen durch Stosswellen Von Paul Schmidt Pp 57 (Köln und Opladen Westdeutscher Verlag, 1959) 5 20 DM [147]
- Annals of the New York Academy of Sciences Vol 77, Article 3 Hematopoietic Mechanisms By Albert S Gordon, Walter S Root and 65 other authors Pp 407-820 5 dollars Vol 78, Article 2 The Biology of the Amoeba By Henry I Hirschfeld and 22 other authors Pp 401-704 4 50 dollars (New York New York Academy of Sciences, 1959) [147]
- Consejo Superior de Investigaciones Publicaciones del Instituto de Química "Alonso Barba", Vol XII, Año 1958 (Colección de los Trabajos Publicados durante dicho año en los Anales de la Real Sociedad Española de Física y Química) Pp ii+354 (Madrid Instituto de Química "Alonso Barba", 1959) [147]
- Trace Element Problems in Nature a Symposium held in the Botany Department, University of Cape Town, May, 1958 Pp iv+65 (Cape Town University of Cape Town Department of Botany, 1959) [147]
- United States Department of Commerce Weather Bureau Forecasting Guide No 3 Hurricane Forecasting By Staff Members U S Weather Bureau Pp v+108 (Washington, D C U S Department of Commerce, Weather Bureau 1959) [147]
- National Academy of Sciences—National Research Council 1957-1958 Pp iv+65 (Washington D C National Academy of Sciences—National Research Council, 1959) [147]
- Smithsonian Miscellaneous Collections, Vol 138, No 1 Pueblo del Arroyo, Chaco Canyon, New Mexico By Neil M Judd Pp vii+222+55 plates (Publication 4346) (Washington, D C Smithsonian Institution, 1959) [147]
- Deutsches Hydrographisches Institut, Hamburg Jahresbericht Nr 13 für das Jahr 1958 Pp 81 (Hamburg Deutsches Hydrographisches Institut, 1959) [107]
- New Zealand Air Department New Zealand Meteorological Service Meteorological Investigations for 1958 Pp i+87 (Wellington Government Printer, 1959) [177]
- Centro Brasileiro de Pesquisas Físicas Notas de Física Vol 4 No 18 A Stochastic Theory of Chromatography By H Macedo, A L Zamith and J Danon Pp 15 Vol 4, No 21 Siderical Anisotropy of High Energy Cosmic Rays near the Equator By I Escobar, N Nerurkar and R Well Pp 12 Vol 4, No 22 The Disintegration of Ga⁶⁷ By J Goldemberg, L Marquez, E W Cybulska, N L Costa, and I G Alkeld Pp 7 Vol 4, No 23 Effect of Non-Locality in Fermi Interactions Due to Vector Mesons on the Decays $\Sigma^- \rightarrow p + \gamma$ and $\mu^- \rightarrow e + \nu + \gamma$ By Prem Prakash and A H Zimmerman Pp 11 Vol 4, No 24 Hyperfragments Produced by K⁺ Mesons from K⁺ Charge Exchange By M Baldo Ceolin H Hurita, S Natoli, U Camerini, and W F Fry Pp 9 Vol 4, No 25 On the Masses of Elementary Particles By Abbas Salam and J Tiomo Pp 4 Vol 4, No 26 The Poles of the S-Matrix of a Rectangular Potential Well or Barrier By H M Nussenzweig Pp 36 Vol 5, No 1 The Decay of TI²¹⁴ By E W Cybulska and L Marquez Pp 9 Vol 5, No 2 Correlated Polarization of Muons in K₂₃-Decay By S W Macdowell Pp 6 Vol 5, No 3 On the Analytic Properties of Partial Amplitudes By S W Macdowell Pp 18 Vol 5, No 4 The Attractive K-Meson Proton Interaction By Erasmo M Ferreira Pp 3 Vol 5, No 5 On Anomalous Magnetic Moment of Nucleons By Colber G de Oliveira Pp 13 Vol 5, No 6 Determination of the Stability Constants of Thorium Nitrate Complexes with Anion-Exchange Resins By J Danon Pp 14 Vol 5, No 7 Paper Chromatography of Inorganic Ions in Nitrate Media 1 Scandium, Yttrium, Actinium and the Lanthanides By J Danon and M C Levi Pp 4 (Rio de Janeiro Centro Brasileiro de Pesquisas Físicas, 1959) [177]
- Cytophotometry by Silver Analysis of Photomicrographs Description of a New Method and its Application to the Study of Corpuscular Haemoglobin By Mikko Niemi (*Acta Anatomica*, Supplementum 34-2 ad Vol 35, 1958) Pp 92 (Basel and New York S Karger, 1958) 13 20 Swiss francs [207]
- Canada Department of Mines and Technical Surveys Geological Survey of Canada Bulletin 48 Contributions to Canadian Palaeontology Fungal Filaments in a Devonian Limestone from Alberta By Wayne L Fry and D J McLaren Petrified Logs of *Cupressinoxylon* from the West Shore of Chilko Lake, British Columbia By Wayne L Fry A Revision of the Devonian Coral Genus *Synaptophylloids* Simpson By D J McLaren Pp vi+33+10 plates 1 dollar Bulletin 49 Marine Jurassic Rocks in Nelson and Salmo Areas, Southern British Columbia By Hans Frobeld Pp vii+20+5 plates 1 dollar (Ottawa Queen's Printer, 1959) [207]
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LETTERS TO THE EDITORS

GEOPHYSICS

Correlation between Earth Current and Geomagnetic Disturbance

THE relation between earth-current and magnetic activity is generally known, but we have not noted any quantitative data in the form of correlation coefficients.

W. J. Rooney¹ presents curves of earth current activity, magnetic activity and sunspot numbers for the epoch 1910-1930 showing close correlation between geoelectric and geomagnetic activity. He states that true earth current disturbances (as opposed to interference phenomena) are always accompanied by magnetic disturbances. Frequent comparison of magnetic and earth current records taken at College Alaska, during the past several years substantiates Rooney's observation. To arrive at a quantitative measure of the relation, correlation coefficients were calculated for each of several months. The correlations were made between the equivalent daily amplitude A_{eq} of the College magnetic activity and the mean daily earth current activity.

The College equivalent daily amplitude A_{eq} in gammas, is determined by converting the eight scaled K indices to field intensity according to the following schedule, and taking the arithmetic mean²:

| | | | | | | | | | | |
|----------|---|----|----|-----|-----|-----|-----|------|------|------|
| K | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
| γ | 0 | 30 | 70 | 130 | 270 | 430 | 800 | 1400 | 2400 | 4000 |

The mean daily earth-current activity was determined by scaling the earth-current records for amplitude activity on the 3 hr periods corresponding to the K scaling and taking the arithmetic mean of the 8 values for the day. Only north-south records were scaled because of the generally unidirectional flow of the earth current disturbances at College. The values of the correlation coefficients for six randomly selected months are given in Table 1.

Table 1

| | |
|----------------|-------|
| September 1957 | 0.916 |
| February 1958 | 0.941 |
| March 1958 | 0.939 |
| April 1958 | 0.973 |
| September 1958 | 0.915 |
| November 1958 | 0.939 |

In conjunction with the calculation of the correlation coefficients, scatter diagrams were plotted and least squares regression lines calculated for each of the six months. There were no widely scattered points. Fig. 1 is the scatter diagram and regression line of earth current activity on geomagnetic activity for April, 1958.

To obtain an additional measure of the relation between these two phenomena the correlation coefficient of earth-current activity in mV/km versus magnetic activity in gammas was calculated for the

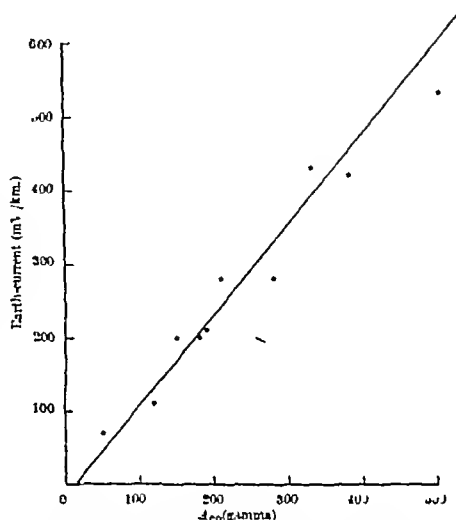


Fig. 1 Scatter diagram and least-square regression line Earth current activity versus magnetic activity at College Alaska, April 1958.

3 hr periods of April, 1958. The correlation coefficient for this set of 240 values is 0.833.

These very high correlation coefficients show that earth currents may be used interchangeably with the magnetic disturbances as an indicator of ionospheric activity. In areas where interference such as street railway systems is not a problem an earth-current recording system can be set up much more readily than a comparable magnetic system. To indicate activity only one recorder and one pair of electrodes oriented in the preferred direction of the earth-current disturbance is required. Furthermore none of the equipment needs to be isolated from the usual laboratory activities which would interfere with the operation of a magnetometer.

This work is supported by the Geophysics Research Directorate of the Air Force Cambridge Research Center. The Magnetic A figures were furnished by the College Magnetic Observatory of the U.S. Coast and Geodetic Survey.

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Micropulsation Measurements in California and Alaska

IN recent years there has been increased interest in micropulsations of the Earth's magnetic field¹⁻⁴. As a part of a study of the micropulsations with periods of 10-30 sec., stations were established near Borrego, California (33° 21' 5" N, 116° 17' W), and near College, Alaska (64° 42' N, 148° 29' 5" W). Horizontal coil antennas of 2-m diameter and 21,586 turns were used. The associated amplifiers had three db band pass points at 0.04 and 0.4 cycles per second and a limiting sensitivity of 0.02 γ.

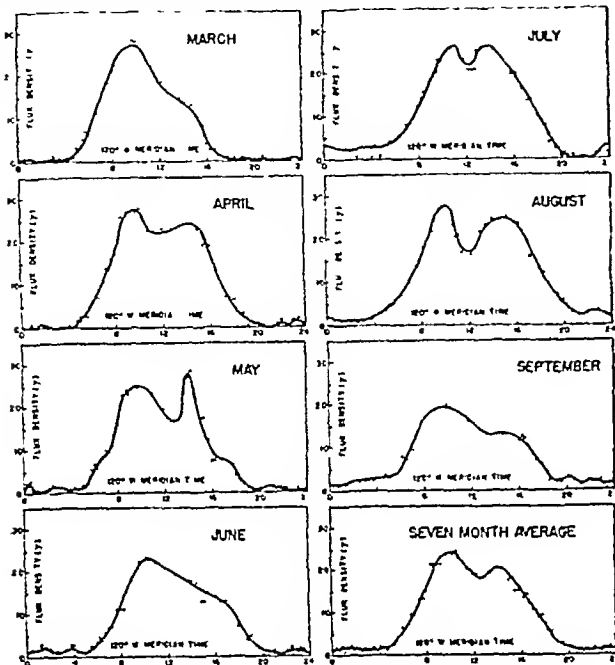


Fig 1 Average diurnal behaviour of micropulsations, California, 1958

Fig 1 illustrates the average diurnal behaviour for 15 min rms amplitudes measured from March until September, 1958, in California. Fig 2 illustrates micropulsations in California and Alaska for comparable times. There were twenty-three such coincident active groups of micropulsations in six days' operation (Table 1). Large night time storms in

Table 1 COINCIDENCES OF GROUPS OF OSCILLATIONS IN ALASKA AND CALIFORNIA 150° W MEAN TIME

| Month and Day | Alaska Time Start | Calif Time Start | Alaska Time Peak | Calif Time Peak |
|---------------|-------------------|------------------|-------------------|-------------------|
| August 23 | 1530 ^a | 1540 | 1530 ^a | 1542 |
| | 1605 ^a | 1602 | 1600 ^a | 1604 |
| | 1733 ^a | 1733 | 1733 ^a | 1734 |
| | 1750 ^a | 1751 | 1750 ^a | 1751 |
| | 1800 ^a | 1807 | 1806 ^a | 1807 |
| August 24 | 0217 ^a | 0217 | 0220 ^a | 0218 |
| | 0554 ^a | 0553 | 0555 ^a | 0554 |
| | 0850 ^a | 0850 | 0701 ^a | 0701 |
| | 0750 ^a | 0751 | 0751 ^a | 0753 |
| | 1120 ^a | 1119 | 1121 ^a | 1120 |
| August 25 | 1125 ^a | 1125 | 1126 ^a | 1125 |
| | 0740 | 0341 | 0341 | 0341 |
| | 2110 | 2111 | 2111 | 2111 |
| | 2343 ^a | 2341 | 2344 | 2342 |
| | 0230 | 0230 | 0237 | 0230 |
| August 26 | 1852 | 1851 | 1857 | 1853 |
| | 1944 | 1944 | 1944.5 | 1944.5 |
| | 2024 | 2024 | 2024 | 2024 |
| | 2035 | 2035 | 2037 | 2035 |
| | 2318 | 2319 | 2320 | 2320 |
| August 27 | 0836 | 0838 | 0838 | 0840 |
| August 28 | 0856 | 0857 | 0857 | 0858.5 |
| | 1651 ^a | 1653 | 1652 | 1654 ^a |

Alaska gave oscillations ten or fifteen times larger than California. Day-time activity amplitudes were similar at the two stations.

In Alaska it was noted that times of great micropulsation activity were accompanied by short wave blackouts. Also during the dark hours, large micropulsations attended visible auroral displays. One occasion of simultaneous oscillations of the 3814 Å auroral line and small micropulsations was observed.

This work, originating at the Institute of Geophysics of the University of California, was sponsored by the Office of Naval Research contract Nour 233 (47), and carried out through the generous co-operation of the Geophysical Institute of the University of Alaska.

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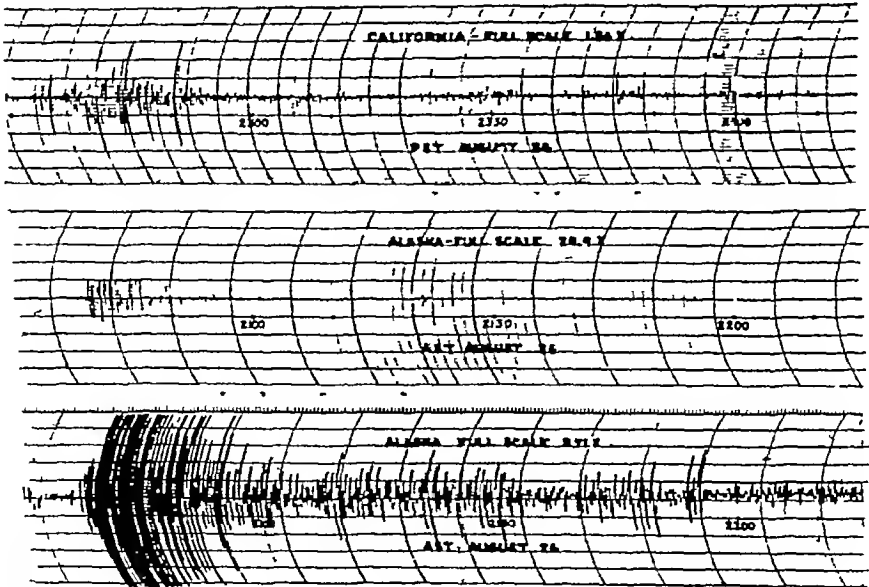


Fig 2 Simultaneous observation of micropulsations in California, and Alaska

Depth of Isostatic Compensation and Mohorovičić Discontinuity, etc. In Continental and Oceanic Areas

On the basis of the probable average density of rock below the oceans and over land, up to 160 km or so estimates of have been made of the depth of isostatic compensation. The depth of the Mohorovičić discontinuity is inferred from an analysis of refraction type travel time curves assuming the existence of layers in which there is a uniform velocity and that there is a discontinuous increase in velocity on crossing the Mohorovičić discontinuity between an upper granitic layer and a lower 'basaltic' layer. Due to this discontinuity critical reflexions occur which may explain arrivals of high intensity at certain distances. The layer of relatively low velocities above the discontinuity is thought to consist of sediments, unconsolidated at the top and consolidated and/or metamorphosed below. Usually the depth of the Mohorovičić discontinuity is calculated as 15-40 km beneath continents and 5-15 km below the oceans.

There are practical difficulties if all this is accepted. The depth of isostatic compensation remains highly hypothetical. The Mohorovičić discontinuity, though regarded as a physical phenomena does not manifest itself everywhere. In a number of cases the critical reflexions associated with it are not observed though as a zeroth-order approximation travel time curves are still analysed on the layer hypothesis. The difference in thickness of sediments in oceanic and land areas cannot be explained by any plausible theory.

The seismic data might therefore be analysed assuming that the computed thickness of sediments under the oceans is more or less correct but that the currently accepted values for land areas are much too high. This is compatible with the seismic data on the basis of a gradual increase of velocity with depth. In actual fact the velocity gradient will change with depth. Further it is likely to be high in the upper layers and to decrease as one goes deeper, getting very small once velocities of the order of 8.8 km/sec or so are reached. This is somewhat unlike the current ideas of velocity variation with depth. The seismic data can be analysed to a first order approximation on the basis of a uniform velocity gradient. Seismologists have preferred not to do so in crustal seismology since the analysis is rather insensitive and an independent justification for going beyond the simpler zeroth order approximation was lacking. An independent justification has now been provided by an analysis of reverberation data which I have carried out (being communicated to the *Proceedings of the Royal Society*). This necessitates a gradual increase of velocity with depth and gives an accurate estimate of the average velocity gradient from the decay of reverberation observed close to a shot point.

In the state of Virginia, in the United States, where Mohorovičić type reflexions are quite prominent for shots at a distance of about 100 km, the average velocity gradient is 0.075 km/sec/km and the penetration of rays responsible for the high intensity arrivals is only 14 km. On the usual hypothesis of two layers the depth of the discontinuity in this area is computed to be about 37 km. The average gradients in some other areas come out to be 0.04 km/sec/km in South Africa and 0.055 km/sec/km

in Tennessee. Those values are somewhat weighted in favour of deeper rock as they have been calculated from the tail ends of reverberation records or from more distant portions of travel time curves. The value for ocean bottom in mid Pacific is about 0.35 km/sec/km and there is an intermediate value of about 0.16 for coastal areas like western California decreasing to 0.09 in relatively deeper sediments.

Values of the order of 8.8 km/sec for the velocity of *P* waves (the highest observed during the recent *Downwind* expedition in the mid Pacific) are found in the oceanic records. One can reasonably assume this to be the velocity in the heavier rock into which the roots of continental blocks have to extend. Presumably the velocity gradient is very small once this velocity has been reached. Now assuming 0.04 km/sec/km to be the smallest average gradient observed, and 5.6 km/sec to be the velocity in the top layers, the depth of isostatic compensation or the depth of deepest penetration of the roots of the land in question seems to be of the order of 80 km, since the velocity difference of 3.2 km/sec will be made up in this depth. The recent work in the South American Andes requires deep roots, and perhaps the Himalayas require still deeper roots. From existing data one can see that the velocity of 8.8 km/sec will be reached at the following depths:

Oceanic areas about 5 km to more than 15 km
Continental areas about 30 km to more than 80 km

The depths which give rise to Mohorovičić type effects over certain continental areas seem to vary from 10 to 20 km. Thus these depths and the depths under oceans where the velocity reaches 8.8 km/sec are of same order, and this perhaps corresponds to the thickness of the sediments. Over land the rock between a depth of about 15 km, that of isostatic compensation, as envisaged above, consists of rock underneath and lighter rock transformed from the deeper rock during continental formation on top. Under the mountains with the deepest roots the lighter rock extends right down to the depth of compensation, but under the oceans it is missing.

The patchy nature of Mohorovičić phenomena can also be understood easily. In certain areas the gradual increase of velocity with depth in sediments may lead to velocities greater than those in the topmost layers of the crustal rock in the area. This might give rise to the so-called low-velocity layer, as well as to focusing due to an increase of velocity after a sudden decrease. The thickness of the sediments on land would be likely to be approximately that in oceanic geosynclines that exist now or which are reflected in oceanic rises for example, the Easter Island rise. The above considerations also help to resolve the paradox of almost equal heat flow from below in oceanic and continental areas.

My thanks are due to Prof R W Raitt of the Scripps Institution of Oceanography and to Dr M A Tappin of the Carnegie Institution of Washington for making some of the data utilized here available to me. I am also grateful to Dr D N Wadia for his encouragement.

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PHYSICS

 α -Radioactivity of Cerium-142

JOHNSON AND NIER¹ have measured the atomic masses of some of the rare earth isotopes and have shown that the mass difference cerium-142—(barium-138 + helium-4) is equivalent to 1.68 ± 0.10 MeV. Similar results for the naturally occurring samarium and neodymium isotopes show that the α -active isotope of each element is the one having the largest possible decay energy. Rasmussen and others² suggest that the two or three neutrons just beyond the closed shell of 82 neutrons have decreased binding energies and hence the α -energy has a maximum about 84 neutrons. Johnson and Nier suggest that the α -decay of cerium-142 may take place with enough energy to be experimentally observable. Porschen and Riezler³ examined a sample of unenriched cerium ammonium citrate using nuclear track plates sensitive to α -particles. No α -activity was observed after a 30-day exposure of 1.2 mgm of the cerium salt. In 1957 Riezler and Kauw⁴ reported an alpha activity for an enriched sample of cerium-142. From their results they calculated a half-life of 5.1×10^{15} years with an uncertainty factor of 2.

A sample of cerium oxide enriched in cerium-142 was made available by the Oak Ridge National Laboratory to check the α -radioactivity by an emulsion technique. Mass spectrographic and semi-quantitative spectrochemical analyses showed the heavy-element contaminant reported was neodymium whose abundance was < 0.3 per cent. This amount of neodymium would not significantly affect the results.

In this experiment we were primarily interested in showing that the α -activity, if detectable, could be ascribed directly to the cerium salt. To eliminate contamination in process chemicals the oxide powder (300 μ gm) was loaded directly on a type G-2 Ilford nuclear track plate. The cerium oxide containing 90.2 per cent cerium-142 was exposed for 125 days. After a thorough examination of the nuclear plate at the end of the exposure period no alpha tracks were visible emanating from the particles of cerium oxide, contrary to the observation of Riezler and Kauw.

A similar plate containing unenriched impure cerium oxide was also exposed for the same period as a control. Several tracks were found emanating from the surface of the particles. In each case the α -track was shorter than those we have observed for the thorium or uranium series when radioactive mineral grains are embedded in an emulsion in a similar manner. The few short α -tracks observed on the control plate are believed to be from a samarium contaminant in the impure cerium oxide.

Although this experiment is considered as only qualitative, it is of interest to make a rough estimate of the half-life. After considering self-absorption, non-uniform loading of the crystals and correcting for geometry we can assume that about ten per cent of the cerium salt is actually exposed to the emulsion. Although no activity was observed one should consider that statistically a count of 1 ± 1 is possible. Thus, if a maximum of two alpha tracks were observed, this would correspond to a minimum half-life of about 10^{16} years. This qualitative half-life, although based on negative results, agrees with Riezler and Kauw within the uncertainty factor they

have quoted. For an α -decay energy of 1.68 MeV one can calculate a half-life of 9×10^{16} years for cerium-142 assuming a one-body model as outlined by Biswas⁵. If the half-life is this long, one could just detect the activity with 10 mgm of the enriched material and probably the order of several hundred milligrams would be required to make a good half-life determination.

This work is part of a programme being conducted by the U.S. Geological Survey on behalf of the Division of Research of the U.S. Atomic Energy Commission, and publication is authorized by the Director, U.S. Geological Survey.

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Colour Centres produced by Radiation in Silica Gel

COLORATION of inorganic solids by ionizing radiations has been well known and studied for many years. The possibility that defects associated with such colour might bear a relation to the processes of adsorption and catalysis has been suggested¹, but never directly observed. We have recently observed that the procedure which produces radiation enhancement of catalytic activity in silicas², that is, irradiating a gel degassed at 500°C or above with comparatively small ($\sim 10^{19}$ eV/gm) doses of cobalt-60 γ -rays or 50 keV X-rays also produces a marked magenta coloration of the gel. The comparative rarity of such observations^{3,4}, and their possible connexion with the radiation enhancement of catalytic activity² have prompted this communication.

The colour produced probably corresponds to the broad absorption band at 500–600 m μ observed in irradiated quartz and vitreous silica⁵, and is stable to light and to temperatures less than 250°. We now find that contact with excess hydrogen or ethylene at room temperature bleaches it instantaneously. The colour is less rapidly discharged by water vapour or ammonia, the action of mercury vapour is somewhat sluggish. Oxygen is without effect. Activation energy is required for the hydrogen bleaching, for the colour is not removed by contact with excess hydrogen at –196°C for 1 hr. At –78°C the gel is decolorized in 15 min. The action of water vapour proceeds by diffusion of the water into the solid, rather than by migration of electrons or holes, for if the coloured grains are exposed to moist air they bleach first around the edges, lastly in the centre. Reheating gradually to 300°C after hydrogen bleaching does not regenerate the colour or desorb more than a few per cent of the adsorbed hydrogen.

Adsorption of hydrogen at room temperature by freshly degassed silica gel is either extremely slow or vanishingly small, hence, by measuring the amount of hydrogen adsorbed after irradiation, one can determine the number of colour centres. The simultaneous

cessation of hydrogen adsorption and disappearance of the last traces of colour corresponds to the end point of a titration. From the sample weight, dose and hydrogen adsorbed, one can follow the production of colour centres and calculate their yield. Such an experiment has shown a yield on freshly degassed gels of 1 centre per 100 eV absorbed, dropping gradually to a value of 0.1 centre per 100 eV with further irradiation as more hydrogen is adsorbed. At this point approximately 3×10^{18} centres/gm have been introduced into the catalyst.

Qualitatively both silica alumina and alumina catalysts show the same phenomenon of coloration and decolorization with adsorption. Before irradiation a degassed gamma alumina is fairly white and adsorbs no hydrogen. After irradiation it is faintly cream coloured and slowly adsorbs hydrogen. The adsorption is too sluggish to follow conveniently but decolorization by excess hydrogen is complete in 1 hr. The change in appearance compared with that of silica gel is very slight. Houdry S 46¹ a silica alumina cracking catalyst (12% per cent aluminium oxide) after degassing at 500°C is off white and adsorbs small (~ 0.03 micromole/gm) amounts of hydrogen. After a long (5×10^{18} eV/gm) irradiation, the sample has a marked tawny appearance with magenta overtones and adsorbs 1 micromole of hydrogen per gm, gradually losing its colour as it does so.

A plausible explanation of these phenomena is that the colour centres are positive holes associated with oxygen excess in the silica, and that these holes are neutralized by interaction with electrons from the bleaching gas. However the initial yield of adsorption sites per unit dose obtained in this work is greater than that of catalytic exchange sites determined previously² by a factor of 10^8 . Hence, even though the effect of irradiation on hydrogen adsorption is clearly demonstrated, the connexion between the coloration bleaching phenomena and the irradiation enhancement of silica catalysts is not yet clear.

This work was carried out at the Oak Ridge National Laboratory operated by the Union Carbide Corporation for the U.S. Atomic Energy Commission.

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Ultrasonic Absorption in Acetic Acid at 450 kc/s by the Calorimetric Method

CALORIMETRIC measurements based on thermosonic principles have successfully been used^{1,2} for the determination of ultrasonic absorption in liquids at frequencies of 5 Mc/s and above. Recently it has been possible to extend this method to measurements in acetic acid at 450 kc/s.

At frequencies of this order, the divergence of the beam is pronounced and when the cell is moved away from the course the whole of the sound beam does not enter the cell, further, for the complete absorption of the beam at these low frequencies a long column of

liquid is necessary, which increases the thermal capacity of the system considerably and results in a comparatively smaller rise of temperature.

These defects have been overcome by using a smaller area of sound emitter compared to the mouth of the absorbing cell and by employing a spherical double walled glass cell with a plano section for the entrance of the beam. The sound beam on entering the cell undergoes multiple reflexions at its inner surface until it is completely absorbed.

The experiment was carried out on acetic acid. In a typical set of observations a rise in temperature of 0.5°C and 2.2°C was observed in two positions of the crystal in 30 minutes. The separation between these positions was 3.5 cm.

The value of α/ν^2 for acetic acid at 450 kc/s and 30°C was found to be about $90\,000 \times 10^{-17} \text{ cm}^{-1} \text{ sec}^2$ being an average of a large set of readings with a variation of ± 10 per cent. This agrees with the value of about $80\,000 \times 10^{-17} \text{ cm}^{-1} \text{ sec}^2$ at 500 kc/s obtained by Lamb and Pinkerton³. Lamb, Andreae, and Bird⁴ however, reported a value of $175\,000 \text{ cm}^{-1} \text{ sec}^2$ below 2 Mc/sec at 17.5°C.

An attempt was made to use this method for measurements in benzene and carbon disulphide, but it was found that owing to the comparatively small absorption in these liquids the difference in the rise of temperature at the two positions of observation was either negligible or very small, and in the latter case, comparable to the necessary corrections. In view of this limitation the method reported here is applicable only to liquids having an absorption coefficient not lower than $10\,000 \times 10^{-17} \text{ cm}^{-1} \text{ sec}^2$ at these low frequencies.

Further work on this problem is in progress.

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MINERALOGY

Revised Equilibrium Diagram for the System $\text{Al}_2\text{O}_3\text{-SiO}_2$

THE most important system in present-day high temperature technology is $\text{Al}_2\text{O}_3\text{-SiO}_2$. The accepted equilibrium diagram for this system was determined in a classic investigation by Bowen and Groig¹, but during the last few years several workers have questioned its correctness²⁻⁶. The data offered in criticism have not, however, been unequivocal themselves. We summarize briefly here the data from some 700 runs in a nearly two year re-examination of the $\text{Al}_2\text{O}_3\text{-SiO}_2\text{-H}_2\text{O}$ system by standard 'quenching' methods of studying silicate phase equilibria.

The starting mixtures were made mainly from hydrated aluminium nitrate and silica sol of very high purity for hydrothermal runs and from high purity silica glass and α alumina for 'dry' runs. The mixtures were all run in hermetically sealed noble metal containers of 80Pt-20Rh and 90Pt-40Rh in a gas oxygen quenching furnace with zirconia refractories, capable of reaching 1900°C. Temperatures were read

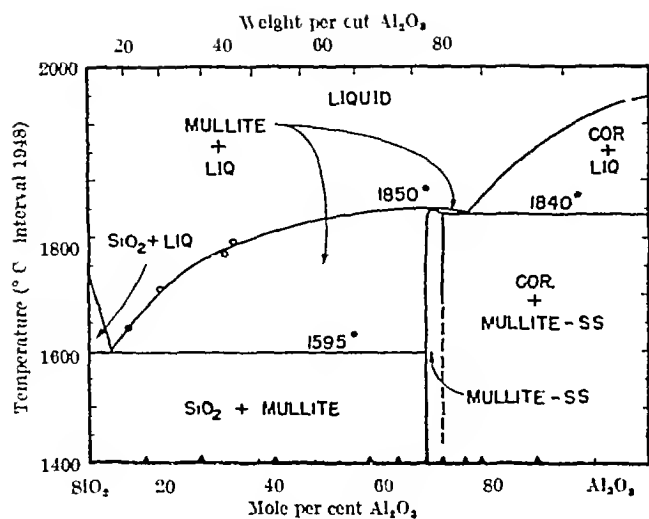


Fig. 1 Revised equilibrium diagram for the system $\text{Al}_2\text{O}_3\text{-SiO}_2$ determined by quenching experiments in sealed noble metal containers. Circles shown represent liquidus determinations from refractive indices of the glasses

by a Leeds Northrup optical pyrometer frequently calibrated at the melting point of platinum, 1769° C (Intl, 1948). The samples, quenched in mercury, were examined petrographically and by X-ray diffraction.

The data from 190 runs above the solidus show that no corundum is formed (indeed the starting-material corundum dissolves) in mixtures containing 50, 60 and 66.7 mole per cent Al_2O_3 , when these are held above the incongruent melting temperature of the Bowen and Greig diagram (1810°, *GL* scale). The phases present at various temperatures and at various compositions, combined into the phase diagram of Fig. 1, prove that the phase mullite melts congruently at $1850 \pm 15^\circ \text{C}$ (Intl, 1948). The equilibrium extent of crystalline solubility appears to extend from 60 to about 63 mole per cent of Al_2O_3 . However, it is relatively easy to crystallize liquids metastably to a 66.7 mole per cent solid solution with the mullite structure. Precise lattice constants (1 part in 5000) have been measured on 21 samples of mullites of various composition crystallized at different temperatures from 800° C to 1850° C. X-ray spacings of mullites can be changed by heat treatment and are not reliable indices of composition. True glasses have been prepared up to the 63 mole per cent mixture and their refractive indices determined (3.2 ratio glass has $n_{\text{D}} = 1.598$), the glass composition as determined from its index of refraction has also been used to locate the liquidus line (see Fig. 1). The composition of the mullite-silica eutectic appears to be unchanged from that given by Bowen and Greig. No clear evidence for the theoretically expected stable two immiscible liquids region was found, although the tendency towards such unmixed structure is clearly seen in the extremely flat liquidus near the mullite composition. Excellent confirmation of the eutectic position between mullite and corundum has been obtained from data on the systems $\text{MgO-Al}_2\text{O}_3\text{-SiO}_2$, and $\text{CaO-Al}_2\text{O}_3\text{-SiO}_2$. The phase boundary has been fixed between the corundum and mullite fields in these systems. It disagrees radically with that suggested by Toropov and Galakhov² and is not inconsistent with the actual results obtained by Bowen, Scharrer, Rankin, Wright, Merwin and others at the Geophysical Laboratory, near the invariant point between mullite, corundum and either andalite ($2\text{MgO} \cdot 2\text{Al}_2\text{O}_3 \cdot 5\text{SiO}_2$) or anorthite.

At lower temperatures at least two new anhydrous aluminosilicate phases have been recognized. One of them had previously been thought to be andalusite⁷; single-crystal X-ray work established a larger cell (orthorhombic, $a = 7.55 \text{ \AA}$, $b = 8.27 \text{ \AA}$, $c = 5.66 \text{ \AA}$) similar to but easily distinguished from andalusite. The other is a high temperature (probably aluminium silicon disordered) form of sillimanite which occurs in volcanic xenoliths. Details of this study are to appear in the *Journal of the American Ceramic Society*.

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CHEMISTRY

Liquid Crystal Systems from Fibrillar Polysaccharides

THE preparation of a neutral aqueous suspension of cellulose crystallites by hydrolysis in strong sulphuric acid (952 gm/l) at 30 or 40° C for 24 hr has been described¹. A similar suspension of crystallite particles of chitin was prepared by treating 20 gm of purified chitin from crab shells for 1 hr in 750 ml of 2.5 N hydrochloric acid under reflux. Afterwards, the excess acid was decanted and distilled water was added. At this stage, the chitin hydrolysate was still essentially a sediment and was well on the acid side when it was given three passes through a 'Minisonic' homogenizer (Sonic Eng. Corp., Stamford, Conn.). From this treatment, a stable isotropic suspension was obtained and the pH had risen to 3.5. The rise in pH is probably due to release, from within the crystallites, of some unacetylated amino groups which complexed with a proton to give NH_3^+ at the crystallite surfaces. The presence of free NH_2 groups in chitin, which is supposed to be a polymer of N-acetyl-D-glucosamine is not unexpected since purification procedures involve alkaline conditions which can saponify acetyl groups. Electron micrographs of the stable suspension show the presence of rod-like particles of similar dimensions to the cellulose crystallites².

These two, stable, colloidal dispersions of cellulose and chitin crystallites were the starting materials for the preparation of the liquid crystals as described below. The concentration of these colloidal suspensions was always less than 1 per cent.

The formation of a permanently birefringent gel was first observed when a suspensions of cellulose crystallites was heated on a steam bath. A reddish brown gel, having the consistency of soft butter, formed on the surface of the heated suspension. In the polarizing microscope it was found to be birefringent but without extinction directions, that is, it behaved

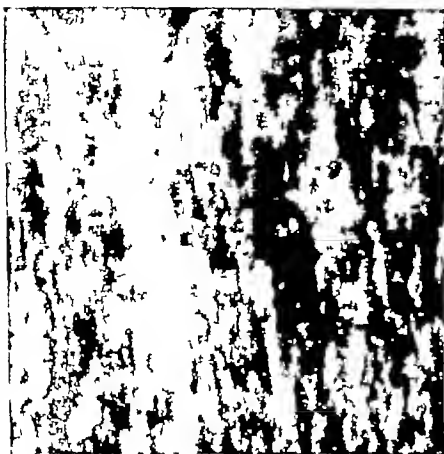


Fig. 1 Birefringent gel between crossed polaroids ($\times 750$)

as if it were a powder of a birefringent crystal. More careful observation showed that as evaporation occurred slowly from the undisturbed surface of the suspension islands of a thin rubber film originating at the walls became visible on the surface. Sections of the film could be lifted on to a microscope slide, and they appeared to have a single though not well defined extinction direction. The same gel could be obtained by centrifuging the suspension at 20 000 *g*, and this method is the one that was generally used to prepare the material. The concentration of the cellulose in the gel under these conditions was about 13–15 per cent by weight and in the presence of salts this value was still greater.

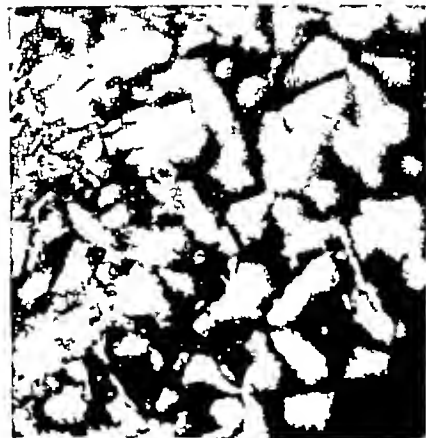


Fig. 2. Dried-down film of salted out birefringent gel between crossed polaroids ($\times 200$)

Viewed between crossed Nicols the gel has the appearance shown in Fig. 1 where the streaked appearance is due to orientation induced by pressing on the coverslip. The streaking is in the direction of the fibre axis. Fig. 2 is a view, between crossed Nicols of a dried-down film of gel which was formed by slow coagulation of a suspension of crystallites in the presence of 0.01 *M* sodium chloride. The film was formed by filtering out the particle aggregates. Rather large birefringent areas are present in this film and the patchwork of light and dark regions is reminiscent of the spherulitic behaviour of high polymers. Fig. 3 is an electron micrograph of crystallites from mercerized ramie which shows the parallel aggregation of the particles that occurs on drying down a dilute suspension. Clearly these areas are the cause of the birefringent regions which are visible in the dried-down films of crystallites.

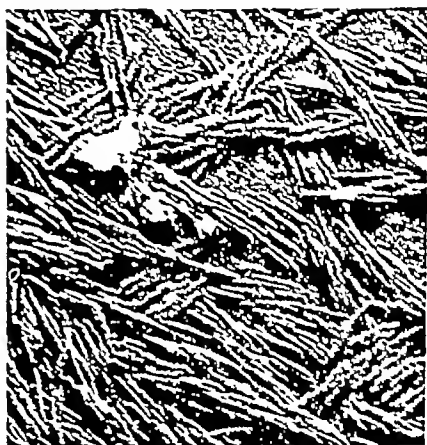


Fig. 3. Electron micrograph made by surface replica technique of crystallite film made by drying down dilute suspension on glass ($\times 5 000$)

In the birefringent gel low angle X ray measurements have shown that the interparticle distance varies as the square root of the concentration in *o/gm*. For a 15 per cent gel it is about 400 Å so that long range forces or entropy effects have to be evoked in order to explain the parallel alignment. The properties of this system are similar in many respects to the well known behaviour of tobacco mosaic virus particles.

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Biological Origin and Configuration of 10-Hydroxy- Δ^2 -decanoic Acid

WE have recently established¹ that 10-hydroxy- Δ^2 -decanoic acid, which constitutes about 15 per cent of royal jelly, is not present in the free state in pollens of representative species, nectar or honey. We suggested that it might therefore be present in combined form or be a specific bee product. In order to investigate the latter possibility we have examined the four pairs of salivary glands of the honey bee (*Apis mellifica*) obtained by dissection under distilled water.

Alcohol suspensions of one hundred thoracic, post-cerebral, and hypopharyngeal glands and fifty mandibular glands obtained from worker bees were filtered, the residual glands extracted with ether (1 ml) in a Mickel tissue disintegrator and the combined alcohol and ether extracts concentrated *in vacuo* to 0.2 ml. Each solution was analysed (50 μ l) by paper chromatographic separation in amyl alcohol/5*M* formic acid². On spraying with a 0.1 per cent alcohol solution of chlorophenol red, an acidic component having R_F 0.88 identical with that of 10-hydroxy- Δ^2 -decanoic acid was detected only in the extract of the mandibular glands. A paper ionophoretogram³ of the extracts run in 0.1 *M* borate buffer, pH 10.0 was dried, suspended in an atmosphere of formic acid vapour in a vacuum desiccator for 1 hr, the excess acid then allowed to evaporate and the residual acidic components detected with the indicator spray. A component having M_R value³ 0.64 identical with that of 10-hydroxy- Δ^2 -decanoic acid was again found to be present only in the extract of mandibular glands. This was also confirmed by paper ionophoresis using 0.20 *M* acetate buffer, pH 5.0 and detection with alkaline silver nitrate⁴.

The finding of 10-hydroxy- Δ^2 -decanoic acid in the mandibular glands of foraging bees is of interest, hitherto the hypopharyngeal glands have been considered the sole glandular source of larval food⁵ although Haydak⁶ noted that their contents assumed the appearance of royal jelly when treated with mandibular gland secretion. Whether a female larva develops into a queen or worker bee is determined by the nature of its food^{7,8}, and it has been suggested that the difference in diet occurs mainly with the older larvae⁷. Two samples of larval food have therefore been analysed. The food from larvae less than 3 days old was obtained by direct pipetting and that from older larvae by filling the cells with distilled water and collecting the mixture after the larvae had floated up to the top. Qualitative paper chromatographic and ionophoretic analysis of other extracts of the larval foods indicated that the food from the larvae less than 3 days old was richer in 10-hydroxy- Δ^2 -decanoic acid than that from the older larvae.

The application of nuclear magnetic resonance spectroscopy has permitted the allocation of the *trans*-configuration to 10-hydroxy- Δ^2 -decanoic acid. The spectra were determined by one of us (L. M. J.) on a 10 per cent solution of methyl 10-hydroxy- Δ^2 -decanoate (obtained from the parent acid by diazomethane treatment) in carbon tetrachloride with Me_4Si as internal standard. It showed absorptions at (1) $\tau = 8.65$ due to ordinary methylene protons⁹, (2) $\tau \sim 6.3$ due to methylene and methyl protons in $-\text{CH}_2\text{OH}$ and $-\text{CO}_2\text{Me}$ and (3) $\tau = 4.2 - 2.5$ associated with olefinic protons and typical of the *ABX*₂ pattern where *A* and *B* are olefinic protons and *X*₂ the adjacent methylene group. The values $\tau_A = 3.02$, $\tau_B = 4.18$ p.p.m. and $J_{AB} 15.8$ c.p.s. were

found. The coupling constant J_{AB} is correct for a *trans*-disubstituted ethylene (cf., $J_{AB} \sim 12$ c.p.s. for *cis*-compounds) and the position of the β -proton ($\tau_A = 3.02$) is close to that expected for a *trans*-compound (cf., $\tau_A = 2.92$ for methyl *trans*-crotonate), the τ values for β -protons are critically dependent on stereochemistry¹⁰.

We thank Prof. M. Stacey for his interest in this investigation and are indebted to Mr. J. Simpson of the Rothamsted Experimental Station for providing the glands and larval food.

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BIOCHEMISTRY

Application of Warburg's Equation to Tissue Slices

THE possibility of using Warburg's equation to measure the diffusion coefficient of oxygen through slices of liver cut with the MacIlwain tissue slicer has been discussed¹.

Warburg's equation related the oxygen concentration outside to that at various points within a slice. The diffusion coefficient of oxygen through liver and the oxygen uptake by liver are also parameters in this equation. The equation is only valid when the respiration rate is independent of oxygen concentration. This is true above the critical oxygen concentration. Since cells furthest from the surface will respire at their maximal rate only when the oxygen concentration outside the slice is such that they are exposed to at least their critical oxygen concentration, it should be possible, knowing the critical oxygen concentration for the slice and for individual cells, the Q_{O_2} and the thickness of the slice, to calculate the diffusion coefficient.

For this application the equation reduces to

$$C_c = C_s - \frac{ax^2}{2D}$$

where C_c = critical pO_2 (in atmospheres) of cells or mitochondria², C_s = critical pO_2 (in atmospheres) of slice, a = ml of oxygen consumed/min./ml of tissue, $2x$ = slice thickness in cm, D = diffusion coefficient.

The measurement of C_r has been described², and with a modification of the electrode it is possible also to measure the critical pO_2 of liver slices³. In the present study we measured the C_r and C_e of liver of six week-old rats. We found that the C_r was never more than 10 per cent of the C_e so in a preliminary examination of our results we neglected C_r so that the equation reduces to $C_e = \alpha \pi^2/2D$. It will be seen that C_e is proportional to the respiration rate and to the square of the thickness. Experimentally with slices of the same thickness the C_e is in fact approximately proportional to the respiration rate. However, in the case of slices having the same respiration rate but of thicknesses in the ratio of 1:5 the C_e are not in the expected ratio 1:25 but less than 1:3. In other words the C_e is largely independent of slice thickness. In the equation π is theoretically the distance of the point of oxygen consumption furthest from the oxygen supply. In practice, however, it does seem possible that π might not equal half the thickness of the slice, since Elias⁴ has shown that liver is composed of branching plates (a muralium) and during the measurement of C_e the agitation of the fluid in the polarographic cell may be sufficient to maintain a flow of oxygenated fluid between these plates. If this is the case then the value of π which should be used in the equation would be half the thickness of the thickest part of the muralium. This would explain the failure of C_e to increase as the square of the slice thickness.

If this explanation is correct we would expect to find that the C_e of slices of more compact tissues might show the predicted relationship with slice thickness. Measurements were made on slices of heart and kidney but they showed the same relationship as did liver slices. It seems therefore that it is necessary to re-examine the assumptions made both by Warburg and ourselves. They are that protoplasmic streaming plays no part in oxygen transport in the cell and that the critical pO_2 of individual cells and isolated mitochondria is identical with that of the same cells in slices.

We are indebted to Prof. A. Haddow of the Chester Beatty Research Institute, for the supply of rat livers.

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Determination of the Interaction of Deoxyribonucleate and Magnesium Ions by Means of a Metal Ion Indicator

THIS communication presents a study of the binding of magnesium ions by deoxyribonucleate using eriochrome black T as an indicator of magnesium ion concentration. Earlier studies by conductometric and spectrophotometric titration procedures were interpreted as showing that in the absence of other salts magnesium was tightly bound by both undenatured and denatured deoxyribonucleic acid¹; this conclusion was based primarily on the presence of breaks in the titration curves which were, irrespective

of the degree of denaturation, stoichiometrically related to the concentration of deoxyribonucleic acid over a wide range of concentrations. However, using similar conductometric procedures, Zubay and Doty² later concluded, from comparison of the increments of conductivity, that under these conditions magnesium was bound tightly by denatured but only loosely by undenatured deoxyribonucleic acid. Titration methods of this type do not of course yield direct information concerning either the extent or tightness of binding. In particular the increments of conductivity found in the conductometric titrations depend not only on the extent of binding but also on the balance of various other factors. In view of these facts and of the importance of ion binding to many aspects of the behaviour of deoxyribonucleic acid it appeared desirable to obtain further information by methods which give a more direct measure of binding. Results obtained using the metal ion indicator show that magnesium is, in fact, bound even more tightly by undenatured than by denatured deoxyribonucleic acid.

A spectral titration procedure was used in which the increase of absorbance at 540 mμ (ref. ³) that occurs on addition of magnesium chloride to a solution containing eriochrome black T ($4.4 \times 10^{-5} M$) is measured. To inhibit water denaturation of deoxyribonucleic acid the concentration of sodium chloride was in every case 0.002 M or greater. Buffer systems used were 0.002 M ethanalamine pH 10.2, and trimethylol aminomethane (tris), pH 9.04; at these pH values eriochrome black T serves as a sensitive indicator of magnesium ion concentration. Similar titrations in which citrate was used in place of deoxyribonucleic acid established that eriochrome black T functions as a reliable indicator of free magnesium ion concentration under these conditions.

Four different preparations of calf thymus deoxyribonucleic acid were used: two were made as previously described⁴ and two were made by the procedure described by Zamenhof *et al.*⁵ All were completely undenatured⁶ according to the several optical criteria cited or described in ref. 4. Likewise, ultra violet absorption measurements showed that they remained undenatured during the titrations: a finding in accord with earlier observations that neither titration nor alkali denaturation of deoxyribonucleic acid begins until somewhat higher pH values (about 10.8–11) are reached. Heat-denatured deoxyribonucleic acid was made by exposing solutions to 55° for 1 hr.

A typical set of titrations at pH 10.2 is given in Fig. 1. The degree of transformation of eriochrome black T to the eriochrome black T magnesium complex is given by α . The amount of magnesium bound by deoxyribonucleic acid is determined by subtraction of the dye curve from the appropriate acid titration. Fig. 2 relates r , the equivalents of magnesium bound per deoxyribonucleic acid phosphorus to $[Mg^{++}]$, the concentration of free magnesium. Values of $[Mg^{++}]$ were calculated from

$$[Mg^{++}] = \frac{\alpha}{(1 - \alpha)(K_{\text{EBT}})}$$

where K_{EBT} is the association constant for eriochrome black T and magnesium at the particular pH estimated by interpolation from values given by Schwarzenbach⁷.

The results show that, at low concentrations of sodium chloride, magnesium is very tightly bound by both undenatured and denatured deoxyribonucleic acid: binding by the undenatured form being tighter.

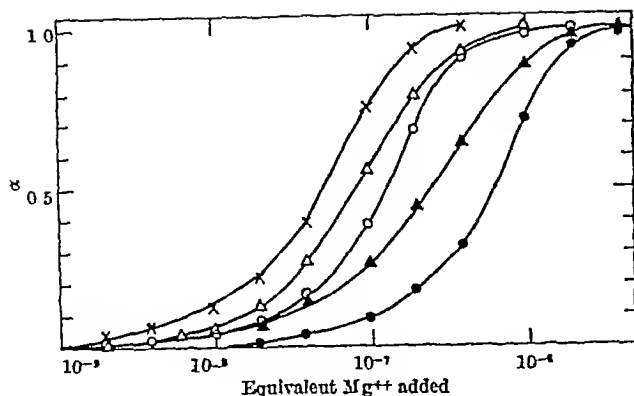


Fig. 1 Effect of deoxyribonucleic acid on the titration of eriochrome black T with magnesium chloride. pH is 10.2, in all cases sodium chloride = 0.002 M. The number of moles of deoxyribonucleic acid phosphorus given below were in each case present in the 3 ml of solution titrated with magnesium chloride: ×, eriochrome black T alone; Δ, 3.84×10^{-7} moles of denatured deoxyribonucleic acid phosphorus; ○, 3.84×10^{-7} moles of undenatured deoxyribonucleic acid-phosphorus; ▲, 3.09×10^{-6} moles denatured deoxyribonucleic acid-phosphorus; ●, 3.09×10^{-6} moles of undenatured deoxyribonucleic acid-phosphorus

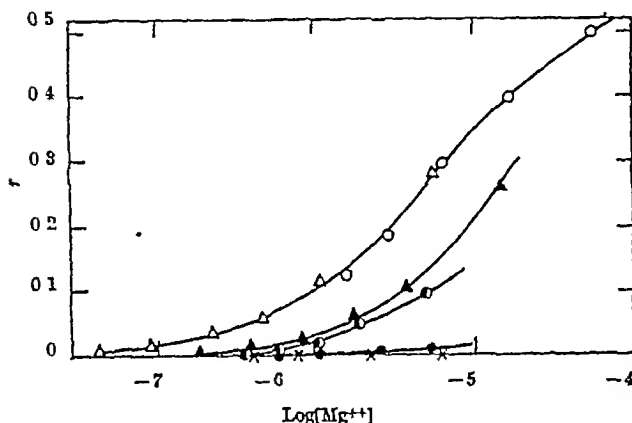


Fig. 2 Binding of magnesium ions by deoxyribonucleic acid. The equivalents of magnesium bound per nucleotide is designated by r . ○, from titrations at pH 9.04. All other points from titrations at pH 10.2: Δ, ○, undenatured deoxyribonucleic acid in 0.002 M sodium chloride; ▲, denatured deoxyribonucleic acid in 0.002 M sodium chloride; ●, undenatured deoxyribonucleic acid in 0.02 M sodium chloride; ×, denatured deoxyribonucleic acid in 0.1 M sodium chloride. Concentration of nucleic acid phosphorus = 1.03×10^{-4} M

The association constant for binding of magnesium and undenatured deoxyribonucleic acid (in 0.002 M sodium chloride) is about 2×10^5 (assuming a maximum binding capacity of 0.6 eq per nucleotide). The binding of magnesium is greatly reduced by increase of sodium chloride and the results suggest that sodium is capable of replacing magnesium on all binding sites. The very large effect of sodium, together with finding that magnesium is more tightly bound by the undenatured deoxyribonucleic acid, in spite of initial blocking of the amino and enolic groups, suggests that binding of magnesium by deoxyribonucleic acid primarily involves the charged phosphates rather than amino or enolic groups. Although only a limited range of $[Mg^{++}]$ values can be covered at a given pH, it appears that binding of magnesium by deoxyribonucleic acid does not vary with pH over the range studied, in accord with expectations from the titration properties of deoxyribonucleic acid. It is to be expected that the same invariance with pH should

apply to the whole range of pH where no titration of deoxyribonucleic acid occurs (around 5–11)

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Estimation of μ g. Quantities of Iron in Culture Medium, using Bathophenanthroline

THE use of bathophenanthroline (4,7-diphenyl-1,10-phenanthroline) as a highly sensitive reagent for the colorimetric estimation of iron has been described by Smith, McCurdy and Diehl¹. They showed that it was almost twice as sensitive as 1,10-phenanthroline, that the ferrous-bathophenanthroline complex could be extracted into a suitable solvent, and that it was virtually specific for iron (cobalt formed a yellow non-extractable complex, copper formed a yellow extractable complex, but only in neutral or alkaline solution). In view of these considerations it was decided to use this reagent to replace 1,10-phenanthroline in the estimation of iron in culture medium, and the following method was developed.

150 ml 'Pyrex' boiling flasks are cleaned by boiling with 10 M sodium hydroxide, rinsing with distilled water, heating for an hour with 18 M sulphuric acid, and finally rinsing with deionized water. Sulphuric and nitric acids are redistilled *in vacuo* from silver nitrate. Perchloric acid is redistilled *in vacuo* and the constant boiling acid collected. *n*-Hexanol is redistilled, and the fraction boiling at 156–158°C collected. Reagent solutions are purified by adding bathophenanthroline and extracting with *n*-hexanol.

The sample of culture medium containing 2–3 μ g of iron, is placed in a cleaned flask, and 0.2–0.5 ml sulphuric acid added, the exact quantity being the minimum amount necessary to ensure a liquid residue after ashing. 2 ml nitric acid is added and the mixture is boiled until charring begins, when the heat is turned off. When the mixture is cool a further 1 ml of nitric acid is added, followed by 1 ml of perchloric acid, and the mixture is reheated until clear, additional nitric acid being added if further charring occurs. When clear, excess nitric and perchloric acids are boiled off.

The digest is cooled and diluted to about 5 ml with deionized water. Phenolphthalein is added, the solution is neutralized with 18 M ammonium hydroxide and then the pink colour is just discharged with 2 M hydrochloric acid. 1 ml of 10 per cent (w/v) hydroxylamine hydrochloride, 1 ml of 0.1 per cent (w/v) bathophenanthroline in 70 per cent (v/v) ethanol, and 1 ml of 40 per cent (w/v) sodium acetate are added and the solution is boiled for 10–20 sec to decompose ferric pyrophosphate². When cool, the contents of the flask are transferred to a separating funnel, rinsing the flask successively with 2–3 ml deionized water, 2 ml ethanol, and 2–3 ml deionized water. After mixing, the colour is extracted into 6 ml *n*-hexanol, allowing 15 min for separation. The extract is transferred

to a stoppered tube graduated at 10 ml, the separating funnel is rinsed with 2 ml ethanol, and the volume made up to 10 ml with ethanol. The tubes are centrifuged, the optical density of the n hexanol extract measured at 533 m μ using 2 cm cells, and iron content read from a standard curve.

Results obtained from an experiment in which three independent operators determined the iron content of a single culture medium sample showed that the error variance between operators, corresponding to a standard deviation of ± 1.4 per cent was not significant compared with the residual (experimental) error of the method, which corresponded to a standard deviation of ± 1.5 per cent. In a further experiment in which a known quantity of iron was added to a sample of culture medium, the figures shown in Table 1 were obtained.

Table 1. RECOVERY OF IRON ADDED TO CULTURE MEDIUM

| Iron in medium, μ gm. | Iron added, μ gm. | Iron found, μ gm. | Iron recovered, μ gm. | Recovery (per cent) |
|---------------------------|-----------------------|-----------------------|---------------------------|---------------------|
| 2.27 | 3.0 | 5.42 | 3.05 | 102 |
| | 4.0 | 6.44 | 4.07 | 103 |

In addition to the estimation of iron in culture medium, the method has also been extensively employed for estimation of bacterial iron in cultures of *Corynebacterium diphtheriae*.

I wish to thank Dr. C. G. Pope for suggesting the use of the reagent, and Mr. E. L. Fenton for statistical analyses.

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Kent. June 10

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Monovalent Cations and the Incorporation of Metabolites by Isolated Thymus Nuclei

INCORPORATION into protein of amino acid by disrupted *Bacillus megaterium* protoplasts¹, pea seedling nucleoprotein particles², and rat liver microsomes³ is markedly enhanced by potassium ions while sodium ions are either inhibitory or without effect. In contrast, incorporation of amino acid into the proteins of isolated thymus nuclei requires sodium ions and potassium ions are inactive⁴. Potassium ions are required for many different enzyme catalyzed reactions but the observations with nuclei constitute one of the few instances of an apparently similar requirement for sodium ions. We have, therefore, examined this requirement in more detail especially to determine whether the sodium requirement is unique for nuclear protein synthesis, or whether related activities such as nuclear nucleic acid synthesis, also require sodium ions.

Nuclei were isolated from calf thymus as described by Allfrey *et al.*⁴ One ml. of nuclear suspension was added to a medium consisting of 0.4 ml. of 0.1 M glucose (containing 0.25 mgm. sodium chloridide and 5.34 mgm. crystalline mercuric chloridide per ml.), 0.5 ml. of 0.1 M sodium phosphate buffer (pH 7.1), and 0.1 ml. of metabolite labelled with carbon 14 (containing approximately 300,000 counts per minute). For experiments with other cations, the sodium

compounds in the medium were replaced by an equivalent amount of potassium or other compounds. The suspension were shaken for 120 min. at 38° C. The nuclear proteins and nucleic acids were precipitated with 13 ml. of cold two per cent perchloric acid. The precipitate was washed four times with two per cent perchloric acid, twice with hot 85 per cent ethanol, twice with an ethanol-ether mixture (3:1), and finally with ether. Deoxyribonucleic acid, ribonucleic acid, and protein were separated by a modified Schmidt-Thannhauser procedure⁵, in which the hydrolysis methods of Kleinschmidt⁶ and Mantley⁷ were employed. The hydrolysed ribonucleic acid was further purified by absorption on and elution from Dowex 1 chloride⁸. Separation of the nucleotides liberated by hydrolysis of ribonucleic acid (electrophoresis in 0.05 M ammonium formate buffer of pH 3.5) showed that all of the radioactivity incorporated in the ribonucleic acid resided in the nucleotides. The hydrolysed ribonucleic and deoxy ribonucleic acids were measured at 280 m μ in a Beckman spectrophotometer by use of an absorbance index of 32.1 and 20.1 for ribonucleic and deoxy ribonucleic acids respectively. Protein concentration was measured by the biuret method⁹. The protein and the hydrolysed nucleic acids were dispersed evenly on glass planchets and assayed for radioactivity with a nuclear model D-47 gas flow counter and standard scaling circuit.

Table 1. EFFECT OF REPLACEMENT OF SODIUM BY POTASSIUM IONS ON THE INCORPORATION OF VARIOUS PRECURSORS INTO NUCLEAR PROTEINS AND NUCLEIC ACIDS.

| Compound | Incorporation in the presence of potassium ions (expressed as per cent of incorporation in the presence of sodium ions) | | |
|---|---|-----------------------|---------|
| | Ribonucleic acid | Deoxyribonucleic acid | Protein |
| Glycine-2- ¹⁴ C | 24 | 20 | 22 |
| Alanine-1- ¹⁴ C | 16 | 16 | 12 |
| Formate-4- ¹⁴ C | 84 | 111 | 65 |
| Adenine-8- ¹⁴ C | 123 | 116 | — |
| Guanine-4- ¹⁴ C | 85 | 110 | — |
| Uracil-6- ¹⁴ C | 123 | — | — |
| Adenosine-8- ¹⁴ C-5' monophosphate | 93 | 85 | — |

Table 1 shows the effects of replacement of sodium ions by potassium ions on the incorporation of various precursors into the nucleic acids and protein of isolated nuclei. It can be seen that the incorporation of glycine or alanine carbons into not only protein, but also nucleic acids is strongly inhibited by replacement of sodium by potassium ions. In contrast, the incorporation of formate carbon into both nucleic acids and proteins exhibits moderate or no inhibition. Likewise, the incorporation of labelled adenine, guanine, uracil, or adenosine 5' monophosphate into nuclear nucleic acids is not generally inhibited by replacement of sodium ions by potassium ions. Thus, it appears that only the utilization of amino acids for either protein or nucleic acid synthesis requires sodium ions. This requirement for sodium ions for amino-acid utilization for both protein and nucleic acid formation is very specific, as sodium cannot be replaced by potassium, ammonium, lithium, rubidium, or caesium ions. The manner in which sodium ions are required only for amino acid utilization for protein and nucleic acid synthesis is not clear. One possibility, that is compatible with the results obtained here, is that sodium ions are required for the transport of amino-acids across the nuclear membrane, but clear evidence for such a role for sodium ions must await further experiment.

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Proof of the Formation of Enzyme-Substrate Complex by 'Crossing-Paper Electrophoresis'

In the first report¹, on 'crossing paper electrophoresis', a direct demonstration of enzyme-substrate complex has been described. The enzymes tested included crystallized pure trypsin, chymotrypsin and ribonuclease.

Objections² were raised, namely, that the formation of enzyme-substrate complex was not demonstrated thereby but merely an overlapping of the line of enzyme and that of substrate appeared, that the enzyme did not interact with substrate but with its split products and so on. We have already answered these objections¹, and up to the present, there seems to be no reason for denying the validity of the principle of 'crossing paper electrophoresis', and hence that of the demonstration of enzyme-substrate complex carried out by this method.

Since the first report was submitted, we have continued experiments with enzymes other than those cited above and obtained what we hold to be an unequivocal proof of the formation of enzyme-substrate complex, using crystallized pure preparations of amylase, papain, arginase, and lactic dehydrogenase.

In Fig. 1 is shown one of the experiments demonstrating the formation of enzyme-substrate complex of papain. A 1 per cent solution of the crystallized papain was applied on the line drawn parallel to the direction of the electrical field and a 0.2 M solution of benzoyl arginamide on the line vertical to it. The line of papain migrated so slowly compared with that of benzoyl-argininamide, that the line of the latter and that of papain came to cross each other with the progress of electrophoresis (hence 'crossing paper electrophoresis').

As has already been shown, two lines of different substances show a deformation at the point of crossing if they interact, because the complex which they form must show different mobility from its parent substances (the principle of 'crossing paper electrophoresis'). In Fig. 1, the line of benzoyl-L-argininamide shows a groove along the line of papain. This must be due to the fact that the former interacted with the latter to form a complex, which would migrate very slowly. Thus the line of benzoyl-L-argininamide would be retarded at the part where it crossed with the line of papain to form the complex. But the part of benzoyl-L-argininamide line where the complex was formed would not remain at the

point of complex formation, as the complex dissociates and equilibrates with the substrate. Thus the groove formed in the line of a substrate will become shallower according to the value of the dissociation constant, if other conditions are the same. In this way the formation of the enzyme-substrate complex of papain with benzoyl-L-argininamide was demonstrated unequivocally.

The same procedures were applied to amylase, pepsin, arginase and lactic dehydrogenase, and the formation of the respective enzyme-substrate complex was demonstrated.

In the case of amylase, the lines of the application of enzyme and substrate were the opposite of those of other enzymes. The reason for this is that the starch has a molecular weight as large as that of amylase and does not migrate. In order to meet the objection that the enzyme might have interacted not with substrate but with its split products, it is most convincing to demonstrate the deformation of the line of substrate. Thus for amylase, a control was necessary, although it is improbable that an enzyme would interact only with the split product of its substrate and not with the substrate *per se*.

In the case of lactic dehydrogenase, the enzyme used for the demonstration was the apoenzyme which could be shown to form a complex with lactic acid in one experiment and with diphosphopyridine nucleotide in the other.

The same experiments were carried out with other enzymes using crude preparations. The enzymes with which the enzyme-substrate complex could most probably be demonstrated were urcase, histidase, glycylglycine dipeptidase, malic dehydrogenase, etc. Experimental results obtained were almost the same as with pure enzymes. But as the enzyme preparations used were crude, the proof is not so convincing as with crystallized pure enzymes, because the sub

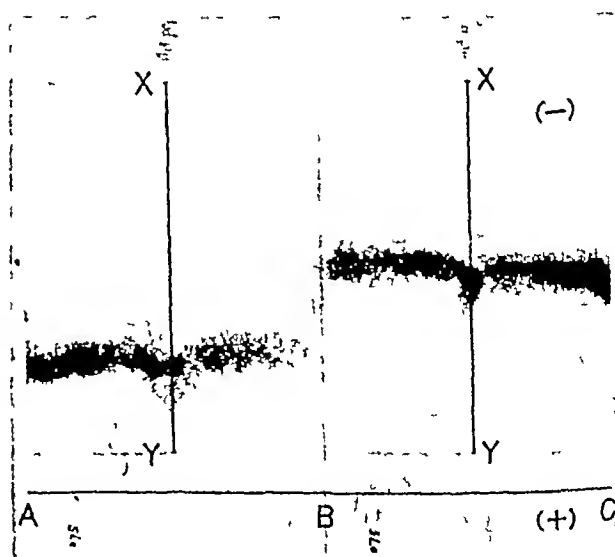


Fig. 1. Electrophoretic crossing of the line of benzoyl-L-argininamide and that of benzoyl-L-arginin with that of papain. 50 mM solution of benzoyl-L-arginine on the line A-B, 0.0075 ml/8 cm. 50 mM solution of benzoyl-L-argininamide on the line B-C, 0.0075 ml/8 cm. 1 per cent papain solution on the line A-Y, and A-Y', on X-Y 0.02 ml/10 cm. and on A-Y' 0.005 ml/10 cm. Acetate buffer containing 2 mM ethylenediaminetetraacetate, pH 3.0, ionic strength 0.05. Electrophoresis at 300 V 15 mA for 60 min. After drying for 10 min at 110°, stained with Sakaguchi reagent Paper, Toyo No. 51. Grooves appearing in the lines of benzoyl-L-argininamide and benzoyl-L-arginine are of the same depth. If the substance on the grooved part of the benzoyl-L-argininamide line were benzoyl-L-arginine, the part had to be retarded as deep as the corresponding part of the benzoyl-L-arginine line.

strates could also interact with non-enzymic inert proteins

The number of enzymes with which the enzyme substrate complex has been demonstrated by the crossing paper electrophoresis is not yet large, even if the demonstrations with crude preparations are included. The proof of the enzyme-substrate complex as is well known, has hitherto been regarded as one of the most difficult problems, as the complex is too unstable to be isolated as such. The demonstration of the complex with some oxidases by the change in light absorption has been regarded as the only possible and sure one. But this is not applicable to other enzymes. However by the procedure of the crossing paper electrophoresis it has now been established that the proof of enzyme substrate complex is no longer a difficult problem. The complex formation of individual enzymes will be demonstrated sooner or later.

Detailed reports will appear elsewhere

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HÆMATOLOGY

Influence of Streptomycin Solutions on the Interaction Between the Agglutinating Sera and the Corresponding Red Blood Cell Receptors

WORK on the influence of different chemical compounds on the reaction between blood group receptors of red cells and the corresponding antibodies has been published but the action of antibiotics on this reaction, however, has not yet been fully examined except by Netter *et al.*¹ who described the effect of antibiotics on enterobacterial lipopolysaccharides utilizing hemagglutination and hemolysis reactions. Our chance discovery of the inhibiting effect of a streptomycin solution on the reaction between anti-D antibodies and D positive erythrocytes led us to study the effect of different streptomycin concentrations on the antigen-antibody interaction in blood group systems. For our experiments we used streptomycin of Czechoslovak origin ('Streptomycin sulphurum', Penicillin Works, Prague). The different streptomycin concentrations were prepared by diluting 1 gm. of streptomycin in 2, 5, 10, 20, 50, 80 and 100 ml. of saline. Agglutinating sera of the systems A₁A₂BO, MN and Rh/Hr were chosen for the reaction. The red blood cells of the corresponding blood groups were washed three times in saline before use.

In the first group of tests the effect of different streptomycin concentrations was investigated in the following manner: after mixing equal parts of antisera (titrated progressively in twofold dilutions) with the corresponding streptomycin concentration an equal amount of a 4 per cent suspension of type red cells was added. The control tests were carried out in the same way by adding the corresponding

amount of saline instead of the solution of antibiotics. In sera of the ABO and MN blood group systems the testsera were carried out in agglutinating tubes (9×80 mm.) and in that of the Rh/Hr system in microtubes (5×45 mm.). After suitable incubation at optimal temperature the results in the ABO and MN systems were read macroscopically and in the Rh/Hr system microscopically. The results are shown in Table 1.

TABLE 1

| Sera | Cells | Control titre* | ml. saline containing 1 gm. streptomycin solution | | | | | | | |
|---------------------|----------------|----------------|---|----|----|-----|-----|-----|-----|-----|
| | | | 2 | 5 | 10 | 20 | 30 | 50 | 80 | 100 |
| A (anti B) | B | 116 | 4† | 8 | 8 | 16 | | | | |
| B (anti A) | A | 164 | 16 | 64 | | | | | | |
| anti-A ₁ | A ₁ | 116 | 2 | 8 | 8 | 8 | 8 | 16 | | |
| anti-O (H) | O | 116 | 2 | 8 | 16 | | | | | |
| Lectinin anti H | H | 164 | 16 | 64 | | | | | | |
| anti-M | M | 132 | 2 | 8 | 16 | 32 | | | | |
| anti-N | N | 18 | 0 | 0 | 2 | 4 | 8 | 4 | 4 | 8 |
| anti-D | CCD | 158 | 0 | 0 | 0 | 2 | 4 | 8 | 16 | 32 |
| anti-B | CCD | 128 | 0 | 0 | 0 | 4 | 16 | 32 | 32 | 64 |
| anti-B+C | CCD | 164 | 0 | 2 | 4 | 8 | 16 | 16 | 32 | 32 |
| anti-C | CCD | 164 | 2 | 8 | 16 | 32 | 64 | | | |
| anti-O | CCD | 1512 | 0 | 32 | 64 | 128 | 128 | 256 | 512 | 512 |
| anti-c | residue | 164 | 0 | 32 | 32 | 64 | | | | |
| anti-r | residue | 116 | 0 | 2 | 2 | 4 | 4 | 8 | 8 | 16 |

*Streptomycin solution was substituted by equal amount of saline.
†Figures indicate titres. 0 no agglutination.

It can be seen that in higher streptomycin concentrations the reaction with most sera (mainly in the Rh/Hr system) is inhibited. The inhibition declines gradually with the decrease in streptomycin concentration but differs according to the type of antibodies used until it gradually disappears in higher streptomycin dilutions.

The next task was to observe whether the streptomycin solution acts on red blood cell receptors or on the antibodies. After exposure of red blood cells type D positive to the action of the streptomycin concentrations at 37° C and for various lengths of time (1, 2, 4, 8, 16, 24 and 48 hr.) the erythrocytes were washed three times and again titrated with specifically reacting anti-D agglutinating antibodies. In the controls we used erythrocytes which had been stored for the same length of time and instead of antibiotics the same amount of saline was added. It was found that the activity of the D receptor is not lowered as compared to the controls. The following experiment confirmed our assumption that streptomycin in 1:2 and 1:5 concentration does not act on the blood group receptor D of the red cell membrane. Red cells which in the first experiment did not produce a positive reaction in the presence of antibody and the streptomycin solution were again incubated after a single washing with saline and the addition of the specific antibody. The ensuing positive result showed that the cells had not lost their agglutinating capacity.

If however normal erythrocytes were exposed to the action of the supernatant from our first experiment the results were negative as opposed to the controls. It can be concluded from our experiments that streptomycin acts apparently on the antibody to which it has a greater affinity than to the red blood cells receptors. This is also in keeping with the findings of Netter *et al.*¹

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Frequency of the New Blood Group Antigen Js^a among South American Indians

THE NEW blood group antigen Js^a was discovered by Giblett¹. Families carrying this antigen showed independent segregation from ABO, MNSS and Rh blood systems. Recently, Layrisse, Sanger and Race² studying families of hybrid populations of Venezuela added proof of its independence of Duffy, Kidd and Diego, and also confirmed its independence of MNSS and Rh.

The distribution of the Js^a antigen suggests that it is a Negro antigen. It has been found to be positive in 19 per cent of Negroes in the United States while not a single positive case was observed in 500 white donors³. No other ethnical human divisions have yet been tested.

Table 1 shows the incidence of Diego and Js blood group antigens in four Indian tribes from the western part of Venezuela. The Paraujano and Goajiro belong to the Arawak Indian stock and the Irapa and Macoita are classified as Carib.

Table 1. FREQUENCY OF THE DIEGO AND JS BLOOD GROUPS IN FOUR SOUTH AMERICAN INDIAN TRIBES

| Tribes | Number tested | Diego | | | | Js | | | |
|-----------|---------------|-----------------------|---------|------------------|-------|-----------------------|---------|------------------|--------|
| | | Phenotypes (per cent) | | Genes (per cent) | | Phenotypes (per cent) | | Genes (per cent) | |
| | | Di (a+) | Di (a-) | Di ^a | Di | Js (a+) | Js (a-) | Js ^a | Js |
| Paraujano | 120 | 10 00 | 90 00 | 5 14 | 94 86 | 2 50 | 97 50 | 1 23 | 98 77 |
| Goajiro | 110 | 10 03 | 89 99 | 5 18 | 94 82 | 0 84 | 99 15 | 0 44 | 99 56 |
| Irapa | 138 | 2 17 | 97 82 | 1 10 | 98 90 | 0 00 | 100 00 | 0 00 | 100 00 |
| Macoita | 57 | 19 20 | 80 70 | 10 17 | 89 83 | 0 00 | 100 00 | 0 00 | 100 00 |

The incidence of the Di^a in Paraujano, Goajiro and Macoita was in accordance with previous studies⁴, however, the low frequency for the Irapa Indians was not expected, since in all Carib tribes tested so far the incidence of the gene Di^a has been between 10 and 24 per cent.

Both Carib tribes show negative incidence of the Js^a, while the Arawak tribes show three positive cases out of 120 Paraujano, and one positive case out of 120 Goajiro, Indians. The studies of other blood group antigens, which will be published in detail elsewhere, demonstrated that both Carib tribes had no Negro admixture, while a Negro gene flow into both Arawak tribes was found, this is in agreement with the physical features and historical tradition.

The results presented here indicate that the Js^a is negative or has a very low frequency in the Indian tribes studied. If in future investigations this finding should be confirmed among other Indian tribes, and perhaps in Asiatic Mongoloids, the antigen will be of great value for studying Negro gene flow into hybrid populations.

We are indebted to Dr. Eloise R. Giblett who generously supplied the anti-Js^a used in these studies.

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A Terminal Peptide Sequence of Human Haemoglobin?

It was reported recently^{1,2,3} that the chemical difference between the normal human haemoglobin A and the abnormal haemoglobins S and C resides in a tryptic peptide, called peptide 4, to which the following structure was assigned: histidyl-valyl-leucyl-leucyl-threonyl-prolyl-glutamyl-glutamyl-lysine. In haemoglobins S and C the glutamic acid residue which is in italics is replaced by a valine and a lysine residue, respectively. Although the evidence available at the time of publication made the above structure appear likely, repeated attempts to confirm it by the Edman stepwise degradation method⁴ have not agreed with this formulation. We now wish to report that the sequence of peptide 4 in the haemoglobins A and C is as indicated in Table 1, with histidine in position 2 and valine as the N-terminal amino-acid. Furthermore, this peptide is likely to be N-terminal in one of the haemoglobin chains. The structure of peptide 4 from haemoglobin S is still under investigation, but it seems likely—especially in the light of the work of Hill and Schwartz (following communication) that its structure is as shown. It should be noted that the sequence around the amino-acid which changes and the changes themselves in these mutational alterations are not affected by the new structure.

The first suspicion arose when one of us (J. A. H.) found that application of Sjöquist's modification⁵ of the Edman stepwise degradation yielded valine as the N-terminal amino-acid for peptide 4 from haemoglobin A^{1,2} and peptide 4b from haemoglobin C³. Only traces of histidine could be obtained at this step. Histidine, or rather its phenylthiohydantoin, was tested for by removing *in vacuo* the acid used in the method and extracting a slightly alkaline solution with ethyl acetate. On the other hand the second step did give histidine, but in poor yield, and the third step yielded mainly leucine in reasonable yield. These amino-acids were identified by two-dimensional paper chromatography after hydrolysis of their phenylthiohydantoin with hydriodic acid⁶. Qualitative analysis⁶ of the two peptides after one and two steps of the Edman degradation showed that valine was much reduced after one step and that after two steps both valine and histidine were absent from the residue. It appears that the peptide 4 begins with the sequence valyl-histidyl-leucyl-. However, repeated attempts to obtain dinitrophenyl-valine after reaction with fluoro-2,4-dinitrobenzene⁷ were unsuccessful. Quantitative amino-acid analyses⁶ after paper chromatography indicated that there is only a single leucine residue in the peptides 4.

At this point a Spinco automatic amine acid analyser, modelled on Moore and Stein's equipment⁸, became available. Analysis of haemoglobin A peptide 4 showed at once and unequivocally that only one instead of two leucines is present together with the other amino acids in their expected quantities.

Haemoglobin A peptide 4 was submitted (VMI) once again to one step of the Sjöquist degradation⁴, but both the N-terminal amino-acid derivative and the remaining peptide were analysed quantitatively⁹, the latter on the automatic amino-acid analyser. The results were clear. After cyclization of the phenylthiocarbonyl peptide under Sjöquist's conditions, an extract of the diluted acid solution showed the spectrum typical of a phenylthiohydantoin⁴. After removal of the acid, the slightly alkaline solution did

not yield any more phenylthiohydantoin, as would have been expected had histidine been present as the N terminal amino acid. After hydrolysis with hydrazine the acid extract showed that valine was practically the only amino-acid present. The rest of the peptide was hydrolysed and analysed quantitatively. All the amino acids were present, except for the valine which was reduced to 10 per cent of its usual value. Clearly the peptide had N terminal valine. Histidine was still present although reduced slightly in amount. The recovery of lysine was only about 50 per cent, due perhaps to incomplete hydrolysis of its β -phenylthiocarbonyl-derivative. On the basis of these results we feel that the structures shown in Table 1 are now correct. Hill and Schwartz (following communication) have independently arrived at the same structure for hemoglobin A peptide 4 in connection with their work on hemoglobin G.

Table 1 STRUCTURE OF HEMOGLOBIN PEPTIDES 4

| | |
|--------------|--|
| Hemoglobin A | Val-His-Leu-Thr-Pro-Glu-Gln-Lys |
| " S | Val-His-Leu-Thr-Pro-Phe-Gln-Lys |
| " G | Val-His-Leu-Thr-Pro-Lys-Gln-Lys |
| " | (Val=valyl, His=histidyl, Leu=leucyl, Thr=threonyl, Pro=prolyl, Glu=glutamyl, Lys=lysine.) |

These results are interesting, because Rhinesmith, Schroeder and Martin¹⁰ found that the β chain of hemoglobin, which is known¹¹ to contain peptide 4, begins with the sequence valyl-histidyl-leucyl followed by a bond which is relatively easily cleaved by mild acid hydrolysis. Such a bond is the leucyl-threonyl sequence shown in Table 1. It seems likely, therefore, that peptide 4 stands at the N terminus of the β -chain of hemoglobin and that the glutamic acid residue which changes in hemoglobins S and G is in position number six along this chain. If this is true, then in some manner as yet not understood these alterations at the N terminus of the β -chain appear to exert a profound effect on the physical behaviour of the whole molecule as shown for example by the drastically low solubility¹² of reduced hemoglobin S.

It is still not clear why the dinitrophenyl method does not yield dinitrophenyl valine from these peptides, yet destroys histidine. Rhinesmith, Schroeder and Pauling¹³ also noted this strange behaviour which in part led to the original formula for peptide 4. Furthermore, our experience reinforces that of other workers on the importance of reliable quantitative amino acid analyses on these peptides and their fragments. It seems that estimation by inspection of chromatograms cannot always decide reliably between the presence of one or two equivalents of a particular amino acid.

We wish to acknowledge the courtesy of Drs. Hill and Schwartz in allowing us to see their manuscript prior to publication.

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A Chemical Abnormality in Hemoglobin G

INGRAM and Hunt¹ reported that normal human hemoglobin (hemoglobin A) differs from certain of the abnormal human hemoglobins by a single amino acid in the primary structure of the β -chains of the globin of these proteins. The peptides from a tryptic digest of hemoglobin A and hemoglobin S were visibly identical except for one peptide (peptide 4) in which a glutamyl residue in hemoglobin A was replaced by a valyl residue in hemoglobin S. We have isolated an abnormal peptide in hemoglobin G² and have compared it to similar peptides obtained from hemoglobins A and S. By amino-acid analysis and sequence determinations, it is evident that hemoglobin G possesses an abnormal amino-acid in the tryptic peptide number 4 of Ingram. The sequences determined for the tryptic peptides from hemoglobins A and G are

| | |
|--------------|---------------------------------|
| Hemoglobin A | Val-His-Leu-Thr-Pro-Glu-Gln-Lys |
| " G | Val-His-Leu-Thr-Pro-Gly-Gln-Lys |

It is apparent that a somewhat different sequence was obtained for the hemoglobin A peptide than previously reported. Only one leucyl residue is present in these peptides and a glycyl residue in hemoglobin G replaces a glutamyl residue in hemoglobin A. Although peptide 4 from hemoglobin S also contained only one residue each of leucine and glutamic acid and an additional residue of valine, the exact sequence has not yet been determined.

Hemoglobin G was obtained from an individual (pedigree number II-7) who was shown by Schwartz *et al.*³ to possess only hemoglobin G, hemoglobin S was obtained from a patient having sickle cell anemia; hemoglobin A was obtained from one of us (H.C.S.). The hemoglobins were prepared from washed red cells and digested with trypsin in a similar manner to that reported by Ingram.² The soluble peptides were examined by both the two-dimensional electrophoresis-chromatography technique⁴ and by one-dimensional electrophoresis on Whatman 3MM paper.

By both of these techniques hemoglobin G differed from hemoglobin A in only one peptide. The single abnormal peptide of both hemoglobin G and hemoglobin S and the corresponding peptide of hemoglobin A were obtained from preparative electrophoretograms by elution of the appropriate bands. These peptides were further purified by one-dimensional paper chromatography in butanol-acetic acid-water (200:30:75). Each purified peptide was then hydrolyzed *in vacuo* in 6 N hydrochloric acid for 24 hr. Amino-acid analyses of these hydrolysates were performed with an automatic amino-acid analyzer⁵ and are shown in Table 1. These peptides possess a composition similar to that of trypsin peptide 4 but contain only one leucyl residue. Also hemoglobin G like hemoglobin S contains one less glutamyl residue

than haemoglobin A. However, the haemoglobin G peptide contains one glycyl residue and is distinguished from the haemoglobin S peptide in that it contains only one valyl residue.

Table 2 summarizes the sequence analysis made on the haemoglobin G peptide. Only the phenylthiohydantoin of valine was found on N-terminal analysis⁷ and it behaved exactly like the synthetic compound on paper chromatography in three different solvent systems. Leucine aminopeptidase⁸ liberated equivalent quantities of valine, histidine, and leucine, and a lesser amount of threonine. On the basis of the specificity of the aminopeptidase,^{8,10} threonine is in position number four in the peptide and proline at position number five. Only the sequence shown is compatible with the several peptides obtained after papain digestion.

Table 1 AMINO-ACID ANALYSIS OF TRYPTIC PEPTIDE 4 OF HEMOGLOBINS A, S AND G

| Amino acid | Hb-A | Hb S | Hb-G |
|---------------|---------------------------|------|------|
| | moles per mole of peptide | | |
| Lysine | 1.0 | 1.1 | 1.1 |
| Histidine | 0.9 | 1.0 | 0.9 |
| Threonine | 0.9 | 1.0 | 1.0 |
| Glutamic acid | 1.9 | 1.1 | 1.0 |
| Proline | 1.0 | 1.1 | 1.0 |
| Glycine | 0 | 0 | 1.1 |
| Valine | 1.0 | 1.7 | 0.8 |
| Leucine | 1.2 | 1.1 | 1.0 |

Table 2 SEQUENCE ANALYSIS OF Hb G TRYPTIC PEPTIDE 4

| Method | Result |
|------------------|---------------------------------|
| PITC* | Val. |
| LAP† | Val His, Leu, (Thr) |
| Papain Peptide 3 | Val, His |
| Papain Peptide 1 | Leu, Thr, Pro, Glu, Gly, Lys |
| Papain Peptide 2 | Gly, Lys |
| Papain Peptide 4 | Leu, Thr, Pro, Glu |
| Papain Peptide 5 | Thr, Pro, Glu |
| Papain Peptide 6 | Glu, Gly |
| Sequence | Val His Leu Thr Pro Gln Gly Lys |

*PITC=phenylisothiocyanate procedure⁷

†Leucine aminopeptidase degradation⁸

A similar sequence analysis of tryptic peptide 4 of haemoglobin A has been made by isolation of the phenylthiohydantoin of valine and the action of leucine aminopeptidase and papain. The results establish the sequence shown above.

From these results it is clear that haemoglobin G used in this study is definitely an abnormal haemoglobin which is chemically distinct from haemoglobin S. It cannot, however, be determined whether the haemoglobin G used in this study is identical with that of Eddington *et al.*¹¹ It is also evident that haemoglobin G possesses an abnormality in sequence at a different position but adjacent to that of haemoglobins S and C, accepting the sequence recently reported by Hunt and Ingram (preceding communication) for each of these as

| | |
|---------------|----------------------------------|
| Haemoglobin S | Val His Leu Thr Pro Val Glu Lys |
| " C | Val His Leu, Thr Pro Lys Gln Lys |

On the basis of genetic evidence, it is probable that the genes for haemoglobins C and S are alleles¹², whereas it has been proposed that haemoglobins S and G are produced by genes which are not alleles.⁴ This genetic evidence and the work presented here would suggest that more than one gene controls the sequence of the β -chain of haemoglobin. If, however, a gene is defined as the unit which controls the synthesis of an entire peptide, for example, the β -chain, then the mutations seen in haemoglobins S and G must reside at different parts of this unit. Work now in progress on the chemical evaluation of the haemoglobins in the members of the family described by Schwartz, *et al.*⁴, should help answer these questions as well as provide useful information on the

genetic control of the primary structure of the haemoglobins.

Another feature of interest in this study is the relationship between the trypsin peptides containing the sequence abnormalities and their position in the whole haemoglobin molecule. The work of Schroeder *et al.*¹³, indicates that the N-terminal sequence of the β -chains of haemoglobin is Val His Leu. From the identity of the first three residues in the peptides of the above haemoglobins and the β -chain it is tempting to suggest that the tryptic peptides studied in this investigation, and by Ingram, occupy the N-terminal end of the β -chains. If this is the case, it might now be possible to evaluate how differences in the sequence of amino-acids effect changes in the physical behaviour of the abnormal haemoglobin molecules.

It is a pleasure to acknowledge the encouragement and interest shown by Dr. Emil L. Smith and the other members of this laboratory in this work. It is also a pleasure to acknowledge the courtesy of Drs. Hunt and Ingram for allowing us to read their manuscript prior to publication. Haemoglobin G samples were kindly furnished by Dr. S. F. Kaufman and the haemoglobin S by Dr. Janet Watson. This study was supported in part by grants from the National Institutes of Health, U.S. Public Health Service. One of us (H.C.S.) is a Postdoctoral Research Fellow, National Heart Institute, U.S. Public Health Service.

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RADIOBIOLOGY

Absorption of Zinc Phosphide Particles

ALTHOUGH human poisoning by the rodenticide zinc phosphide is said to be fairly common in the Far East there are only four cases described in the medical literature and of these only one had fatal outcome^{1,2}. From these cases it appears that death may occur in one of two ways, either within a few hours of ingestion or as a result of liver damage several days later. We recently investigated a case in which the clinical and chemical evidence suggested poisoning of the latter type. The outstanding feature was the liberation of about a microgram of phosphine at room temperature from 20-gm. samples of liver and kidney after acidification of the tissue. Detection and identification of the phosphine were by the method of Curry, Rutter and Lum Chin-Hua³. The findings indicated

that zinc phosphide was present in these organs and at first eight it was difficult to visualize the mechanism and route of absorption of this poison from the alimentary tract

It seemed possible, however, that because of the very small size of some of the particles of commercially available zinc phosphide (less than 0.1 μ) these particles might pass through the intestinal wall into the bloodstream. We observed that in aqueous suspension in the presence of fat or oil the particles are preferentially absorbed on to the surface of the fat or oil and despite their high density can even be made to float. When zinc phosphide is added to a commercially available evaporated milk the particles are held indefinitely in fine suspension by the fat globules and we used such a suspension to feed the poison to rats and guinea pigs. In dilute acid, zinc phosphide rapidly liberates phosphine and we showed by experiments on rats that when these animals were fed a dose of zinc phosphide in excess of the LD50 then, if death resulted, it occurred rapidly and moreover phosphine was detectable in the liver. In lower doses, when the animals were killed more than 24 hours after ingestion, no phosphine was detectable in the liver, but on adding acid to this tissue however, a very faint brown stain was obtained when the gases were passed through a filter paper soaked in methanolic silver nitrate. Such small quantities were present that it was not possible to obtain confirmatory reduced phosphomolybdate blue colour. We therefore attempted to demonstrate particles of zinc phosphide in the liver of poisoned rats in three ways: (a) by histological examination, staining for zinc, (b) by concentration and examination for sub-microscopic particles using electron microscopy, and an electron diffraction examination of the particles, (c) by using radioactive zinc phosphide so that increased sensitivity of detection was obtained.

We wish to discuss here only the results of the work using zinc phosphide labelled with phosphorus 32 since these provided excellent evidence for the presence of phosphine in the livers of poisoned rats.

10 mgm aliquots of irradiated commercial zinc phosphide each having a phosphorus activity of 0.8 mc were fed in suspension to 6 approximately 250 gm rats. One rat (RA/2) died less than 20 hours after ingestion another (RA/1) about 22 hours after ingestion while rats RA/3, 4, 5 and 6 were killed by coal gas 26 hours after ingestion of the poison. The livers from rats RA/2 and RA/1 were analysed separately those from rats RA/3, 4, 5 and 6 were combined before analysis.

Table 1. β RAY COUNTS AT VARIOUS TIMES

| | Time (hr) | | | | | |
|---------------------------|-----------|-------|-------|-------|------|-----|
| | 0 | 1 | 1½ | 3 | 5½ | 20 |
| Rat RA/3 | 6,500 | 5,500 | 3,200 | 1,200 | 500* | 200 |
| Rat RA/1 | 450 | 300* | 600 | 200 | | |
| Rat RA/3, 4, 5 and 6 (a)† | 50 | 35 | 30 | 110 | 64 | |
| Rat RA/3, 4, 5 and 6 (b)† | 30 | 0* | 153 | 63 | 21 | |

* Time at which acid was added.

† Background = 35 c.p.m.

‡ Readings repeated background = 1 c.p.m.

Carbon dioxide was passed in the cold through suspensions of the cut up livers in water and the resulting gases were passed through a filter paper soaked in silver nitrate which was changed at half hourly intervals. When the β counts from the silver phosphide were low, or absent, dilute mineral acid was added and the procedure was repeated. Table 1 shows the results that were obtained.

The increase in counts following acidification in rats RA/1 and RA/3, 4, 5 and 6 shows that phosphine is to be found in liver following its oral administration. Rat RA/2 obviously died from phosphine poisoning. Rat RA/1 had phosphine and phosphide present in its liver while the four other rats had recovered from the effects of phosphine and had none left in their livers but they had absorbed significant quantities of phosphine.

Further experiments showed that the main urinary excretion product in these poisoned rats and guinea pigs was hypophosphite and that on histological examination their gastric and intestinal mucosae were intact.

Because of their toxicological importance and the evidence for particle absorption we felt justified in publishing these preliminary observations.

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Enzymes and Radioactivity in Erythrocytes of Different Ages

Fractionation of erythrocytes of different ages by differential hemolysis is a useful approach to the study of enzymatic aspects of the maturation of the erythrocyte in the peripheral blood. Young red cells are thought to be resistant to osmotic hemolysis and older cells to be very fragile.¹ Recently Simon and Topper² have shown by serial osmotic hemolysis that young erythrocytes have both fragile and resistant components. In the present paper the activities of glutamic oxaloacetic transaminase and lactate dehydrogenase have been related to red blood cells of various ages.

Male Sherman strain rats were injected with either sulphur-35 amino acids or ferrous-59 citrate to act as markers of the age of the red cells³ and were bled at various intervals after injection. After removal of plasma and buffy coat, erythrocytes were washed six times with buffered isotonic saline at room temperature. Serial osmotic hemolysis, some what modified from the method quoted above², was carried out by suspending the washed red cells in 0.9 per cent buffered saline, and removing a small aliquot to represent the whole population. The remainder of the suspension was centrifuged (600 g for 3 min) and the supernatant saved as the most fragile fraction. The residual red cells were then resuspended in 0.7 per cent buffered saline for 5 min followed by separation of the supernatant which represented the next most fragile fraction. Surviving cells were successively cycled through solutions each more dilute than that preceding until hemolysis was complete. The last fraction obtained represents the most resistant cells. The successive supernatants and the aliquot of whole hemolyzate

were recentrifuged for 10 min at 2500 *g*. These resultant supernatants were analysed for haemoglobin (optical density at 540 $m\mu$), activities of glutamic oxaloacetic transaminase⁴ and lactic dehydrogenase⁵, and for radioactivity. The activities in each fraction were expressed per mgm of haemoglobin. The relative specific activity was calculated by dividing the specific activity of a substance in the fraction by the corresponding specific activity in the whole.

Fig 1 depicts the distribution of sulphur-35 radioactivity in haemolysate fractions at various intervals after injections. The vertical axis represents relative specific activity. The right-hand horizontal axis gives the interval after injection in days. The left-hand horizontal axis represents the order of fragility, with the most fragile to the left and the most resistant to the right, a probit scale is used to expand the extreme values of haemolysis for better visualization.

At one day, shown by the first plane, the bulk of radioactivity is in the most resistant 10 per cent at the right, and smaller quantities are in the most fragile 1 per cent at the left. At 4 days, the second plane, the right hand peak has started to shift to a less resistant area, and this continues so that at 10 days, the third plane, and later, the most resistant erythrocytes, on the right, have little radioactivity. The peak of sulphur-35 radioactivity in the most fragile area, to the left, persists somewhat longer in these haemolysates. In other experiments, not here shown, haemoglobin of the haemolysates was purified by recrystallizing three times and removing exchangeable sulphur-35 with cysteine at alkaline pH and dialysing. With this purification the peak of radioactivity in the most fragile erythrocytes is clearly present at early times, though somewhat diminished, and disappears more promptly than when haemolysates are studied directly. At 60 days, represented by the next to the last plane, there are two peaks, one at 0.5 and the other at 85 per cent haemolysis. It should be pointed out that neither of these peaks coincides with those at the extreme ends associated with young cells.

The last plane shows the averaged distribution of activity of the two enzymes for ten experiments. This distribution is, of course, independent of the interval after injection of any radioactive markers. Highest glutamic oxaloacetic transaminase activity is present in the most resistant 20 per cent of erythrocytes, at the right, and in the most fragile 1 per cent at the left. Lactic dehydrogenase is most active in the most fragile 1 per cent at the left. In the resistant fraction on the right it is enriched to a value of 1.75, somewhat less than the enrichment found for glutamic oxaloacetic transaminase in this area. Thus the peaks of enzyme activity at the two extremes correspond to the distribution of younger red blood cells depicted in the front planes. A similar correlation between enzyme and radioactivity marking young

cells was obtained with both rat and human erythrocytes after radioactive iron administration. Only early intervals after injection were studied with this isotope. The present work demonstrates that older rat red cells are as inhomogeneous with respect to haemolytic susceptibility as are the young cells.

The fact that haemolysis of very young erythrocytes was obtained in 0.9 and 0.7 per cent saline suggests that the phenomenon of fragile young erythrocytes may at least be partially explained by an increased mechanical fragility of these cells.

Previous workers have amply demonstrated that reticulocytes and young erythrocytes contain a large complement of enzymes, some of which disappear on maturation⁶. The present results demonstrate that the young red cells, found in both the most fragile and most resistant fractions of haemolysis, contain high orders of activity of the two enzymes studied here, GOT and LDH.

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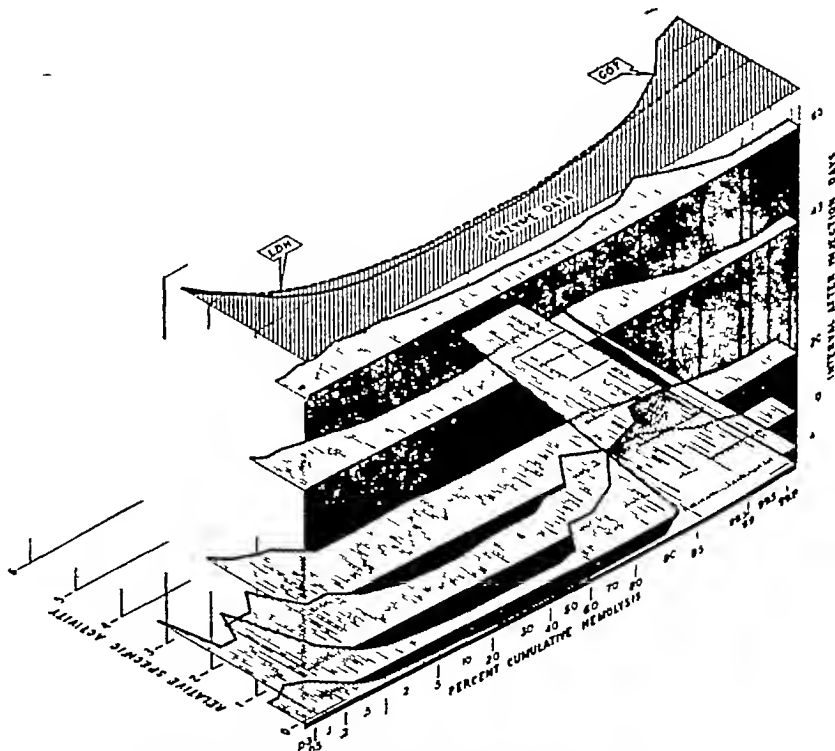


Fig 1. Distribution of sulphur-35 radioactivity and enzyme activity in haemolysates of rat erythrocytes of different ages.

PHYSIOLOGY

Responses to Localized Distension of the Oesophagus in Decerebrate Sheep

The reflex nature of contractions of the oesophagus stimulated by oesophageal stretch has been described in a number of species. In our experiments in addition to the oesophageal responses to distension of itself the effects on parotid salivary secretion, reticulum and rumen movements have been examined in decerebrate preparations of sheep. The distension was delivered and the responses to it recorded from balloons introduced through the mouth or through an incision in the mid cervical oesophagus into the lower cervical or thoracic regions of the oesophagus. In three experiments on preparations anaesthetized with pentobarbitone sodium after decerebration the thorax was opened and the responses of the thoracic oesophagus observed directly. The effects of oesophageal distension on the reticulum, rumen and salivary responses were judged by its modification of previously established reflex responses of these structures.^{1,2}

The balloons used were 2-3 cm long and were distended to diameters up to 2-3 cm with air. When retained in the same position moderate distension of such a balloon evoked a series of contractions of the oesophagus. These increased in frequency up to degrees of distension beyond which oesophageal contractions were not observed. If the balloon was left free to move it was delivered, after its distension, by a series of contractions into the reticulo-rumen. The contractions were not accompanied by bucco-pharyngeal or upper cervical oesophageal movements of swallowing. The responses of the oesophagus to distension of itself were not observed after the intravenous administration of *d* tubocurarine chloride (0.1 mgm/kgm), decamethonium iodide (0.5-0.75 mgm/kgm) or after the vagus nerves were cut in the neck. They persisted after the administration of atropine sulphate (1 mgm/kgm). Contractions of the oesophagus evoked by stimulation of the peripheral end of a vagus nerve cut in the neck similarly persisted after the administration of atropine but were not obtained after *d* tubocurarine or decamethonium had been given. Striated muscle was identified in the regions of the oesophagus the responses of which were studied.

The effects of oesophageal distension on parotid salivary secretion, reticulum and rumen contractions varied according to its degree and the region stimulated. Moderate distension, particularly of the first 2-3 cm and of the last 2-3 cm, of the thoracic oesophagus was frequently followed by increased parotid salivary secretion and by the initiation, or if already present, by an increase in the frequency, of reticulum and rumen contractions. Greater degrees of distension inhibited previously established parotid salivary secretion and rumen responses. The most efficacious stimulus was the distension of a balloon in the lower part of the cervical oesophagus when it was left free to be moved by the oesophageal contractions into the stomach. With balloons held in the one position the greatest effects were obtained from distension of the last 2-3 cm of the thoracic oesophagus, similar but weaker responses were evoked from stimulation of first 2-3 cm of the thoracic oesophagus. The effects were obtained after oesophageal contractions were annulled with *d* tubocurarine. Less regularly similar but weaker responses

were evoked from intermediate regions of the thoracic oesophagus and from the lower 2-3 cm of the cervical oesophagus.

Retracting stretch alone or combined with that of the reticulo-ruminal orifice modified the oesophageal contractions stimulated by distension of itself. The effects varied from an absolute inhibition to a temporary cessation of oesophageal contractions during each contraction of the reticulum and rumen stimulated by stretch of the reticulum and reticulo-ruminal orifice. In four experiments distension of a balloon in the reticulum led to an increased frequency of the contractions of the most caudal regions of the thoracic oesophagus.

These results suggest that the two functionally distinct regions of the thoracic oesophagus characterized as sphincters by Dougherty and Meredith³ from cinefluorographic observations may be particularly significant from a sensory point of view, and also add to the evidence which suggests that the activity of the oesophagus in ruminants may be modified by conditions or activity in the stomach.^{4,5}

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Curative Effect of Selenium Upon the Incisor Teeth of Rats deficient in Vitamin E

The original description of the protective action of selenium against the oxidative diathesis in chicks on torula yeast diets was given by Schwarz *et al.*¹ Following this significant finding, a good deal of research has been done on the possible vitamin E properties of this element and Schwarz *et al.*'s findings were confirmed.² Selenium was also found to be protective against liver necrogenic diets in rats.^{3,4} It did not reverse the diluoro acid haemolysis test⁴ and was ineffective in preventing resorption gestation in rats⁵ or in averting muscular dystrophy in rabbits, on vitamin E free diets.⁶ The selenium was usually given as sodium selenite or selenate, selenious acid, or selenocystine. The levels used in the diets varied from 0.1 to 10 p.p.m. selenum.

A characteristic degeneration of the enamel organ and whitening of the normally orange-coloured incisor teeth of the rat occur in vitamin E deficiency. Aterman⁷ has recently reported that sodium selenite in a liver necrogenic diet at a level of 9 p.p.m. selenum and fed to weaning rats did not protect the incisor teeth against depigmentation, though it averted liver necrosis.

I have conducted experiments which show that selenium has a protective action upon the enamel organ and tooth pigment, but my methods differed

from those of Aterman Rats weighing 50–60 gm were put on to the diet previously employed¹ which consisted of 77.5 per cent potato starch, 20 per cent dried brewer's yeast, and 2.5 per cent cod liver oil. On this diet marked histological changes in the incisal enamel organ and whitening of the teeth occur in 30 days and these changes are completely averted by α -tocopherol administration. Animals kept on this diet for as long as 120 days show consistently marked enamel organ degeneration and white teeth².

44 rats were put on this diet for 40 days, by which time all their upper incisor teeth were white. Six were then killed and the enamel organs examined histologically. All enamel organs showed extensive degeneration and in all but one the ameloblasts were iron-free. This loss of iron occurs in vitamin E deficiency³, and its reappearance is the earliest sign of recovery after α -tocopherol administration. 18 rats were dosed with 3 mgm of α -tocopherol daily ('Ephynal', Rocho) and 6 were killed 40, 60 or 80 days later. These all showed the reappearance of iron-staining granules in the ameloblasts and the recovery of the enamel organ as described². At forty days all teeth were yellow at the gingival margin and they were uniformly orange by 80 days. Of the remaining 18 rats, 9 were put on to the basal diet to which sodium selenite had been added to a level of 0.3 p.p.m. selenium, and 9 on to the basal diet plus sodium selenite at a level of 0.9 p.p.m. selenium. The animals on 0.3 p.p.m. selenium grew as well as the vitamin-dosed animals, but 0.9 p.p.m. selenium retarded growth to some extent. 0.3 p.p.m. selenium was not as effective as 0.9 p.p.m. for tooth recovery. 3 animals on the 0.3 p.p.m. diet had after 40 days teeth either completely yellow or yellow on the upper half, and their enamel organs were recovering and had iron containing granules. This curative action of selenium was not kept up, and at 60 days the teeth were mottled yellow and the enamel organs had degenerated and by 80 days all teeth were white. On the 0.9 p.p.m. level of selenium, 5 rats at 40 days had recovered their incisal orange pigment in whole or in part. At 60 days 3 more rats showed pigment being replaced and at 90 days only 1 of the 3 remaining rats had white teeth. All the animals with pigment recovery had regenerating enamel organs and iron containing granules in their ameloblasts.

It thus appears that while not as uniformly effective as α -tocopherol, selenium does have a significant role in curing the effects of vitamin E deficiency in the rat incisor tooth. Possibly the requisite level for this increases with age.

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Subcutaneous Absorption of Urethane in Dehydrated and Fasted Mice

THE absorption of the non-electrolyte urethane from subcutaneously injected solutions is depressed in mice treated with oestrogenic hormones in pharmacological doses¹. This is possibly due to the higher amount of connective tissue ground substance found in such animals when compared with controls. Both the hexosamine content and the concentration of water in the connective tissue is increased following treatment with oestrogen. To elucidate the influence of alterations in the content of hexosamine and the concentration of water on the absorption from subcutaneously injected solutions of a non-electrolyte, the following experiments were carried out.

Absorption experiments were performed on mice (7–8 weeks) by injecting 0.30 ml./25 gm of a 10 per cent w/v urethane solution subcutaneously into the skin on the back. The absorption time was expressed as the time in seconds from the subcutaneous injection until the animals could be laid on the side without resistance (light anaesthesia). Experiments were performed on controls and on two groups of pretreated animals. One group was fasted and another group was dehydrated. A full description of the dietary regimen used will be given by one of us². Hvidberg found that the fasting method used here was followed by a 7.3 per cent reduction in the content of hexosamine in the subcutaneous connective tissue, while the water content was lowered by 12.5 per cent. The method of dehydration gave a similar reduction in the amount of connective tissue hexosamine (7.5 per cent), while the water content was reduced by about 33 per cent. The amount of water and hexosamine is calculated on the basis of the dry fat-free tissues.

In the present experiments we found the absorption to be accelerated to the same degree in both fasted and dehydrated mice compared to the figures found for normally fed controls (Table 1). When hyaluronidase was added to the injected solution of urethane (500 IU/ml) the absorption of the drug was enhanced to a statistically highly significant degree in all three groups of experimental animals (Table 2). When the absorption times in the three groups in Table 2 are compared, a nearly equal rate of absorption is found in all groups. The absorption time in the fasted mice with hyaluronidase is not statistically different from the controls. In the dehydrated group (Table 2) there is slight enhancement of the absorption when compared to controls ($P > 0.05$), but no difference exists between the rate of absorption in dehydrated and fasted mice.

The conclusion must be that both dehydration and fasting enhance the subcutaneous absorption of urethane to a high degree when compared to controls (Table 1). When hyaluronidase is added to the injected solution this difference between the experimental groups and controls is eliminated (Table 2). Therefore we believe that the enhanced absorption is due to a reduction of the hyaluronic acid content in the connective tissue ground substance, which shows itself by the above lowering in the amount of hexosamine. This seems to be confirmed by the equal enhancement of the absorption in dehydrated and fasted mice (Table 1) in which the amount of hexosamine is reduced to the same degree. A possible influence of the water content of the connective tissue on the subcutaneous absorption of urethane is not

likely because of the great differences in the concentrations of water in the connective tissue from dehydrated and fasted mice while the rate of absorption is equal in both groups

Table 1. TIME (SEC) FROM THE INJECTION OF A 10 PER CENT URETHANE SOLUTION SUBCUTANEOUSLY TO MALE MICE (0.30 ml/25 gm) UNTIL THE ANIMALS COULD BE LAID ON THE SIDE WITHOUT RESISTANCE

| Pre-treatment | No of experiments | Mean | Standard error of mean | P |
|---------------|-------------------|------|------------------------|--------|
| Controls | 20 | 1110 | ±75 | — |
| Fasted | 15 | 650 | ±81 | <0.001 |
| Dehydrated | 10 | 650 | ±84 | <0.001 |

Table 2.—TIME (SEC) FROM THE INJECTION OF A 10 PER CENT URETHANE SOLUTION CONTAINING 500 I.U. HYALURONIDASE/ML. SUBCUTANEOUSLY TO MALE MICE (0.30 ml/25 gm) UNTIL THE ANIMALS COULD BE LAID ON THE SIDE WITHOUT RESISTANCE

| Pre-treatment | No of experiments | Mean | Standard error of mean | P |
|---------------|-------------------|------|------------------------|-------|
| Controls | 1 | 435* | ±31 | — |
| Fasted | 16 | 390† | ±33 | >0.1 |
| Dehydrated | 17 | 350* | ±33 | >0.05 |

*Significant different from the corresponding figures in Table 1 according to $P < 0.001$

†Significant different from the corresponding figures in Table 1 according to $P < 0.005$

Dehydrated and fasted animals are in conditions of stress. Cortisone given in pharmacological doses to mice is followed by an enhanced absorption of urethane¹ while the concentration of hexosamine in the connective tissue is unaltered when compared to controls.² However, it is not likely that the enhanced absorption in dehydrated and fasted mice is due to a rise in the production of adrenocortical steroids. The absorption-enhancing effect of cortisone is still pronounced when experiments are performed with solutions containing hyaluronidase, while dehydrated and fasted animals absorb urethane as normal animals when the injected solutions contain hyaluronidase. While the explanation of the absorption-enhancing effect of cortisone is possibly a reduced self-depression of the subcutaneous absorption,^{3,4} the enhanced absorption in dehydrated and fasted animals is more likely produced by the above alterations in the amount of connective tissue ground substance. The concentration of water in the connective tissue seems of less or no importance for the rate of subcutaneous absorption of a non electrolyte such as urethane.

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In Vitro Study of the Anthelmintic Property of *Artemesia monosperma* grown in Egypt

The various species of the genus *Artemesia* have been subjected to pharmacological investigation for the purpose of ascertaining their useful application as therapeutic agents. As there was no mention in the literature to the physiological activity of the santonin free, *Artemesia monosperma*, Del¹, it was deemed of interest to investigate this common Egyptian desert

plant for any possible anthelmintic properties. It was decided that investigations should be made *in vitro* to determine the effects of some preparations of the plant on both *Ascaris* and the intestine and to show whether it possesses a vermifugal or vermifugal property.

Ascaris leonina and strips of the small intestine were carefully taken from freshly killed but infected dogs and kept in Tyrode's solution. The intestinal strips, each about 1 in long, were suspended in oxygenated Tyrode's solution at a constant temperature of 38°C using a glass jar bath with an inner vessel of 50 ml capacity. The same technique was also applied to the *Ascaris* using either the whole worm or its upper part. After recording the normal movements of the intestine and *Ascaris* on a smoked drum paper, the effect of different doses of alcoholic and watery extracts of *Artemesia monosperma* was tested by the addition of their solutions to the organ bath.

The results obtained showed that both extracts produced inhibition of the intestinal motility and stimulation of the movements of the parasite. The effect became obvious and more pronounced as the concentration of these preparations was increased. When comparison was made between the effective doses of these two extracts it was noticed that the watery extract was more potent than the alcoholic extract.

Thus it is concluded that although the drug would appear to be non lethal to the *Ascaris*, it is obnoxious to them and stimulates the musculature causing excessive and acute movements. Such movements may relinquish their hold on the intestinal mucosa so that they are easily expelled by a subsequent purgative. Moreover, the inhibition of the intestinal motility demands the administration of a purgative, and thus helps the expulsion of the already over-stimulated moving parasites from the intestines.

From this investigation it seems possible that *Artemesia monosperma* possesses highly anthelmintic properties. It is recommended therefore, to be given in the form of a watery extract followed after an interval of an hour by a purge which will expel the excited parasites from the intestines.

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Potassium and Lactose in Milk in Relation to the Physiology of Milk Secretion

In a previous communication¹ we reported the interrelationships of the concentration of sodium, potassium, lactose and water in samples of milk taken at intervals over a period of three months from short-horn cows in mid lactation. It was shown that the water of milk can be represented as a two-phase system in one phase referred to as the sodium lactose phase potassium is absent and sodium and lactose vary inversely, in the other, referred to as the sodium potassium phase lactose is absent and sodium and potassium vary inversely. The relative proportions of the two phases were calculated to be on average about 2.5 : 1.0 but it was not possible to deduce from

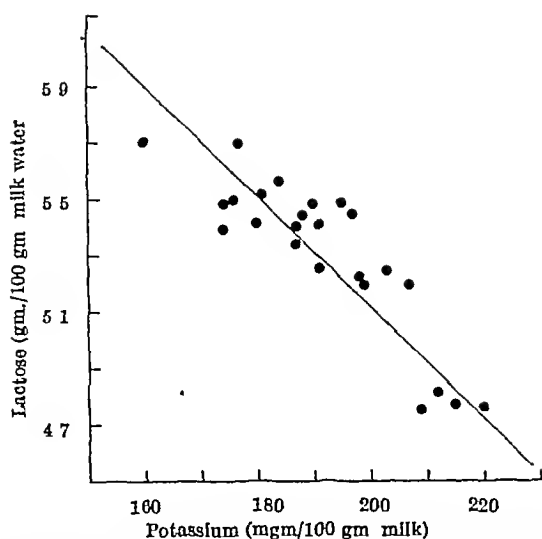


Fig. 1 The relationship between the lactose and potassium contents of the milks of heifers in early or mid-lactation and free from infections of the udder. The line is $y = 8.93 - 0.0191x$, ($P < 0.001$), standard error of estimate, ± 0.16 .

information then available whether, and to what extent, the relative proportions of the two phases varied from animal to animal, or within the milk of an individual animal from time to time.

In continuation of these experimental studies, analyses are now being made of samples of the milk of six Friesian heifers at frequent intervals throughout their whole lactation. A feature of the results has been the constancy of the potassium content of the milk of the individual animals throughout the first 4-5 months of lactation, even during the period of transition from colostrum to normal milk when the changes in other constituents were large. The mean potassium content (mgm/100 gm), with its standard error, for the milk of each of the six heifers, based on analyses of samples of milk collected on twenty separate occasions throughout the first four months of lactation, was 156.3 ± 0.9 , 157.8 ± 1.4 , 159.6 ± 0.8 , 163.7 ± 1.3 , 168.8 ± 1.2 and 174.9 ± 1.3 . Thus, the potassium content of milk appears to be individually characteristic in healthy heifers during the period of full lactation. The lactose contents of the milks showed marked increases during the first two to three weeks of lactation, but in the succeeding three to four months the values for each animal showed a constancy similar to that observed with potassium.

Analyses of the milk of a large number of other healthy heifers in mid-lactation have given potassium contents ranging from 140 to 200 mgm/100 gm of milk and a close inverse relationship between the potassium and lactose contents of the milks has been found (Fig. 1). Previous studies^{2,3} of variations in the potassium and lactose contents of milk have been based on analyses of milk samples obtained from animals varying widely in age and stage of lactation, or on comparisons of the composition of the milk from the separate quarters of the udder of cows infected with mastitis: the data showed a direct relationship between the concentrations of potassium and lactose in milk. With increasing age, advanced lactation and infections of the udder, the potassium and lactose contents of milk decrease and the content of sodium increases, due, it is thought, to a dilution of milk with a transudate of blood plasma². In these earlier studies, variations in composition arising as a result of this dilution have been of such a magnitude that the inverse relationship between potassium and

lactose now observed has been masked.

The present observations with healthy heifers in mid-lactation, showing the constancy of potassium and lactose concentrations in the milk of individual animals and the inverse relationship between the values for potassium and lactose obtained with different animals, suggest that the ratio of the two hypothetical water phases in milk is fairly constant for an individual animal, but varies considerably from animal to animal.

The concept of the water of milk arising in two ways is now seen to be consistent with the mechanism⁴ for the formation of milk within the cells that line the alveoli of the udder. The sodium-potassium phase corresponds to typical intracellular fluid and the sodium-lactose phase would arise by the synthesis within the cell of lactose, together with proteins and fat, coupled with the movement of water into the cell to maintain osmotic equilibrium. The way in which the cell contents are expelled into the lumina of the alveolus has yet to be established, but it is reasonable to suppose that at the moment of expulsion the ratio of intracellular to secretory fluid will be fairly constant in any individual animal, and yet vary from animal to animal, an explanation of the constancy of the potassium content of the milk of an individual animal and of its variation between animals is thus afforded.

The fuller implications of these observations, which include the probability that the rate of synthesis of lactose may determine the rate of milk secretion, will be discussed elsewhere.

We wish to thank Dr S. J. Rowland for his interest in this work and for his helpful advice and criticism.

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BIOLOGY

A New Technique for Isolating and Cloning Cells of Higher Plants

It has recently been shown by several authors¹⁻⁵ that plant tissue cultures grown in liquid media are composed of a population of single cells and small cell clusters. Such cultures represent an excellent source of large numbers of single cells and would be very useful for several types of experiments if the single cells could easily be isolated and grown.

Studies in this direction were made with callus tissue cultures of *Nicotiana tabacum* L. var. Samsun and *Phaseolus vulgaris* L. var. Early Golden Cluster. The tissues were grown in 250-ml. Erlenmeyer flasks on a shaker (120 r.p.m.) in 100 ml. of White's medium⁶ supplemented with 7 per cent coconut milk and 0.5 ppm 2,4-dichlorophenoxyacetic acid. It was found that it was possible to obtain suspensions of uninjured cells by successive filtration of the freely suspended content of the shaker flasks through fine gauze (width of mesh, 0.3 and 0.1 mm) under sterile conditions. More than 90 per cent of the cells present in the filtrate consisted of single cells. The remainder was composed of cells that had divided into two daughter cells just prior to filtration or of two small cells which were attached to each other.

To isolate the single cells from the suspensions the following plating method was used. The filtrated cell suspensions were mixed with molted White's agar medium (0.6 per cent), supplemented as indicated above, and plated in Petri dishes or they were plated on the top of an agar layer in the dishes. The dishes were sealed with rubber bands to prevent desiccation and infection. They were maintained at a constant temperature of 22°C in diffuse light. By making the agar layer about 1 mm thick the cells could

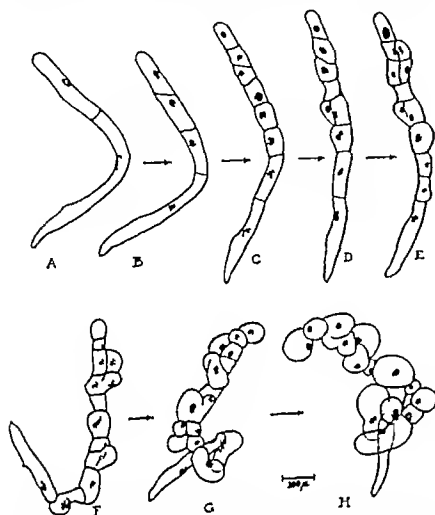


Fig. 1. Diagrammatic drawings, from time-lapse photographs, showing the formation of a cell cluster from an isolated tobacco cell. The pictures were taken after 24, 48, 72, 75, 83, 96 and 120 hr.

easily be observed through the bottom of the dishes at low magnification ($\times 100$) with an inverted microscope.

Microscopic examination showed that cells of *N. tabacum* and *P. vulgaris* isolated in this way were alive that they exhibited an active protoplasmic streaming, and that the first cell divisions occurred 2-4 days after plating. Within 4 weeks about 20 per cent of the single cells had established small tissue clones which could be isolated and grown further. By means of continuous observation, cell divisions and the development of cell clusters from single cells could be followed. Fig. 1 shows, for example, some stages in the development of a cell cluster from a thread-like tobacco cell. As can be seen from Fig. 1, the cell cluster was built up by repeated divisions and growth of the original cell.

The results of the experiments presented above demonstrate that it is possible to grow tissue clones from isolated single plant cells without the presence of a 'nurse tissue'. The described technique has the further advantage of a greater technical simplicity compared with the nurse tissue method used by Muir, Hildebrandt and Riker⁴, for the growth of single cell clones, and the arrangement used by Torrey⁵ for the cultivation and microscopic examination of isolated cells. Full details of this report will be published elsewhere.

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Diffusion of a New Habit among Greenfinches

MANY readers of *Nature* have taken part in a co-operative study of an apparently new feeding habit¹, about which there are now some fairly clear cut conclusions. Two or more greenfinches (*Chloris chloris* L.) will fly some distance to the garden shrub *Daphne mezereum* L., usually in June, to devour every one of its hundreds of large seeds in a strikingly avid and fearless manner. Green and immature fruits are preferred, when the stone of these drupe fruits is not quite so hard. Once a garden has been visited in this way, there is a 95 per cent chance that it will continue to be visited regularly and without intermission.

Bushes in urban gardens are more subject to this despoliation than those in rural gardens ($P < 0.01$). In the south of England the phenomenon is of much more recent occurrence than further north ($P < 0.01$). Indeed, it seems not unlikely that the habit may have originated in some Pennine industrial settlement in the eighteenth or early nineteenth century. At any rate, according to present data by 1900 the habit extended only from Sellark to south Lancashire. By 1930 it extended from Perth to London. And by 1955 its distribution had increased to as far as Inverness in the north, to Deal in Kent, to Ashburton in Devon, as well as to Dublin and Belfast. Since 1925 the number of gardens affected has apparently been doubling every six years. The two vice counties where the incidence is at present greatest are the London ones of Middlesex and south Essex.

Despite extensive inquiries, only negative reports have been received from continental Europe. The habit seems to have originated in this off-shore island, and—rather like the melanism in some moths—it may be an indirect consequence of industrial development and urbanization. In view of its apparent absence from the Continent, and of the fairly slow and orderly spread of this habit in the British Isles, the hypothesis arises that the increase may be solely due to cultural diffusion, following a discovery by a single greenfinch, some one to two centuries ago. This possibility is not inconsistent with the general biology of the greenfinch², though it can in no way be regarded as proved. Certainly the overwhelmingly greater number of fresh despoliations to-day will be due to diffusion rather than to independent discovery. Calculations suggest that the new habit may already have been carried from Britain to the main land. In several gardens, in France for example, *Daphne* bushes may be being stripped already. The

first reports of this arrival, perhaps in the 1960's, will be of interest

Curiously enough, an exactly similar habit of despoliation has now been reported from New Zealand⁴, where both species have been introduced. Retrospective inquiry may be able to suggest whether perhaps some north British settler helped to introduce the habit as well

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An Unusual Breeding Habitat of the Linnet

CONTRARY to the normal habits of the linnet (*Acanthis cannabina*) this species has been found nesting annually in clumps of rushes (*Juncus effusus*) on a hill pasture in north-east Cheshire, grid reference SJ 956925. The rush sites are apparently chosen in preference to more normal sites of which there is no shortage. The habit has so far not been observed elsewhere in the district and would appear to be unusual anywhere.

The pasture is situated on a foothill of the Pennines and faces north-west, sloping from 700 to 800 ft above sea-level. About 12 acres in area, it provides rough grazing for cattle. It is very wet in parts with much rush. On the drier parts are scattered clumps of gorse and there are several hawthorn trees at the lower end. The surrounding land consists mainly of pasture together with some meadow and arable land.

The linnet is a common breeding bird in the district, nesting usually in gorse but also in low, thin hedges of hawthorn and holly, particularly those bordering lanes.

The nests in the rush beds are usually placed near to the top of a clump of rushes, although, in 1954, one nest was placed in a small tuft of grass on very wet ground. The nests are typical of the linnet except that dried rush stems are used in the base material.

The first nest was found in 1952. It was deserted and contained two eggs of linnet and one of cuckoo (*Cuculus canorus*). The pasture was next visited in 1954 when more nests were discovered built in clumps of rushes. Nests have been found each year since. There is no lack of more normal sites even on the pasture itself, and the rush sites are apparently chosen in preference to these.

This year (1959) the first two pairs to breed nested in rushes. These were followed by three pairs which nested in gorse and a sixth pair which also nested in a clump of rushes. Both reed bunting (*Emberiza schoeniclus*) and snipe (*Capella gallinago*) nest in close association with the linnets. The nest and eggs of the linnet are very conspicuous in this unusual habitat, whereas those of the reed bunting, in their natural habitat, are well camouflaged.

While the linnet is known to nest in sea purslane and other tall maritime plants on salt marshes¹, and in marram grass on the Norfolk coast², the rush sites do not appear to have been described before. In the Orkney Islands, the linnet has been found breeding on the ground in cultivated districts, in tall heather, and occasionally in reedy marshes³.

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HISTOLOGY

Histochemical Study of Monoamine Oxidase in the Developing Rat Brain

THE activity of monoamine oxidase was biochemically determined in various portions of the brain^{1,2} and the strongest activity was reported to occur in the hypothalamus. Shimizu, Morikawa and Okada³ recently reported the exact histochemical distribution of this enzyme in the brain of adult rodents using the tryptamine-tetrazolium method⁴. According to our observation, the enzyme action occurred not only in the hypothalamus, interpeduncular nucleus, habenular nucleus and tractus retroflexus of Meynert as other investigators^{4,5} stated, but also most strongly in the locus coeruleus and moderately in the dorsal nucleus of the vagus nerve, midline nuclear group of the thalamus, nucleus of the brachium conjunctivum, central grey matter, nucleus ambiguus and area postrema. From the histochemical result it is assumed that monoamine oxidase may be involved in the metabolism of the visceral regions of the brain rather than in the exclusive participation in the function of adrenergic neurons.

The present study was concerned with the developmental changes of monoamine oxidase in the rat brain using histochemical means. Fresh frozen sections were obtained from the brain of rats at varying ages, foetal ages of 15 and 20 days, newly born, 1, 3, 5, 7, 10, 14, 21 days, 1 and 2 months after birth, and adult. The sections were stained by the tryptamine-tetrazolium method of Glenner, Buriner and Brown⁴. As tetrazolium INT (2-*p*-iodophenyl-3-*p*-nitrophenyl-5-phenyl tetrazolium chloride) was mainly used but nitro-blue tetrazolium was also occasionally used.

At the foetal age of 15 days the enzyme action of the brain was almost negative except for definite regions of the pons, which reacted faintly and probably corresponded to the locus coeruleus and its continuation. On the foetal 20th day moderate to strong action occurred in the locus coeruleus (Fig. 1), and a faint staining was present in the habenula, periventricular grey of the hypothalamus and nucleus ambiguus. In the newly born rat a slight initial action appeared in whole portions of the brain excepting the above-mentioned regions. The locus coeruleus and nucleus ambiguus nearly reached the adult level of the enzyme activity directly after birth, the former showing unusually intense reaction (Fig. 3) and the latter a moderate one (Fig. 2). 1-5 days after birth the enzyme activity was generally similar to that of the newly born rat or slightly increased. From the 7th to 10th postnatal days activity in most regions began to increase in intensity and extent, and about 3 weeks after birth the enzyme activity of each region attained respective adult level. In the adult brain the most intense action was observed in the locus coeruleus, and moderate to intense action was encountered in the following regions: the subfornical organ, supraoptic crest, habenula, midline nuclear group of the thalamus, periventricular grey and medial nucleus of the hypothalamus, tractus retroflexus of Meynert, interpeduncular nucleus, nucleus of the brachium conjunctivum, dorsal nucleus of the vagus nerve, nucleus ambiguus, inferior olivary nucleus, area postrema and ependymal layer of the lateral, 3rd and 4th cerebral ventricles. The enzyme action remained weak or negative throughout the development in the neo-



Figs 1-4 Histochemical distribution of monoamine oxidase in the developing rat brain. Fresh frozen sections were incubated in the following mixture for 30 min at 37°C: 25 mg/ml, tryptamine hydrochloride, 4 g/l sodium sulphate, 5 mmol INT (Figs 1-3) or nitro-blue tetrazolium (Fig 4) 5 ml 0.1 M phosphate buffer pH 7.5, 15 ml distilled water.

Fig 1 Pons at foetal age of 20 days. Showing a moderately strong action of the locus coeruleus (arrow) ($\times 6$).

Fig 2 Medulla oblongata directly after birth. Moderate staining is observed in the nucleus ambiguus (arrow) ($\times 9$).

Fig 3 Pons directly after birth. Intense staining is seen in the locus coeruleus of both sides. Dendritic layer is slightly positive ($\times 6$).

Fig 4 Locus coeruleus at age of 2 weeks. Several strongly positive nerve cell bodies (perikarya) (arrows) and irregular and coarse formazan granules between them (neuropil) ($\times 260$).

cortex, striatum, thalamus nuclei (excepting the habenula and midline nuclear group) mamillary body subthalamus nucleus substantia nigra red nucleus and nuclei of the somatic cranial nerves. In the sections treated by the tryptamine INT method, the formazan crystals were so large and irregular that exact localization of the enzyme action could not generally be determined. If nitro blue tetrazolium was employed as hydrogen acceptor, it became clear that the formazan granules occurred not only in the perikaryon but also in the neuropil (Fig 4). But it was undecided whether the coarse formazan granules within the neuropil are due to the true enzyme action in the same localities or diffusion from the strongly reactive perikaryon.

Very little work has been done on the development of amino oxidase during growth. Biochemical study by Birkhäuser¹ has shown that monoamine oxidase of the thalamus, caudate nucleus and cortex is evidently less reactive in the small children than the adults. According to Eppe² the kidney cortex and medulla were poor in amino oxidase in the newly born child, but showed an increase of activity until the child was 3 months old when the mean activity remained constant. Eppe found no variation of activity with age in the liver and mucosa of the ilium.

From our observation it became apparent that each region of the brain does not always follow the same developmental pattern in the make up of monoamine oxidase. The locus coeruleus and nucleus ambiguus showed the characteristic pattern different from other portions of the brain. Namely the locus coeruleus demonstrated an intense action (nucleus ambiguus a faint action) already in the late foetal life, attained maximal intensity in the newborn and maintained nearly unchanged level of activity throughout postnatal development up to the adult. The remaining portions of the brain were negative or slightly positive for the enzyme activity in the late foetal or new

born life, began to increase their activity from 7th to 10th day and reached adult activity in 3 weeks after birth.

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A Dense Lamellar Structure Found in Conjunction With Cell Membranes in the Anterior Pituitary Gland

RECENTLY it has been shown that the cell membrane in many different types of tissue cells is a triple layered structure ~ 75 Å across and consisting of two dense layers ~ 20 Å wide separated by a somewhat wider less-dense space. Robertson¹ has suggested that this 75 Å unit represents one bimolecular leaflet of lipid the polar surfaces of which may be covered by non lipid material. In view of this work it was thought interesting to report the occurrence of



Fig 1 A dense lamellar body lying across two adjacent plasma membranes. The mean distance from the centre of one dense line to the centre of the next is ~ 40 Å. At either end of the structure one of the dense lines may be seen to run directly into the plasma membrane. ($\times 40,000$).

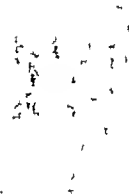
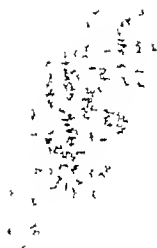


Fig. 2 Three dense lamellar bodies lying close together on two adjacent cell membranes ($\times c$ 570,000)

phospholipid-like material in close conjunction with cell membranes

The material used in this study, small blocks of tissue from the anterior pituitary of the mouse, was fixed in buffered isotonic osmium tetroxide and additionally stained by soaking in a saturated solution of phosphotungstic acid in absolute alcohol for 12 hr, after dehydration in an alcohol series. The tissue was embedded, after preliminary soakings for up to two weeks, in 'Araldite'. Sections were cut on a Huxley ultramicrotome and collected on 200-mesh copper grids which had not been coated with a supporting film. Such sections when carefully cured in the electron beam are entirely stable for high-resolution microscopy. Examination of specimens without a supporting film gives a considerable increase in both contrast and resolution. Although the sections used in this study were measured in an interference microscope to be about 1000–1200 Å thick, the resolution obtained was better than 30 Å. Sections were examined and photographed in a Metropolitan-Vickers EM 6 electron microscope.

In survey micrographs of anterior pituitary tissue the plasma membrane of each cell can be seen to be 'dotted' with very small, distinct, electron dense bodies, which at instrumental magnifications of 36,000 or higher can be resolved into periodic structures con-

sisting of numerous dense lines ~ 20 Å wide separated by somewhat wider clearer spaces. The mean repeat distance in these structures is ~ 40 Å and this is constant in all the bodies so far examined. Frequently a ~ 75 Å wide unit of the lamellar body, consisting of two dense lines bounding a lighter zone, may be seen to run directly into the plasma membrane upon which the lamellar body lies.

Stoeckenius² has recently published micrographs of myelin figures obtained from solutions of phospholipid spread on water, and a comparison indicates that these dense lamellar bodies and *in vitro* myelin figures are remarkably similar both in appearance and in the ~ 40 Å repeat distance.

It seems possible therefore that these dense lamellar bodies may represent accumulations of phospholipid lying in close conjunction with cell membranes and this assumption is consistent with the current belief that phospholipid is a major constituent of cell membranes.

My thanks are due to Mrs A. Cosslett for her kind interest and help in cutting the sections and measuring their thickness, and to Dr D. B. Cater for his advice and encouragement.

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PATHOLOGY

Infectivity of Polio Virus Ribonucleic Acid for Embryonated Eggs and Unsusceptible Cell Lines

THE isolation of ribonucleic acid from various viruses grown in animals or in tissue culture systems has been reported recently. These preparations have been shown to be infectious for susceptible cell monolayers.¹⁻⁵

In the course of experiments with a ribonucleic acid preparation extracted from polio virus, we have investigated the possibility of adapting polio virus type I to the chick by inoculating infectious ribonucleic acid into embryonated eggs. Our aim was supported by the idea that numerous specific properties of virus being linked to the protein component, it could be possible that, by losing its protein coat, the infectious particle would also lose its specificity for certain cells and be able to invade cells unsusceptible to polio virus. The progeny of such infectious units might eventually exhibit new properties as to its virus-cell relationship.

Ribonucleic acid used in our experiments was prepared by the technique of Gierer and Schramm⁶, from polio virus type I (Mahoney strain) grown on monkey kidney cells. This virus strain was selected for its lack of infectivity for the chick. The infectious activity of the ribonucleic acid preparations was tested on monkey kidney cell monolayers using the plaque technique of Dulbecco.⁷ The average yield of infectious ribonucleic acid was about 0.01 per cent of the treated polio virus titre. We confirmed the observations of others²⁻⁴ that an optimum infectious titre is obtained when ribonucleic acid is used in 1.0 M sodium chloride.

Table 1 INFECTIVITY OF RIBONUCLEIC ACID (RNA) PREPARATION BEFORE INOCULATION IN EGG (PLAQUE FORMING UNITS PER ML.)

| Time of recovery (hr) | RNA | | | | | | RNA with RNA ^a | | | | | |
|---|------------------------------------|----|-----|-----|----|-----|--------------------------------------|---|---|---|---|---|
| | 73 | 80 | 103 | 116 | 07 | 123 | 0 | 0 | 0 | 0 | 0 | 0 |
| INFECTIVITY OF ALLANTOIC FLUIDS RECOVERED AT DIFFERENT TIMES AFTER INOCULATION OF RIBONUCLEIC ACID (0.2 ML INOCULUM)* | | | | | | | | | | | | |
| Time of recovery (hr) | Allantolite fluid alone | | | | | | Allantolite fluid + RNA ^a | | | | | |
| | No. of plaque forming units per ml | | | | | | No. of plaque forming units per ml | | | | | |
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 24 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 48 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 00 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

C = Confluent area (more than 250)

* Inoculation into 20 embryonated eggs at the eighth day of incubation. 5 samples are harvested at each time numbered after 4 days. Plaque-forming unit counts are

the saline acts by inhibiting the activity of cellular ribonuclease⁸.

In the first series of experiments ribonucleic acid (0.2 ml) was inoculated into the allantoic cavity of embryonated eggs at the eighth day of incubation. These eggs were kept at 37°C, and samples of allantoic fluid were harvested at different times. The infectious activity of these samples was tested on monkey kidney cell monolayers.

Table 1 summarizes the results of a typical experiment. Most of the allantoic fluid samples are infectious for the tissue culture system. The yield of these samples exhibits a large variation: maximum plaque forming units being observed 12-24 hours after inoculation.

The main point is that the infectious activity of this material is not inhibited by ribonuclease. Furthermore it shows a much higher thermostability than ribonucleic acid preparations.

A standard preparation of ribonucleic acid loses all its infectivity after 6 hr at 37°C. For these reasons, we believe that the allantoic fluid samples contain whole polio virus. This opinion is sustained by the fact that attempts to produce passively coated ribonucleic acid, by mixing ribonucleic acid preparations with BSA serum albumin or normal allantoic fluid *in vitro*, did not succeed in protecting ribonucleic acid infectivity against ribonuclease and temperature.

Another important point is that the average number of plaque forming units observed is consistently higher than the plaque forming unit titre of the inoculated ribonucleic acid preparation. In the reported experiments 0.2 ml ribonucleic acid is inoculated into a total volume of allantoic fluid of about 0.1 ml. This dilution factor of 1/30 implies that normally the allantoic fluid samples should not contain more than 3 or 4 plaque forming units/ml. The fact that we found consistently a higher number of plaques about 20-80 times more can be explained in two ways.

(1) If the ribonucleic acid preparations contain more infectious units than we actually observe in our tissue culture system it could be possible that these units have acquired a particular protection from the chick embryo fluids so that more infectious ribonucleic acid is found in the allantoic fluid samples. This hypothesis has not been confirmed by *in vitro* assays. The combination of ribonucleic acid and normal allantoic fluid failed to maintain the infectivity of ribonucleic acid. This failure is probably due to the presence of ribonuclease in allantoic fluid.

(2) That some ribonucleic acid particles are able to invade and to replicate into cells which normally are not susceptible to polio virus. The new particles

emerging from the infected cells after multiplication, are whole polio virus and therefore are not infectious any more for the chick embryo cell system. In conclusion this hypothesis would suggest a one cycle multiplication performed by a certain number of ribonucleic acid particles, the other ones being inactivated either by enzyme or by heat. This hypothesis would account at the same time for the increase and for the variation in the number of plaque forming units observed in our experiments⁷.

In further series of experiments we have demonstrated that polio virus present in allantoic fluid samples is not infectious for the chick so that our original aim of adapting polio virus to the chick by this method did not materialize.

An important question is raised by our results with the fact that ribonucleic acid would be able to replicate in unsuspensible cells. The question is to what extent the cell susceptibility to a particular virus is dependent upon the reaction between the specific viral protein and the corresponding cellular receptors. This could be investigated by a systematic study of the comparative susceptibility of different cell lines to viruses and their ribonucleic acid preparations.

Preliminary experiments in this field have demonstrated that this one cycle multiplication of polio virus ribonucleic acid did not happen in a continuous cell line (DET) from a rat tumour⁸. These results indicate that infectious ribonucleic acid is not able to produce polio virus in any type of cell.

As a general conclusion it appears that infectious ribonucleic acid does not require the presence of a special cellular affinity to invade cells and, therefore is able to perform a replication of virus in certain unsuspensible cells. But virus-cell relationship also depends on the available nucleic material present in a particular cell.

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Within the nucleus the highest specific activity is restricted to certain chromosomal sites (Fig 1). All these sites correspond to those found to be rich in ribonucleic acid by the meta-chromasy after staining with toluidine blue. Some, but not all, of the highly labelled bands appear puffed in the morphological sense, so that even very fine ribonucleic acid bands may show a high uridine incorporation. Activities found in different bands of the same chromosome cover a wide range. The pattern of incorporation does not vary appreciably from nucleus to nucleus within one preparation (except the 'special' cells mentioned above, and except when deoxyribonucleic acid replication occurs). The differences between individuals, however, appear to be considerable. Two of the three large 'Balbiani-rings' of the 4th salivary gland chromosome of *Chironomus tentans* regularly show intense labelling, even if only 15 min have passed after injection of the uridine. The highest activities were observed in the nucleoli, but the incorporation of the uridine does not occur throughout the nucleolus as a whole

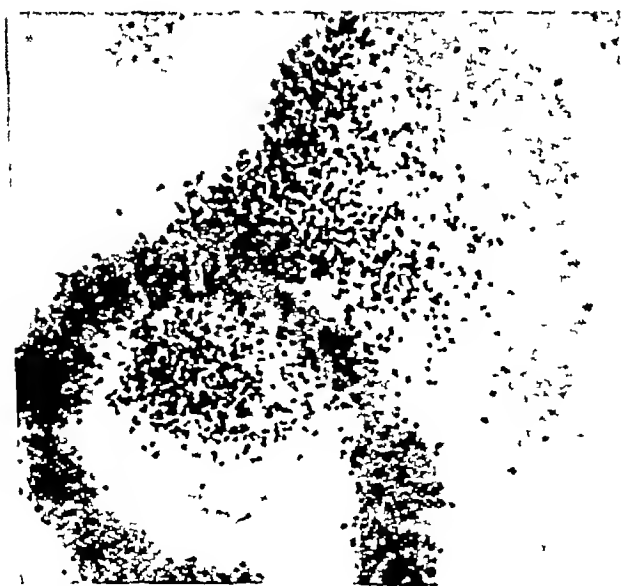


Fig. 1. Salivary gland chromosome I of *Chironomus tentans* 40 min after injection of uridine labelled with tritium into 4th instar larva. Preparation focus and photographic layer focus.

Fig. 2. Nucleolar labelling by uridine-labelled with tritium spreading out from the 2nd chromosome organizer region 60 min after injection of the uridine.

It appears at first in the neighbourhood of the two nucleolar organizers, located in the 2nd and 3rd

chromosomes, respectively (Fig 2). As incorporation time progresses, larger areas around the two synthesizing regions become labelled. This way of uptake of the radioactive material may provide a measure for the rate of synthesis. Its speed varies in different larvae. In some animals the nucleoli are found to be completely labelled after 40 min, in others only after 6 hr. The differences seem partly to be due to sudden changes in temperature.

The experiments permit the following conclusion: The nucleolar ribonucleic acid is synthesized at the nucleolar organizers only. Synthesis of ribonucleic acid proceeds continuously, and with respect to its own ribonucleic acid the nucleolus represents nothing but a 'station of transit'. Many other sites of the chromosomes are also involved in synthesis of ribonucleic acid, the bulk of the ribonucleic acid being produced by a few very active loci. This latter observation confirms earlier interpretations of the phenomenon of differential puffing in dipteran giant chromosomes⁴. According to these earlier hypotheses the functional differentiation of cells consists in the development of specific patterns of gene activity.

Finally, ribonucleic acid synthesizing structures show no activity after short application (up to 2 hr) of radioactive amino-acids (glycine-¹⁴C, tryptophan-³H, methionin-³⁵S). Protein synthesis seems not to be correlated with synthesis of ribonucleic acid. The connection between synthesis of deoxyribonucleic acid and protein in chironomid salivary glands is subject to further investigations.

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Cytochemical Study of Mitochondrial Structure

A CHARACTERISTIC morphological pattern of organization of mitochondrial structure has been repeatedly described by Palade¹, Sjöstrand², Rhodin³ and various other workers using electron microscope studies, according to which each mitochondrion consists of a limiting membrane, cristae and the mitochondrial matrix with granules or particles in it. During the cytochemical study of the oocytes of the various fresh water fishes, I^{4,5} have defined a cytochemical pattern of mitochondrial structure. The mitochondria of the fish oocytes are granular filaments with uniform thread-like contour. Such a structure is revealed both vitally under phase contrast microscope⁶ and cytochemically in the tissue prepared according to Baker's⁷ lipid preserving formaldehyde calcium fixative. A similar structure is seen in the tissue fixed in osmium solution or osmium-containing fixatives, that is, Champy's and Lewitsky's (Flemming-without-acetic) fluids. However, their filamentous structure is completely destroyed in fat solvents or fixatives consisting of fat solvents and strong acids, for example, Bouin and Carnoy's fluid, after which treatment their fine granules are observed to be randomly scattered in the cytoplasm. The mitochondrial filaments are coloured deep blue in sudan black B but this deep coloration is confined more rigidly at the periphery and at the

interspaces between the fine granules of mitochondrial filaments. The granules in the mitochondria remain distinct by their feeble coloration in sudan black B. The peripheral sudanophil material is positive to Baker's⁷ acid hematin technique revealing phospholipids, but is completely negative to all other lipid tests. Its exclusive lipid nature is further revealed by its negative reactions to Mazia's⁸ mercuric bromophenol blue test for proteins and by periodic acid schiff technique for carbohydrates. The granular component of mitochondria consist of abundant proteins, and in addition show some lipo-proteins revealed by Pearse's⁹ extractive technique. Thus the mitochondria structure consists of a basal phospholipid sheath, in which numerous protein granules are embedded.

The above structure of mitochondria revealed by cytochemical data can be correlated with the structural pattern concluded by electron microscopy, which seems to be an image study of the structure produced by a definite arrangement of phospholipid molecules of the basal sheath under the influence of the fixative containing osmium tetroxide. The various membranes observed in the electron micrographs of different workers may be formed due to the tendency of phospholipid molecules to arrange themselves in bimolecular membranes under the effect of phospholipid/water complex, and osmium metal. Schmidt¹⁰ believes one end of the phospholipid molecule is hydrophil while the other is hydrophobe and the hydrophobe ends of two molecules associate with one another whereas the hydrophil ends associate with water. The membranes seem to be formed in the basal sheath by the arrangement of these phospholipid bimolecules which come to lie in lateral association with each other due to intermolecular forces (Fig. 1). As suggested by Baker¹¹ the binding of the bimolecules is further strengthened and they are pulled more nearly parallel with one another due to the chelation of osmium at the unsaturated links of fatty acid chains which are very common in naturally occurring phospholipids. According to Criegee¹² such chelation of osmium occurs due to oxidative effect of osmium tetroxide on fatty acid chains. The binding of phospholipid bimolecules into definite membranes by intermolecular forces and by osmication seem to be possibly noticeable only in the ultrathin sections used in electron microscopy. The parallel or double membrane system noticed in the electron micrographs may be formed by two osmophilic layers with a narrow osmophobic layer in between. The calcium also strengthens molecular binding due to which the true filamentous form of mitochondria remains intact in formaldehyde-calcium fixative. However, the filamentous structure of these inclusions is destroyed in acids and fat solvents due to the dissolving out of the basal phospholipid sheath.

The cristae of Palade¹ which are nothing but osmophilic phospholipid material of basal sheath in the interspaces between the protein granules, have also the tendency to form molecular membranes observed in the electron micrographs. However the form of cristae¹ may be varying in relation with the size, density and arrangement of the protein granules in the basal sheath. The granular component of mitochondria had been described by various authors under different names as large microsomes, small mitochondria, submicroscopic granules etc due to their varying appearance though some of them interpreted them as artefacts. These granules are speculated to be the true functional units of mitochondria controlling



Fig. 1 A hypothetical illustration of the arrangement of phospholipid bimolecules forming membranes (m) and cristae (c) in the basal sheath (b.s.) of the mitochondria containing protein granules (p.g.)

the enzymatic activity, and may be constantly changing under their important functional process. However some enzymatic activity is likely to be noticed in phospholipid basal sheath because of the diffusion of enzymes through it.

This work was carried out in Punjab University Laboratories, India

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GENETICS

Fertility Factor in *Salmonella typhimurium*

14 crosses between *Salmonella typhimurium* strain LT7 and *Escherichia coli* strain K 12 Hfr. It was found that recombination occurred only when the *Salmonella* strain carried a mutator factor, presumably a mutator gene (*mut*). Earlier studies had shown that the main effect of *mut* is to increase the rate of spontaneous mutation of virtually all genes with which it was tested¹.

Hybrids from the experiment *S. typhimurium* *mut* × *E. coli* HfrCS 101 were crossed with *E. coli* HfrCS 101. Frequency of recombination in the hybrid × *E. coli* experiment was 10⁻⁴ to 10⁻⁵, that is 10² to 10³ times higher than the frequency in the *S. typhimurium* × *E. coli* cross. Two explanations of this phenomenon were considered and tested: (1) that the greater fertility of the hybrid was due to the presence of chromosomal or cytoplasmic material derived from the *E. coli* parent (2) that it resulted from mutation of a fertility factor in the *S. typhimurium* parent either chromosomal or cytoplasmic stimulated by the *mut* gene.

The following test was designed to determine whether it was possible to obtain a highly fertile *S. typhimurium* strain that had never been in contact with *E. coli* a result which would favour explanation (2). *S. typhimurium* having the genotype constitution *pro* 4 214 *mut* was plated (in 0.1 ml. samples contain

ing about 200 cells) on nutrient agar plates. After 24-hour incubation at 37°C, the colonies present on these plates were replica-plated on minimal-lactose proline medium which had just been spread with 0.1 ml of an overnight broth culture (about 2×10^8 cells) of *E. coli* HfrCS-101. The selection markers in this test were *met* (methionine requirement) in CS-101 and *lac*⁻ (inability to utilize lactose) in the *Salmonella*, and both these markers are so stable that no spontaneous revertants were observed. After 48-hour incubation at 37°C, samples were taken from colonies on the original nutrient agar plates which showed *lac*⁺-recombinants on the printed plates. Cultures grown from single colonies derived from these samples were tested for fertility. The tests showed that many of the original colonies, grown without any contact with *E. coli*, possessed high fertility. The cells derived from them recombined at frequencies between 10^{-4} and 10^{-5} with all Hfr strains tested (CS-101 C³ H⁴, and P4X₆), and showed recombination also with the non-Hfr strain K-12 F⁺ RT-18 (*met*) with frequencies between 10^{-7} and 10^{-8} . The last-mentioned strain was obtained from Prof. P. Fredericq, and strain P4X₆ was kindly supplied by Dr. F. Jacob.

These results indicate that a population of *S. typhimurium mut* is a mixture of fertile and infertile cells (about 1/100), and that only the former recombine with *E. coli* Hfr. Since attempts to obtain a fertile strain from *mut*⁻ bacteria were not successful, it appears probable that the *mut* gene increases the frequency of changes from the infertile to the fertile condition.

As mentioned above, recombination occurred in experiments with the fertile strain of *Salmonella* and an F⁺ strain of *E. coli*, although at lower frequencies. Therefore, it is possible that the fertile strain of *Salmonella* is F⁻ whereas the original strain is F⁺, and that the percentage of change from F⁻ to F⁺ is increased by the presence of the mutator factor.

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Induced Mutations of X-Ray Irradiations in *Culex fatigans* Wied (1828)

To explore the possibility of linking a visible morphological character with the resistant gene for the study of population genetics of resistance of insects to insecticide, mutations were induced in *C. fatigans* by exposing them to X-rays.

Normal laboratory-bred *C. fatigans* pupae were allowed to hatch individually in 3 × 1 in specimen tubes. The mosquitoes on hatching were fed on 10 per cent glucose solution for 48 hr. 108 female and 74 males were irradiated with a total dose of 4150 r (kV, 150, m amp, 15, fod, 40 cm, filter, nil) during 60-min exposure. 32 and 48 per cent mortality occurred among the irradiated male and female mosquitoes respectively within 24 hr after exposure. The surviving mosquitoes were allowed to mate, and the females were afterwards fed on a bird. 25 egg rafts were obtained of which 23 hatched out.

Out of a total of 3251 eggs, 2055 larvae were obtained (174 eggs were embryonated but did not hatch and 1022 eggs were unembryonated). The total number of

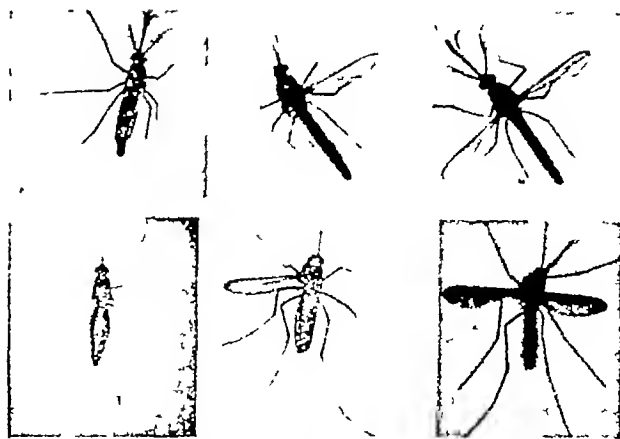


Fig. 1 Male and female *C. fatigans*: a, both wings closed (normal); b, one wing spread (right or left); c, both wings spread.

adults thus obtained were 1456. These were carefully examined for any morphological aberrations. The following were noticed:

- (1) 7 female and 4 male mosquitoes with wings intact but incapable of flight
 - (2) 3 female and 4 male mosquitoes with short wings
 - (3) One single female with an additional branch to long wing vein No. 4
 - (4) A single male with both wings spread out.
- Efforts to rear the mosquitoes with the first three mutations failed.

A single male with the spread wing (*spw*) aberration, however, was successfully mated with 4 normal females in a glass jar 6 × 3 in. The females were afterwards fed on a bird. Three egg rafts were obtained, out of which only one hatched to produce 72 larvae (a high mortality among the embryonated eggs was recorded). These were reared in the laboratory to obtain the F₁ generation. 31 females and 19 males hatched out, of which 5 females and 4 male mosquitoes had one wing spread out (+/*spw*). These were inbred to obtain the F₂ generation. Details of the F₂ adults hatched are given in Table 1.

| Total No of mosquitoes hatched | | No with both wings spread out (<i>spic/spic</i>) | | No with one wing spread out | | No with both wings closed (+/+) | |
|--------------------------------|----|--|----|---|--|---------------------------------|---|
| | | | | Right wing spread out (+/ <i>spic</i>) | Left wing spread out (<i>spic</i> /+) | Normal | |
| F | M | F | M | F | M | F | M |
| 32 | 74 | 16 | 53 | 5 | 9 | 4 | 7 |
| | | | | | | 3 | 4 |

Male and females of the F₂ generation with both the wings spread out (*spw/spw*—phenotypes) were inbred. 13 egg rafts were obtained. Out of a total 1695 eggs 415 larvae hatched. A total number 295 adults were thus obtained. 89 mosquitoes had both wings spread out, 100 had only one wing spread out, and 106 had both the wings closed.

'Spread-wing' is a non sex-linked mutation controlled by a single gene, most likely neutral and with high penetrance. As is evident from Fig. 1, this mutant character is easily detectable with the naked eye. The only other known mutations in this species are micro-mutations as described above and by Kitzmiller².

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MASS MEDIA OF COMMUNICATION AND SCIENTIFIC DEVELOPMENTS

IN his Rede Lecture "The Two Cultures and the Scientific Revolution", Sir Charles Snow pointed out that a knowledge of science among the public was one of four essential conditions if Britain was to meet the challenge of the scientific revolution and, by seizing the opportunities that revolution offers, avoid a steep decline in our standard of living. This knowledge was necessary not only for politicians and administrators but also for the whole community who should know enough science to have a sense of what the scientists are doing. This involves, as Sir John Cockcroft has pointed out, a definite effort to remove the language barrier between the public and the scientist, which makes it difficult even for those who are aware that science affects the life of the community to understand how science works and its implications for the community. Sir John thought that in the everyday business of administration scientists had mostly succeeded in their effort to explain their work in plain language to politicians, civil servants, diplomats and business men but this is only a part of the problem of communication. It is no less important that science should be better understood by the man in the street.

This is in part a problem of formal education. Increasingly it is also a matter of using effectively the ways of communication at our disposal, and this means especially the mass media of the popular Press, sound broadcasting and television. Only if wide and effective use is made of these media can we hope to keep the public sufficiently informed about scientific and technical advances for such discoveries to be put to either personal or public use, and, no less important, for the possibilities of abuse to be eliminated or minimized. Nor is this entirely a matter of appropriate techniques or of the standard of public education. We need to know much more about the way in which scientific information reaches the public and how much of it really penetrates to the public consciousness, and about the general attitudes, or even prejudices, regarding science and scientists which certainly exist in the minds of the public.

These questions have been examined in a series of surveys sponsored by the National Association of Science Writers, Inc. of the United States (Five Longview Road, Port Washington, N.Y.), and although the reports relate strictly to the United States, their findings and conclusions are unlikely to be entirely invalid in Britain. The surveys point to obstacles which exist no less in Britain than in the United States and they suggest ways in which communication could be improved here also, and dangers which threaten in differing degree rather than in differing kind. Moreover, while a similar survey in Britain might not establish the existence of a large reservoir of interest in science reporting, with readers, listeners and viewers prepared to surrender other news and entertainment features to become better

informed about science, it might well disclose the existence of sufficient interest to halt the present lowering of standards. Indeed, failure to do so would provide a damning indictment of our educational system and point to an early decline to a third or fourth rate power.

The first of these reports, *Science, the News and the Public*, describes a sample survey of 1919 American adults selected to represent a cross section of the public conducted by the Survey Research Center, University of Michigan and also sponsored by New York University, to ascertain who got what science news, where they got it and what they think about it. The second report, *The Public Impact of Science in the Mass Media*, describes a nation-wide survey conducted by the same Center and supported by a grant from the Rockefeller Foundation with the specific objectives of ascertaining the size and composition of the major mass media audiences, how science news fits into the news-reading patterns of the newspaper audience, and the conceptions and attitudes of the public relating to science and scientists, determining the size and characteristics of the science audiences of the media describing the content of science news which has been read, heard and seen, obtaining the science audiences' evaluation of the way in which science news is presented, analysing the social and psychological factors that affect the consumption of science news, examining the effect of differential wording of science news items on the level of reader interest and estimating the distribution of science information among the public. This survey was based on a pilot study in 1955 of a non-random sample of 200 respondents. The third report, *Satellites Science and the Public*, describing a national survey of the impact on the public of early satellite launchings, is a follow-up of the main survey. It was conducted a year later, and it is focused on the changes revealed in the answers to questions regarding the Earth satellites put before and after the launching of the first satellite.

The first report provides evidence that in the United States the mass media could reasonably increase the present cover of scientific developments, and it is argued that, with increasing numbers of students in high school and college, many of whom will be studying science, there should be a great expansion in the demand for science coverage in the channels of popular communication. Much of the information in the mass media does reach the public mind, and on the evidence of this survey an impressive amount of this science information is retained. The report once again directs attention to the room for improvement in the popular reporting of scientific developments, but beyond the observation that reporters and script writers, given more training and time in assignments, would be able to provide more details, greater background, better interpretation

and, possibly, higher accuracy, the report does not pursue this important theme. It is conceded that such changes might help to correct present distortions in the public image of science and scientists and promote the idea that they are part of, not divorced from, contemporary living, but the conclusion stands that science is not constantly covered in the United States and that Americans lack information on which to decide intelligently public matters involving science, scientists, and possibly their own existence.

These conclusions are substantially supported by the larger study. Available evidence suggests that even allowing for a possible boom in science news stimulated by the launching of Earth satellites, the mass media are transmitting only a microscopic part of the supply of scientific information potentially available. Since 76 per cent of the sample could recall one or more science items they had read or seen recently, 64 per cent recalling at least one item from the newspapers, 34 per cent from magazines, 13 per cent from radio and 41 per cent from television, it would seem that the demand has been greatly under-estimated.

In the United States the mass media together cover all but 1 per cent of the private dwelling units of the country and at least a quarter or a third of every social category uses three media. Papers appear to be the primary source of general views, and while the greatest change in the media used during the past decade has been the rapid spread of television, the written media have held their audiences well. The combined science audience appears to include three out of four adults, and newspapers are the most important source of science news and radio the least. Papers, magazines and television are mutually supplementary as sources of science news, but radio is weak both as a primary and secondary source. Newspapers appear to take a key role in transmitting both science and medical news to this large science audience and there is generally a positive reaction towards science as it is presented in the mass media.

The report then analyses in a separate chapter more particularly the newspaper audience, the magazine, radio and television audiences being considered in a following chapter. While it is clear that science news is not read solely by the intellectual *élite*, the survey suggests that reading of non-medical science news is associated with a cosmopolitan and rather intellectual orientation towards news content, while medical news tends to be read by those with a more personalized local point of view. Education and income-levels are reflected in science reading of both types and also in the extent to which actual news items are recalled. Even in the social categories least prone to read science news, a sizeable minority is reached by the presentation of science in the Press.

As regards magazines, the survey points to a relatively *élite* audience compared with the other media, and in general magazine readers of science in the United States appear to be highly satisfied with the way their medium presents science. The newspaper is

the most important supplementary medium for these readers. The radio audience of science, however, appears to be scanty, and although the audience is spread very evenly through the population, the completeness and accuracy of science news on the radio receive adverse comment. Again, the newspapers provide much supplementary information for this group. Television has not yet challenged the lead of the newspaper, and its potentialities for the transmission of science news are regarded as largely unexplored, but there is evidence in this report that a good deal of care will be required in developing this field if science information is to be presented without exaggeration and distortion.

Subsequent chapters consider briefly the forms and channels in which science news is presented in relation to effective presentation, but the data are too scanty for more than tentative evaluations of presentation to be made. The evidence indicates that additional interest is more readily stimulated the more a person is already interested in science, but nevertheless more vivid or stimulating presentation does affect those who are not already interested or trained in science. Education in science is, however, important as providing both the necessary background and a sensitivity to scientific topics. The evidence presented in this report fully supports the argument that sufficient general science should be a part of the education of every citizen to enable him or her to understand how science works, what it is about and something of its meaning in the world to-day.

This factor can obviously determine attention or indifference to science news and the report seeks to analyse these motives. Most of those interviewed were willing to have other news cut to get more science news in the papers, but the reasons for interest in science most cited were fairly broad, and orientation to science seemed to serve the broader functions of making sense of the world and helping to manage one's relations to it. This, of course, indicates the importance of presenting science in its context and not presenting pieces of information or facts in isolation.

Finally, the survey examines the current attitudes to science and the world which go so far to determine the public understanding or misunderstanding of science as it is presented to them to-day. When asked to strike a balance of the effects of science on the world the public overwhelmingly stresses the good effects. These are seen primarily as improvements in health, standard of living and technological advance, and the direct ill-effects on the world are seen almost entirely in terms of the destructive potential of nuclear energy. Concern about the detrimental effects of science on the social order and the deviating traits of scientists was an underlying theme, and the report, besides noting that people who are highly concerned about such issues are likely to advocate limiting scientific research, points out that in times of crisis these ambivalent attitudes could lead to a more negative picture of science.

The report on the survey of the public impact of early satellite launchings shows that almost half the adult population of the United States became aware of the satellites in a single year 90 per cent had heard of the satellites by mid 1958 compared with less than 50 per cent a year earlier Less than one third of those aware of the satellites thought of them as having primarily an immediate scientific purpose, about one fourth knew of no purpose Both awareness of the satellites and of their scientific purpose was related to the education, income and number of media used by the person and the evaluation of science and scientists was overwhelmingly favourable in both these comparative surveys Within the newspaper audience there was a moderate increase in readership of science

The comparative survey provides further evidence that awareness of a scientific event or finding can be stimulated in all strata of the public if enough news concerning the event can be made available to the audience, and that it is probable the public reaction to a scientific event is largely determined by a desire to understand and master the world as seen by the individual Increase of interest in a particular area of science due to a major break through in knowledge or achievement is unlikely to stimulate interest in other scientific areas unless the public sees definite links between the areas The pattern of public reactions to science and scientists is a complex and pervasive phenomenon, and the generally favourable attitude to science and scientists is regarded as more stable than the public's notions of the boundaries of scientific endeavour Science and scientific events however, do not operate in a vacuum and some aspects of the public's evaluation of science are liable to change It seems likely that the public is less concerned with what science is than with what it accomplishes

These generalizations are scarcely new to the scientific writer and are indeed part of the everyday technique of communication On the actual technique of communication, however, these reports throw little light They are of interest to British readers rather for the attention they direct to certain dangers as well as to trends and objectives in the use of mass media and perhaps especially to the fundamental importance of education They underline indeed the importance of the investigation of the educational potentialities of the mass media on which Mr J Trenaman has been engaged for the past three years with the support of the Nuffield Foundation and provide substantial evidence that effective use cannot be made of the mass media, and perhaps especially of television, if our educational system is defective Shortcomings there will not be remedied by the mass media

Indeed, if one generalization is to be drawn from these reports, it is that the mass media are unlikely to prove a reliable method of increasing the public understanding of science unless the mass audience has itself already been prepared by its general formal education to understand what science is about and the place it takes in the world to-day Without

thus the dangers of abuse, particularly of broad casting and television, to which renewed attention was directed in the debate in the House of Lords on June 3, and by Mr H Carleton Greene, the recently appointed director general of the British Broadcasting Corporation, in an address* to German business men on April 18, and by Dr M Conran in his article on the Third Programme, will remain formidable There is little in the American survey to suggest that Field Marshal Smuts was unduly pessimistic in regarding the disappearance of the sturdy independent minded, freedom loving individual and his replacement by a servile, standardized, mass mentality as the greatest human menace of our time Indeed, it is almost inherently impossible for the mass media themselves to check this process Lord James of Rusholme in the Lords debate remarked that one cannot use all the techniques of mass persuasion appeal consistently to the facile the uncritical and the escapist, and still talk of freedom

The debate in the House of Lords did not resolve this issue It focused attention rather upon the question of public responsibility, and strong support was forthcoming for the view that television as well as sound broadcasting should be made entirely responsive to the public interest and whether in the public or in the private sector subject to impartial review Lord James was forthright on the importance of this sense of public responsibility and of television and broadcasting being independent of any political or commercial pressure, so that new facilities could be freely used and in new ways if we are to foster an educated democracy as critical, as knowledgeable and as free as we can make it

There was little support in the debate for further extension of television programmes but some for the improvement of programmes and for technical research Lord Hailsham seemed to stand alone in his reply for the Government in professing satisfaction with the present position and no concern about the possibility of abuse or debasement of standards This was Mr Carleton Greene's main concern however, and arguing that radio and television are too powerful in the potential long term effects for their control to be entrusted to either politicians or business men, he points out that once the fairness and impartiality of a broadcasting system become suspect its authority as a source of information is destroyed He quotes American experience to show how liable this is to happen in commercial television and he suggests further that available evidence points to the conclusion that commercially controlled broadcasting tends, in the long run to undermine the intelligence, at any rate, of its constant listeners and viewers, and makes it more difficult for them to appreciate programmes which demand some thought and application It makes them passive rather than active

This can be particularly serious for children and the possibility is the more disturbing in that the American survey confirms so strongly the determining

* Two Threats to Broadcasting Political and Commercial Control By H Carleton Greene Pp 8. (London British Broadcasting Corporation 1959)

influence of early education brought out in Mr Trenaman's study. The most powerful influence in effective communication is the full-time education received in childhood and early youth, and alike in resisting the detrimental or anti-social influences of broadcasting or in realizing the potentialities of these new media for adult education this is the decisive factor. It far outweighs the importance of technical improvements in the use of television or sound broadcasting for educational purposes, and though Mr Greene's address at first sight seems to bear only indirectly on the American inquiry, it should be clear that any attempt to improve the use of the mass media to disseminate scientific information and advance the public understanding of science could well fail if it did not take account of this factor, and if it ignored the consequences of political and sectional pressure debasing the media.

Mr Greene does not ignore the beneficial results which a public service broadcasting system can bring and he points out that B B C television has, contrary to expectation, had in England a favourable effect on reading habits rather than otherwise. The use of radio and television in schools, however, is quite a separate issue. What needs to be emphasized first is the crucial importance of an adequate system of education in the schools if the level of public understanding of science is to be raised. That comes first, and no improvements in the techniques of presentation and of using the mass media can compensate for shortcomings there. Further, with the realization of the opportunities which television and also sound broadcasting should increasingly offer, if wisely used, for communicating scientific information, there should be a keen appreciation of the irreparable damage that can be done both to the reputation and effectiveness of the medium and to public intelligence if these media are rashly and irresponsibly used.

EGYPT AND GREECE IN MEDICAL HISTORY

Ancient Egyptian and Cnidian Medicine

The Relationship of Their Aetiological Concepts of Disease. By Robert O Steuer and J B de C M Saunders. Pp xii+90 (Berkeley and Los Angeles University of California Press, London Cambridge University Press, 1959) 22s 6d net.

THE authors of this interesting and constructive, though highly specialized, book introduce the problem which they seek to expound by the statement that "throughout the history of medicine the physician has searched for a theory of disease through which he might organize a diversity of data and thus justify his practice by establishing a scientific system." This is an elaborate way of saying that for centuries doctors have been looking for an easy way of practising by rule-of-thumb. Even in ancient Egypt this search had begun, although many medical historians have regarded the contribution of Egypt to modern medicine as negligible, because it was magico-religious, and entirely devoid of any rational approach. The recent re-examination of the existing medical papyri has placed Egyptian medicine in

quite a different category, and has confirmed the view, previously advanced with little supporting evidence, that the Greeks, acknowledged to be the first to base their medical practice upon observation rather than upon theory, drew many of their ideas from the Egyptians. The first to profit from the Egyptian impact was the pre-Hippocratic School of Cnidos (on the mainland opposite the island of Cos). Cnidian medicine, however, was apt to confuse symptoms with diseases, and it was not until Hippocrates of Cos insisted upon the need for observation, and upon the importance of prognosis rather than diagnosis, that the great era of Greek medicine was inaugurated.

The present work deals with the link between Egypt and Cnidos. Both were preoccupied with the idea of putrefaction as a cause of disease, and with the means of preventing it. The prevention of corruption had been carried to a fine art by those who embalmed the human body after death, and this process of mummification was based upon the principle which was followed also by those who sought to heal the living body by getting rid of putrefaction within it. It was alleged that disease was caused by the *materia peccans* in the faecal content of the bowel. It logically followed that treatment must consist of eliminating the noxious agent or putrefying matter by purgatives or enemata.

The writers of the book under review give many examples of this etiological concept, culled from various papyri, especially the "Papyrus Anonymus Londinensis", besides a number of Greek writings. Although the Cnidian notions appear to have been supplanted by the idea of the humours, favoured by Hippocrates and the Coan School, the two opinions were to some extent united when it was admitted that even the humours might be corrupt or putrefying. This idea paved the way for the doctrine of the ethereal 'miasma' as a cause of disease, an idea which held the field for centuries in various guises until at length the pathogenic nature of bacteria was demonstrated. The relationship between the ideas of Egypt and those of Greece is a significant chapter in the history of medicine, and Dr Steuer and Prof Saunders are to be congratulated on their careful and well-documented study of the putrefactive principle in ancient writings. Besides the 55 pages of text, there are an appendix expounding the views of Galen on the matter, and another, suggesting that air-borne disease may have been envisaged even in ancient Egypt. There are twelve pages of informative notes and a bibliography, as well as an adequate index.

DOUGLAS GUTHRIE

THE MOVING FRONT OF CARBOHYDRATES

Advances in Carbohydrate Chemistry, Vol 13

Edited by Melville L Wolfrom in association with R Stuart Tipson. Pp xi+387 (New York Academic Press, Inc, London Academic Books, Ltd, 1958) 88s.

VOL 13 of "Advances in Carbohydrate Chemistry" presents ten reviews on specialized topics of carbohydrate chemistry. Trends of present-day sugar chemistry are reflected in the titles of some contributions and are interwoven in the text of others. Interest in amino-sugars has grown considerably over the past two decades with the recognition that

biologically active mucopolysaccharides and mucoproteins such as heparin, blood group specific substances, virus haemagglutinin inhibitors and gonadotropins contained N-substituted 2-amino-2-deoxy sugars. Furthermore, sialic acids containing as nucleus an amino sugar, have established themselves as regular components of mucoproteins and some mucopolysaccharides of animal origin and as constituents of the membrane of certain bacteria. Interest in the impact of alkali on simple sugars, oligosaccharides and polysaccharides has been revived by the discovery of enzymes catalysing aldose-ketose isomerizations, by the realization that the glycosides of β hydroxy aldehydes and β hydroxyketones are sensitive to alkalis and by the recognition that the products of alkali degradation of polysaccharides afford valuable information as to the linkage of the constituent units. Finally, the problem of the conformation of the individual sugars enters into nearly every discussion on the reactivity of the carbohydrate concerned.

The topic of sugar ring conformational analysis attended to in previous volumes is extended by F. Shafizadeh to the formation and cleavage of the oxygen ring in sugars. Shafizadeh discusses various aspects of the interconversion of the cyclic forms and acyclic forms of a sugar. The inductive effect of the hydroxyl groups on the reactive function and the steric effects are well exemplified. The nitrous acid deamination of amino sugars provides further proof of the profound effect the nature of the adjacent group and the configuration and conformation of the molecule have on the reaction. A concise summary of the preparation and physical properties of the methyl ethers of D and L-glucosamine, D-galactosamine, D-allosamine and D-altrosamine is provided by R. W. Jeanloz, who has made many contributions to this field. The availability of these ethers renders it possible to apply the methylation procedure of structural analysis to oligo and polysaccharides containing amino-sugars.

In the chapter on sialic acids, F. Zilliken and M. W. Whitehouse give a useful account of the composition, structure determination and distribution of the various sialic acids (N-acetylated neuraminic acids). The presentation would have gained in appeal if the authors had stressed the unique arrangement of the functional groups in neuraminic acid (the common parent compound) and interpreted the remarkable properties of this group of substances on the basis of this arrangement. With regard to the linkage of sialic acid in animal mucoproteins it is safe to say that the acid is invariably found as a terminal unit, it seems improbable that it serves as a chemical bridge between polypeptides and polysaccharides (p. 238). There is no evidence that the influenza virus particle has any other enzymic activity than that of an neuraminidase (see p. 260). Perhaps I may be allowed to point out that the molecular structure of neuraminic acid proposed in 1955 was conceived not so much on speculation as on the hard facts that N-acetylneuraminic acid was convertible under mildest alkaline conditions to pyrrole 2-carboxylic acid and that the same pyrrole was obtained by aldol condensation of D-glucosamine with pyruvic acid. These findings (*Nature*, 176, 881 (1955)) left no doubt on the position in neuraminic acid of the key functional groups and favoured Blix's (1955) rather than Zilliken's (1955) empirical formula of N-acetylneuraminic acid.

The Lobry de Bruyn-van Ekenstein transformation of sugars in all its aspects and side-reactions

(formation of deoxyosones) is very logically presented by J. G. Speck. The accumulated results show that these transformations proceed by an enolization type of mechanism and that a common intermediate is formed in the aldose-ketose isomerization and the 7-deoxyosone production. The alkaline degradation of polysaccharides also begins at the reducing end of the molecule with enolization and proceeds step wise through the anhydroglycose chain. In such a peeling process the reducing end group is liberated from the chain by elimination of the rest of the chain as a glycoxy anion. The released end group forms an α dicarbonyl structure which is rearranged by a Cannizzaro type of reaction to yield saccharinates. R. L. Whistler and J. N. BeMiller have cogently summarized this field. The reaction schemes clearly indicate the dependence of the type of saccharinate formed (ordinary, meta or iso-saccharinate) on the structure of the glycosyl units of the polysaccharide. Incidentally, treatment of unsubstituted N-acetyl-D-glucosamine by mild alkali results in the formation of D(+)-5-dihydroxyethyl 3-acetamido furan, and not in that of glucosaxoline (p. 305). The life work of J. W. E. Glaffelt on four-carbon saccharinic acids is reviewed by J. D. Crum.

The story by G. V. Caesar of starch nitrate the oldest known and industrially the most important starch derivative reads like a 'thriller'. J. Goodman reports on glycosyl ureides and L. Stolefi contributes a chapter on polysaccharide hydrocolloids of commerce. The important formazan reaction with its implications for the structure of sugar phenylhydrazones and phenylosazones and with its use as a tool for elucidating the structure of polysaccharides is comprehensively described by L. Mæster.

It seems most appropriate that the opening chapter is dedicated to the memory of Carl Neuberg, who has made outstanding contributions to many of the topics discussed in this excellent volume.

ALFRED GOTTSCHALK

PRELUDE TO SPACE RESEARCH

Vistas in Astronautics

First Annual Air Force Office of Scientific Research Astronautics Symposium (Co-sponsored with Convair Division, General Dynamics Corporation). Edited by Morton Alperin and Marvin Stern. (International Series of Monographs on Aeronautical Sciences and Space Flight, Division 7, Astronautics Division, Vol. 1.) Pp. xxi+330. (London and New York: Pergamon Press, 1958.) 105s. net.

IN February 1957 satellites and space exploration were things of the future and the organizers of the Astronautics Symposium held in that month at San Diego were at pains to secure serious papers on the subject from recognized scientists rather than to encourage speculative contributions. Consequently the title of this book which provides a record of the papers read at the Symposium, is slightly misleading: most of the papers remain earthbound (if we stretch this phrase to include satellite orbits), only a few flatter off into the depths of space.

The book is divided into six sections of roughly equal length. The first entitled Re-entry includes an excellent paper by C. Gazley describing the deceleration and heating of a body entering a planetary atmosphere from space and several contributions on the aerodynamics of re-entering space vehicles.

Part 2, on "Tracking and Communication", includes a detailed description of the 'Microlock' radio instrumentation system for satellites. The third section, on the environment of a space vehicle, has several expert surveys of particular topics, such as F. L. Whipple's paper on the "Meteorite Risk to Space Vehicles" and H. V. Neher's terse 1½ pages on cosmic rays. In Part 4 the possible propulsion systems for space travel are fully discussed. Part 5 is devoted to orbits, and includes a 39-page paper by H. Oberth, on "A Precise Attitude Control for Artificial Satellites". Part 6 is entitled "Human Factors", and covers space medicine and legal problems.

The individual papers in the volume differ greatly in their length, tone, technicality and worth. The book can be recommended for its many good technical papers, most of which have stood the test of time well, but there are a few half-page contributions which scarcely deserve permanent reproduction in book form, and the frontispiece, a full-page photograph of the brigadier-general commanding the Air Force Office of Scientific Research, seems rather out of place in a technical book. D. G. KING-HELE

EXPLOSIONS IN SOLIDS

Fast Reactions in Solids

By F. P. Bowden and A. D. Yoffe. Pp. ix+164. (London: Butterworths Scientific Publications, New York: Academic Press, Inc., 1958) 40s, 7 dollars.

THIS book is a sequel to the authors' earlier (1952) monograph "The Initiation and Growth of Explosion in Liquids and Solids". It deals with subsequent work on the same problems and more particularly with the mechanism by which a crystalline explosive decomposes when subjected to heat, light shock or nuclear radiation. Like its predecessor, the book does not attempt to give a comprehensive treatment of the whole field but rather to focus attention on salient developments in the study of explosives and especially on those areas to which the work of the authors and their colleagues has contributed. In this it is most successful and it is a stimulating and attractive volume.

Chapter 1 is a brief (4 pages) introduction and sketches the plan of the book. Chapter 2, which gives an account (13 pages) of the slow decomposition of crystals, is based mainly on silver azide. Chapter 3 is longer (25 pages) and more diversified. Under the general title of thermal explosions it gathers a varied, though not always clearly organized and interrelated, collection of theory, sample calculation and experiment. It is an important chapter to the remainder of the book, for the ideas of thermal explosion theory outlined here are repeatedly applied in this and subsequent chapters. The importance of a molten zone to reaction propagation is also introduced. In Chapter 4, the structure and stability of the inorganic azides are reviewed (12 pages) in terms of electron sharing between the metal atom and the azide group; this concept is one of the important new points of view this book adopts. Chapter 5 (31 pages) on initiation of explosion by shock is closest in theme to the previous monograph. An account is given of recent work on initiation by impact, flying particles and shock waves, by friction and by ultrasonic vibration. Mechanical initiation is thermal in origin, but 'mechanical' factors such as the disintegration

of liquids and solids play a part. Chapter 6 (25 pages) reaches a basically similar conclusion about initiation of explosion by flash photolysis. The azides are again the principal subject and the concepts of Chapters 3 and 4 are applied in interpretation. Decomposition and ignition by nuclear particles and high-energy radiations are dealt with in Chapter 7 (11 pages). High energy particles provide a convenient method of introducing large amounts of energy into molecularly small regions of the crystals, and the experimental evidence so far is that the activation of a small number of adjacent molecules may not be enough to cause explosion. In Chapter 8 (7 pages) the mysterious, spontaneous explosions which occur during crystallization of lead and mercurous azide are described and discussed. The first part (7 pages) of Chapter 9 on the fast growth of explosion deals with thin films and the deflagrations and "low velocity detonations" which occur. The second part (9 pages), which contains some very striking photographic records, discusses small single crystals undergoing explosive decomposition.

This is the arrangement of the text. Each chapter after the first has its own 'conclusion' summarizing in broad generality the trends the authors feel significant and it is often helpful to read these before their chapters. Perhaps the reader would have been helped still more had the principal subdivisions of the chapters been listed with the contents. The text is prefaced by a useful list of names and formulae of most of the explosives discussed and followed by a set of eight appendices which are up-to-date short tables of various properties. There are good author and subject indexes.

It is not the duty of a monograph of this nature which concentrates on recent work in a changing field to supply an extensive background; the appearance last year of M. A. Cook's formidable "Science of High Explosives" helps to meet this need. This book is modern and reliable and the few errors other than trivial misprints that exist, such as the apparent application of le Chatelier's principle to a non-equilibrium process, the occasional use of 'inorganic compound' where 'ionic solid' is intended and of the erroneous $\text{Cu}_2(\text{N}_3)_2$ and $\text{Au}_2(\text{N}_3)_2$, may arise from compression and from production of such an up-to-date monograph. Above all, the experimental work from the authors' laboratory has a lucid quality which permits it to speak for itself without laborious argument. Perhaps 'photogenic' is an apter word to do greater justice to the brilliant photographs which have been obtained and which so admirably illustrate the text.

PETER GRAI

APPLICATIONS OF STATISTICS IN PHYSICS

Statistical Physics

By L. D. Landau and E. M. Lifshitz. (Course of Theoretical Physics, Vol. 5). Translated from the Russian by E. Peierls and R. F. Peierls. Pp. x+484. (London: Pergamon Press, Ltd., 1958) 80s net.

IN abandoning the general practice of considering classical statistics, quantum statistics and thermodynamics as virtually separate subjects, the authors have produced a book in which the three have been combined with considerable success. Although no

concessions have been made to the mathematically under privileged, the importance and significance of the underlying physical principles have not been neglected so that the honours degree student, irrespective of his mathematical attainment, will find much to stimulate his interest in, and to clarify his ideas on, thus the most fundamental branch of physics.

The initial chapters are devoted to the establishment of general principles by first laying the statistical foundations, then deriving the principal thermodynamic quantities and relations associated with the macroscopic state and finally obtaining the standard distribution functions, both classical and quantum. Then follow admirable comprehensive treatments of particular applications to closed systems in thermodynamic equilibrium, some examples of which are perfect and real gases, condensed bodies, solutions, chemical reactions, fluctuations and surface phenomena. A chapter on the symmetry of macroscopic bodies could well be omitted as the treatment is too condensed for all but professional crystallographers and for them it is unnecessary.

There are some weaknesses in the general presentation. The style is occasionally laboured and an improvement in the continuity could be effected by including in the text the material added in numerous footnotes. Further it is surely unnecessary to derive first a dimensionless expression for entropy into which later must be inserted Boltzmann's constant. Again after the excellent exposition of the basic statistical principles it is surprising that reference should be made to both the specific heat and the Gibbs free energy per molecule. Finally the authors depart in several instances from the conventional in their use of thermodynamic terms in particular by adiabatic they always mean 'reversible adiabatic'.

H STEEPL

THE GREAT LAKES

Geology of the Great Lakes

By Prof Jack L Hough Pp xviii+313 (Urbana, Ill University of Illinois Press, 1958) 8 50 dollars

FORTY FOUR years have passed since Leverett and Taylor published their classic work on the history of the Great Lakes. During much of the last twenty seven of these Prof Hough has been engaged on studies of the various aspects of this great group of inland waters. There has been a growing need for a summary of the large amount of work that has been accomplished in the interval.

The book is divided into two parts. The first deals with the topography and hydrology of the present lakes and the deposits on their floors, as well as the pre glacial and glacial history of the region in general terms. The latter is inevitably a simple outline which forms the basis for the more important second part of the book.

Part 2, comprising rather more than half the book, deals with the history of the stages of evolution of the lakes as bodies of open water fluctuating in extent with changes in the position of the oscillating front of the ice sheet to the north. The series of outlets of the lakes to the Mississippi, to the Mohawk and Hudson valley, to Lake Erie and the St Lawrence, and to the St Lawrence via the north east corner of Lake Huron and the Ottawa River came into action repeatedly. The story now unfolded is substantially more complicated than the account of Leverett and

Taylor, and the work is very much better documented, in consequence of the research by many workers, including substantial contributions from the author himself. This applies particularly to revised and more detailed correlation of events over the vast area involved.

Particularly noteworthy parts of the book are the detailed but concise critical assessments of the evidence on which correlation is based, a valuable correlation chart based with an absolute dating scale on carbon 14 measurements, and among the many text figures 23 diagrams, summaries of the successive stages in the fluctuation of the extent and outlets of the lakes throughout late and post-glacial time. The large scale southerly tilt of the area consequent on the isostatic rise as a result of the progressive deglaciation of the area introduces complications in the history in the correlation of shore lines and this is accentuated by the erosion of considerable lengths of the old beaches during later stages of the history of the lakes.

The author is to be congratulated on a major contribution to late glacial geology of the region. The text figures are clearly produced and there is an excellent bibliography. S E HOLLINGWORTH

ANTING

Phoenix Re-born

By Dr Maurice Burton Pp 224+16 plates (London Hutchinson and Co (Publishers) Ltd, 1959) 35s net

FOR many years anting in birds has held considerable fascination for students of bird behaviour. So, too has the myth of the Phoenix and when Maurice Burton saw a tame rook disporting himself on a heap of burning straw it led to an association of ideas which was ultimately responsible for the production of this book. After thorough exploration of the Phoenix legend, Burton carried out experiments with his tame rooks and a pet jay to determine their reactions to certain substances and to heat. He also examined the literature to see whether records of bird and other animal behaviour might reveal anting incidents which had been unidentified. Eventually Burton reached certain conclusions which show a clear connexion between Herodotus's account of the Phoenix and the anting of birds.

One thing is common to all the substances which cause the anting posture: this is heat or the impression of heat. In this remarkable book Burton compares the reaction of birds to different substances, examines the theories of anting and comes to the conclusion that anting must be regarded as a posture adopted in moments of unusually intense excitement. This may be stimulated autochthonously or through the agency of an external stimulus producing heat or the impression of heat in the mouth. Ant hatching and thermophily are also shown to be closely related to anting proper and all these are related to such habits as the self anointing of hedgehogs, the effects of catmint and other odorants on carnivores as well as numerous idiosyncrasies of behaviour among individual birds and mammals not excluding man himself.

The charm of the book lies not only in the emergence of a new theory to an old puzzle, the telling also stamps "Phoenix re-born" as an ornithological thriller of outstanding interest. T H HAWKINS

Introduction to Functional Analysis

By Prof. Angus E Taylor Pp xvi+423 (New York: John Wiley and Sons, Inc., London: Chapman and Hall, Ltd., 1958) 100s net

LINEAR functional analysis arose partly from Hilbert's theory of space of an infinity of dimensions and its axiomatic formulation by John von Neumann, and partly from Banach's development of Fréchet's work on abstract spaces. Good recent books include those by Zaenen and by Riesz and Nagy. Prof Taylor's introduction will not displace these books, but can serve as a useful survey of basic methods. In lecture form, the material has been tried out on several graduate courses in the United States, and hence is particularly helpful in the early chapters. In the first, the algebraic formulation is kept clear of topology, linear spaces, operators and functionals are defined and illustrated by a wealth of examples of each type, so that the novice is gently helped to surmount his initial difficulty of forming some concrete idea of these abstract concepts. The second chapter is a reference section on topology, then in the third, the linear space and the topological space are related to provide the concept of the linear topological space, again with many carefully detailed instances of such spaces. The reader who studies these three chapters closely will be rewarded with a firm grasp of fundamentals and should then cope readily with the somewhat increased pace of the later chapters giving the general theory of linear operators, spectral analysis and the standard results for self-adjoint, normal and unitary operators. The old-fashioned analyst will be pleased to see contour integration employed in the spectral theory, a method much emphasized in some of Taylor's own papers. The final chapter, on integration and linear functionals, is intentionally only a sign-post to further reading in this field. The book should be particularly valuable to those who need to get some knowledge of the unifying and co-ordinating power of this potent theory without having to make a specialist's study of it. T A A BROADBENT

The Birds of the Palearctic Fauna

A Systematic Reference Order Passeriformes. By Dr Charles Vaurie Pp xii+762 (London: H F and G Witherby, Ltd., 1959) 105s

IT has been claimed that birds are systematically better known than any other class of animals, but even for the relatively familiar Palearctic region a new 'base-line' has become desirable. This is here provided in respect of the passerine birds—a second volume is now being prepared to cover the rest—in succession to the corresponding part of Hartert's "Die Vögel der palaarktischen Fauna" of 1903-32. Unlike Hartert, the present author does not give descriptions of species, but only the main points distinguishing one sub-specific form from another, synonymies are brought up to date rather than repeated in full. English names are given for all species, with the French and German equivalents where these exist.

The present less-rigid outlook on intraspecific systematics is reflected in the emphasis placed on the 'clinal' nature of much of the geographical variation, and previously described races which the author regards as mere stages on a cline or as otherwise unsatisfactory are relegated to the synonymy, races which the author accepts are graded as "well" and "moderately well" differentiated but are otherwise given identical treatment. Of special value are the

detailed accounts of the ranges of all forms, and these are usefully reinforced by information about the habitat of each species. There are also brief indications of extra-limital distribution and of the existence of extra-limital races, the latter being mentioned by name when not too numerous. There are doubtless some points on which other experts may differ, but the volume can be welcomed as an up-to-date authoritative work of reference on the systematics and zoogeography of the palearctic passerine avifauna. LANDSBOROUGH THOMSON

The Open Sea—its Natural History

Part 2 Fish and Fisheries, with Chapters on Whales, Turtles and Animals of the Sea Floor. By Sir Alister Hardy (The New Naturalist: a Survey of British Natural History) Pp xiv+322+48 plates (London: William Collins, Sons and Co., Ltd., 1959) 30s net

THOSE who enjoyed Sir Alister Hardy's first book on "The Open Sea" will also enjoy his second, for it has the same virtues—it is written with infectious enthusiasm and with a wide knowledge of fish and fishermen. He has sailed in both the old and the new *Discovery*, in trawlers on fishing trips and in fisheries research vessels of many lands, so that he brings a vivid sense of actuality into his writing.

Beginning with a brief résumé of the fundamentals of life in the sea, the author goes on to describe what a fish is and how it lives and moves. Then follow chapters on particular fish and fisheries. The herring is given pride of place with a short account of its history and of the research work on it right up to the present day. After two chapters on the bottom fauna, we return to fishing with descriptions of different types of gear and chapters on plaice, clasmobranchs and gadoids. The over-fishing problem is not neglected, and indeed in many places throughout the book the author shows how the knowledge we already have could be applied to improve or increase the fisheries. He ends with the plea that the division of the North Sea into northern and southern spheres of research should be abandoned in favour of a united effort covering the whole area.

There are chapters also on the animals of the ocean floor, on parasites, particularly of fish, on reptiles (not omitting the sea-serpent) and on marine mammals.

No attempt has been made to cover the systematics or physiology of fish. This is a natural history of the creatures living in the open seas around Britain and there can be few who will read it without learning something new and interesting.

Mention must be made of the excellent illustrations. Many of the plates are reproductions of the author's own delightful water colours. The photographs, many by Dr D P Wilson, are outstanding and include some wonderful shots of whales and courting fish. S M MARSHALL

Flora of Peru

By Rogers McVaugh (Field Museum of Natural History Botanical Series, Vol 13, Part 4, No 2) Pp ii+569-818 (Chicago: Field Museum of Natural History, 1958) 3.75 dollars

THIS part continues the Flora of Peru with the account of the difficult family, Myrtaceae, contributed by Prof Rogers McVaugh, of the University of Michigan. The bulk of the species belongs to two large genera, *Myrcia* and *Eugenia*. The author is to be congratulated on his carefully prepared keys and long specific descriptions. There are no illustrations

SPECTROSCOPIC IDENTIFICATION OF ALPHA-EMITTING NUCLIDES IN BIOLOGICAL MATERIAL

By PROF W V MAYNEORD, CBE, and C R HILL

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London SW3

IN connexion with a programme aimed at the identification and measurement of the radioactivity of the human body and its environment¹⁻⁴, an attempt has recently been made to undertake spectral analysis of the alpha activity of normal biological materials. The most satisfactory general method of analysing alpha activity is to measure the size of the individual pulses due to electrons which are produced when the alpha particles are made to spend their full energy on ionizing a free electron gas. In the past, attention has been directed largely to materials having moderately high specific activity and the gridded parallel plate ionization chamber has been the instrument most commonly used⁵⁻⁷. This type of chamber is not, however, suitable for the analysis of materials of very low activity for which a large source area and a low background counting rate are essential. In order to provide a large source area, Lonati *et al* have designed an instrument in which the source material is spread on a large metal sheet, which is afterwards rolled to form the outer member of a cylindrical electrode system, a grid being situated between the emitter and collector⁸. The background counting rate of their instrument is still appreciable and due in part at least, to the large areas of metal surface exposed to the counting volume, and to contamination on the grid wires. The use of a cylindrical or spherical arrangement can, however, largely obviate the need for a grid in overcoming line broadening due to positive ion effect⁹ and has been exploited successfully by Ghiorso in an early instrument¹¹. If, in a gridless chamber, the sensitive volume is surrounded by material having a very low alpha emission the background counting rate corresponding to alpha particle energies may be made very small. Such an instrument has been built by us at the Institute of Cancer Research, Royal Cancer Hospital and has proved to be capable of analysing the alpha activity of a wide range of normal biological materials.

Description and Performance of the Instrument

The instrument consists essentially of two concentric cylindrical electrodes of length 53 cm and radii 15 and 0.2 cm, respectively. The material to be analysed is mounted on the metalized surface of a sheet of aluminized cellulose acetate, lining the inner surface of the outer electrode, and a potential of minus 3 kV applied relative to the inner collecting electrode. The electrode system is enclosed in a vacuum tight steel tank containing a mixture of 90 per cent argon and 10 per cent methane at atmospheric pressure. Under these conditions the theoretical spectral line width due to positive ion effect is 210 keV at 5.5 MeV. The line width obtained in

practice is rather greater as a result of contributions from amplifier noise and self absorption in the uncollimated source. As a result of mounting the source on aluminized cellulose acetate film (which itself has a surface emission of about 3 alpha particles per hr per 1,000 cm² compared to stainless steel 100 brass 100, aluminium 150) and of the relatively small area of other surfaces exposed to the counting volume, the background counting rate due to surface emission is only 20 counts per hr in the energy range 4-9 MeV and for a useful source area of 4,000 cm². Due, however, to the presence of radon, originating, it is believed mainly from the surface of the pressure vessel (which was originally built for another purpose and is impossible to clean satisfactorily), the actual background is somewhat higher than the above figure. By continuously circulating the chamber gas over charcoal cooled in a solid carbon dioxide-alcohol bath the radon background which appears as a three line spectrum of radon, radium A and radium C is maintained constant at 70 counts per hr giving a total background of 90 counts per hr.

The ionization chamber is used with *EKCO* 1049 B head and main amplifiers and a *ODC* 100-channel pulse height analyser. This combination provides good stability of recording and when purity of the chamber gas is maintained by continuously flowing over calcium turnings at 350°C overall drift can be kept within 100 keV over a period of several days.

Preparation of Sources

The sources which normally consist of a partially insoluble ash of uncertain chemical composition, are prepared by grinding (by hand or in a ball mill) followed by spraying in the form of a suspension in water on to the cellulose acetate sheet, previously wetted with dilute "Teepol" solution. A thin layer of sodium silicate solution is usually sprayed on top of the film so formed (0.03 mgm./cm² sodium silicate) to act as an adhesive¹². By this process it is possible to prepare sources which under a microscope appear to consist mainly of particles of about one micron diameter spread with good uniformity.

Results

As illustrations of the use of this technique spectra obtained with our equipment are shown in Figs 1-4.

A popular breakfast cereal, stated to contain "100 per cent whole wheat" and having a total specific alpha activity of 32×10^{-12} c per gm of ash (Fig 1) evidently contains two long lived alpha-emitters, radium 226 and thorium 228 (Rd/Th), and their daughters. Most of the radon 222 escapes from the thin source and is removed from the system by the radon trap, so that it and its daughters do not appear

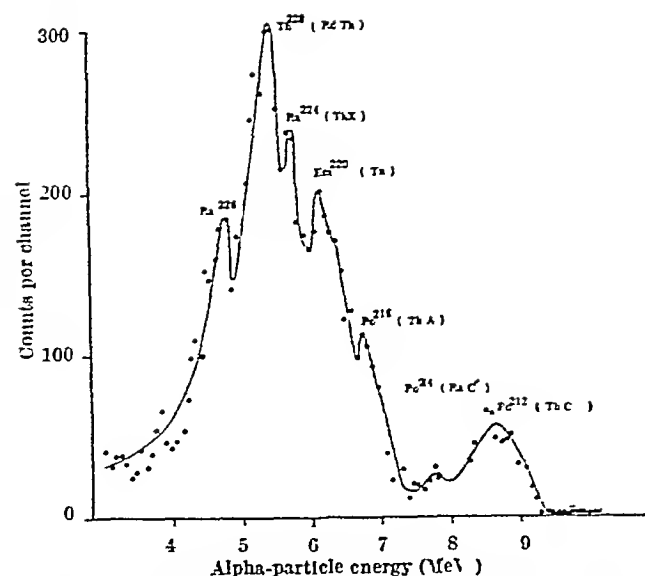


Fig 1 A breakfast food. '100 per cent whole wheat' Counting time 24 hr

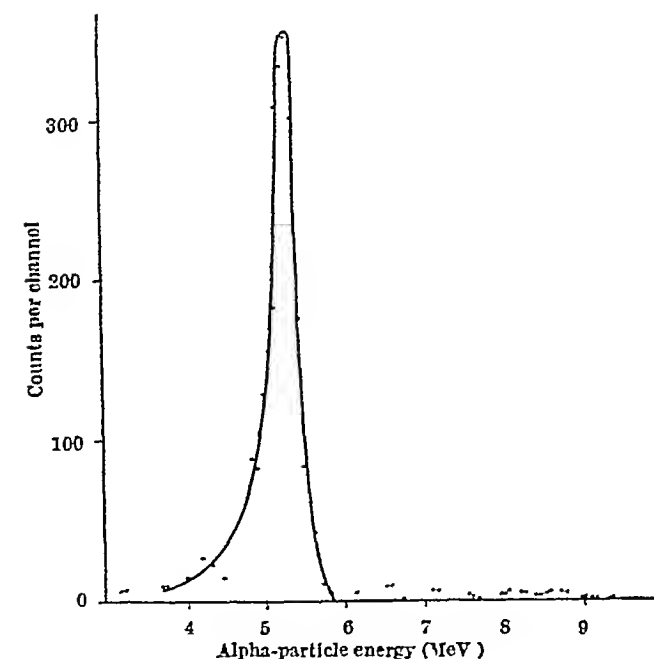


Fig. 2. Grass ash Total specific alpha-activity 6.4×10^{-12} c/gm Counting time 36 hr

from the spectrum to be in equilibrium with radium-226. Uranium-238 and thorium-232 are absent and the thorium-228 must therefore be presumed to originate from radium-228 (MsTh 1) rather than by metabolic uptake of the element thorium. A similar spectrum, but showing relatively higher radium-226, has been obtained for Brazil nuts, which are known to have very high alpha-activity³, these results have been published elsewhere⁴.

Measurements have been made in these laboratories of the total alpha-activities of grass samples taken from various localities¹², and values found in Great Britain have ranged from 1.0 to 170×10^{-12} c per gm of ash. Spectra of the form shown in Fig 2 have been obtained from all the grass samples that we have analysed so far, which have been collected from several different parts of the country. It will be seen that this spectrum is of different form from that of Fig 1, most of the activity being concentrated in a small energy-range. While it is not possible from our spectral evidence alone to decide with confidence

whether the nuclide concerned is polonium-210 (5.30 MeV) or plutonium-239 (5.14 MeV), evidence from chemical analysis and from the build-up of activity with time, after ashing at 500°C , has established that the nuclide is, in fact, polonium-210 in the presence of lead-210 (RaD). From this spectrum we conclude that polonium-210 accounts for some 90 per cent of the total alpha-activity of the grass ash.

In view of the known tendency for the kidney of several species to take up polonium^{14, 15}, we have examined the kidney of a sheep that had been grazed in the district from which the grass sample

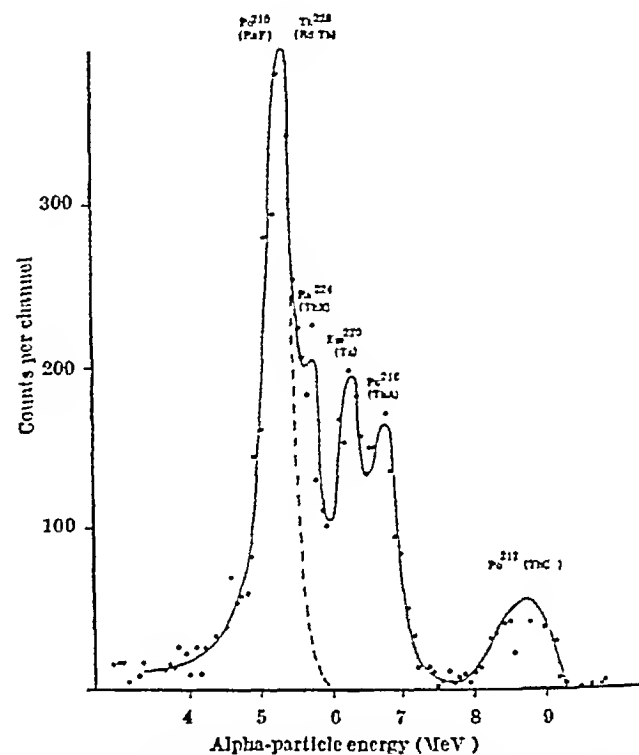


Fig 3 Sheep's kidney Total specific alpha-activity 6.0×10^{-12} c/gm ash Counting time 48 hr

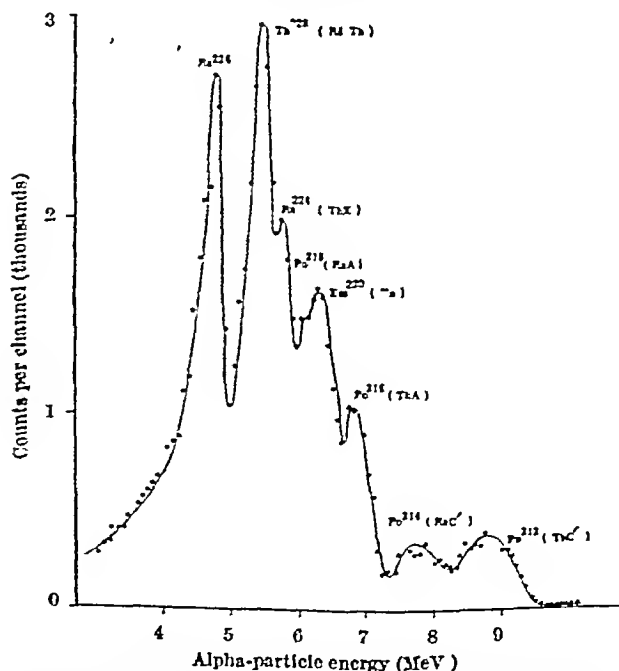


Fig 4 Bone of a worker exposed to the ingestion of radium and mesothorium Total specific alpha activity 214×10^{-12} c/gm ash Counting time 24 hr

of Fig 3 was obtained. The total specific alpha activity was 6.0×10^{-12} c per gm of ash (ash content of wet kidney 1.1 per cent) and the spectrum (Fig 3) shows that about half the total is due to thorium 228 and its daughters, an observation confirmed by an independent method of estimating thorium series nuclides¹. In addition, there is a single line of the same energy as that appearing in the grass, presumably again polonium 210. The presence in the kidney of thorium 228 is interesting in view of the absence of thorium 232 and radium 226, although the latter is clearly present in a spectrum taken of the bone of the same animal. The explanation would appear to be that radium, but not thorium, is absorbed by the sheep from its environment and that thorium 228 originates within the sheep by decay of radium 226, being afterwards transported and fixed in the kidney.

The spectroscopy of normal human bone is beyond the capacity of our present equipment, but interesting results may easily be obtained for the bone of those having radium burdens of the order of one-tenth of the maximum permissible level. Fig 4 shows the spectrum of the bone of a worker who had been exposed to the ingestion of both radium 226 and radium 228 and whose body burden of the former isotope was estimated² at 5.9×10^{-4} c. The presence of radium 226 and of radium 228 with its daughters is clearly demonstrated.

Potentialities of the Method

It seems clear that this type of alpha ray analysis will prove of great value in the study of the radioactivity of biological materials. We are therefore constructing equipment that should be capable of

analysing, with improved resolution, the ash of most living tissues.

We are greatly indebted to our colleague, Dr R C Turner, with whom we have had many fruitful discussions concerning the interpretation of these spectra. Our thanks are due to Mr J O Crookall for the chemical evidence concerning polonium and to Mr S P Newbery for invaluable help with the electronic equipment. We are also indebted to Dr U Facchini and his colleagues of C.I.S.E. Milan, who kindly analysed a number of samples for us in their gridded parallel plate chamber before our own instrument was completed.

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⁹ Lonati R. D., Facchini U., Iori I., Houliermans F. O. and Ton

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¹¹ Ghiorso A., Jaffey, A. H., Robinson, H. P. and Weisbord B. H. "The Transurium Elements" II 1226. Ed Seaborg G. T. et al. (McGraw Hill 1949).

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¹³ Marsden E. *Nature* 153 924 (1950).

¹⁴ Lacazez A. and Lattes J. O. R. *Acad. Sci. Paris* 178 488 (1924).

¹⁵ Stannard J. N. and Smith F. A., Univ. of Rochester Report Atomic Energy Project Contract W-7401-Eng 49 (1957).

THE OHIO STATE UNIVERSITY 360-FT RADIO TELESCOPE

By PROF JOHN D KRAUS

Ohio State University

FOR some years mapping of the radio sky has been a principal activity at the Ohio State University Radio Observatory. Since it was anticipated that this would also be the case if a larger telescope became available consideration was given some years ago to a telescope design especially suited for mapping work which would provide the largest possible aperture per unit cost consistent with large sky coverage. The design evolved consists of a fixed standing parabola with a flat reflector which can be tilted to deflect the celestial radiation into it. The general arrangement is shown in Fig 1. Since the parabola is fixed and supported directly from the ground a minimum of structure is required. The only moving part is the flat reflector, which is pivoted at ground level and is required to move through only one half of the range of declination covered. Although primarily a meridian transit instrument, east-west movement of the feed antenna can provide a small measure of tracking in hour angle. This is not essential, however, in most mapping work.

Scale Model

Experimental work on the design began in 1953 when Robert T. Nash constructed a scale model of

the telescope as part of his thesis work toward a master's degree at the Ohio State University. The parabola of the scale model measured 12 ft in horizontal length while the wave length of operation was 1.25 cm. By scaling both the physical size and the wave length in this manner, antenna patterns can be measured that will duplicate those of the full size system¹. Specifically, the system duplicated is a telescope with a parabola 2 000 ft by 200 ft operating at 2 metres wave length or a telescope with a parabola 700 ft by 70 ft operating at a wave length of 70 cm. A photograph of the model is shown in Fig 2.

Antenna patterns measured by Nash agreed closely with calculated values^{2,3}. In fact, the performance of the model was so satisfactory that Nash used it as an actual radio telescope for many observations of the Sun and Moon at a wave length of 1.25 cm⁴.

Construction of the Full-Size Unit

In 1954 a request was made to the United States National Science Foundation for funds to construct a standing parabola radio telescope with a flat reflector of adjustable tilt, the parabola to be 720 ft long by 70 ft high. The minimum wave

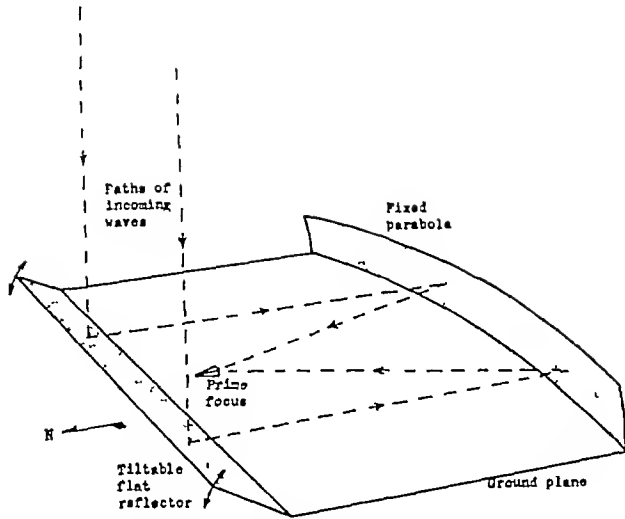


Fig. 1. Principle of operation of the standing parabola radio telescope with flat-sheet reflector. The declination angle of reception is changed by tilting the flat reflector while scanning in right ascension is accomplished by the Earth's rotation.

length of operation was to be about 70 cm and the dimensions were deemed sufficient to provide a significant full-scale test of the design. In 1956 a grant was received from the National Science Foundation for half the amount requested for a parabola 720 ft by 70 ft. As a result, the plans were modified to build the central half of the telescope so that the parabola would be 360 ft long by 70 ft high and the flat reflector of adjustable tilt also 360 ft long with the possibility that outer sections might be added at some future date. At the suggestion of the Radio Astronomy Panel of the National Science Foundation, the original plans were also modified to make the telescope operate at the hydrogen line (21 cm wave-length). To maintain surface tolerances at this wave-length required a structure with several times as much steel as in the original design, with a corresponding increase in cost. Two subsequent grants by the National Science Foundation in 1957 and 1958 have brought the total funds provided for the construction of the telescope close to 250,000 dollars.

A sketch of the final design of the telescope is shown in Fig. 3. This sketch is substantially correct, the main discrepancy being that the actual system for elevating the flat reflector uses a winch arrangement instead of a hydraulic cylinder as suggested in the sketch.

The Ohio Wesleyan University provided a 20-acre site for the radio telescope situated about 4 miles from Delaware, Ohio, and near the Perkins (optical) Observatory. The new radio observatory location is known as the Ohio State-Ohio Wesleyan Radio Observatory.

Construction on the telescope began in 1956 with work on the parabolic reflector. The mechanical design of the structure has been the responsibility of Robert T. Nash and the construction also has been carried out under his supervision. The construction crew

has consisted of about ten men, most of whom have been Ohio State University students who have worked on the telescope on a part-time basis. The parabola was completed in 1958 and work started on the flat reflector. A view of the completed parabola is shown in Fig. 4. At the time of writing (July) the foundations for the flat reflector are mostly in place and sub-assemblies of the steel structure nearly completed. One section of the flat reflector has been assembled and preliminary tests of the hoisting and locking system carried out.

Specifications

The parabola (360 ft \times 70 ft) is a section of a paraboloid of revolution with axis coincident with the ground plane and passing through the prime focus. The focal distance is 420 ft. The aperture area is 25,200 sq ft or about 0.6 acre. This area is equal to that of a circular aperture parabolic dish antenna nearly 180 ft in diameter. The reflecting surface of the parabola consists of vertical copper-clad steel wires 0.081 in. in diameter spaced 1 in. between centres. The entire wire supporting structure of the parabola is hung from the main parabola framework by adjustable brackets in order to facilitate adjustments of the parabola surface if required. The ultimate surface deviation of the parabola is expected to be less than $\frac{1}{4}$ in.

The flat reflector is constructed in movable units 20 ft wide (east-west) by 100 ft long in the slant direction. Under normal loading conditions the maximum deflection of this structure from a flat surface is expected to be of the order of $\frac{1}{4}$ in. Such movable units are to be mounted with a 40 ft spacing between centres. Each unit is to be equipped with an individual 3 hp electric winch and fast-acting pneumatically operated brake and lock. The winch elevates or lowers the flat reflector unit so that the declination may be changed at a rate of about 5° per min. Twenty-foot beams hinged on each end



Photo Dept. of Photography, Ohio State University

Fig. 2. Photograph of scale model built to test the design. The standing parabola is at the right and the flat sheet reflector at the left, with the horn feed antenna at the prime focus just to the right of the base of the flat-sheet reflector.

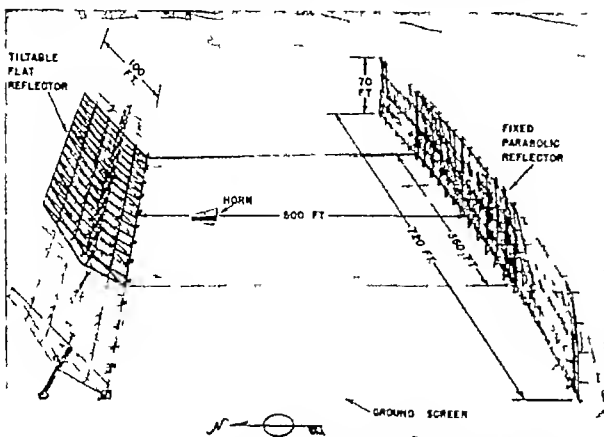


Photo: Dept. of Photography, Ohio State University

Fig. 3 Sketch of the standing parabola radio telescope with flat-sheet reflector being built at the Ohio State University. The central section of the telescope shown in heavy lines is the part now under construction with the end sections in phantom view showing possible future additions.

will bridge the space between movable units. The actual reflecting surface will consist of the same type of wire with the same spacing as used in the parabola. Although each movable unit of the flat reflector is itself rigid, the flat reflector as a whole is non rigid since the hinged connecting beams permit each unit to be moved a couple of degrees independently of the adjacent units. The surface of the flat reflector will be monitored with an optical telescope placed at a point on the axis of rotation (along the base of the flat reflector) west of the reflector, and units adjusted individually until the desired declination of all units is attained.

The steel in the parabola and flat reflector has a total weight of about 300 tons while the concrete in all the foundations totals about 1 200 tons. The horizontal ground plane between the parabola and the flat reflector will consist of thin aluminum sheet a few thousandths of an inch in thickness on flat Poly foam slabs floated on the surface of a water filled pond. It is anticipated that the surface of this ground plane can be maintained flat to less than $\frac{1}{4}$ in.

The antenna feed system at the prime focus will be situated on a peninsula covered with conducting sheet which extends south from the base of the flat reflector into the pond. At the higher frequencies horn antennas will be used as was done with the scale model (see Fig. 2), while corner reflectors will be used at lower frequencies. It is planned to operate the telescope at wave-lengths from 15 cm to 15 metres, a range of 100 to 1. The polarization is vertical. The presence of the horizontal ground plane which acts as an electrical image plane reduces the required height of the feed antenna to one fourth of the value which would be needed if no ground plane were present. Owing to the large horizontal dimension of the standing parabola the required horizontal dimension of the feed antenna is also small. As a result, the aperture blocking or area of obstruction presented by a single feed antenna is very small amounting in a typical case to only about one tenth of one per cent of the aperture of the parabola.

Accordingly, a multiple feed can be employed without objectionable blocking of the aperture to provide simultaneous operation over a wide range of wave lengths. It may even be possible by means of a multiple feed to construct a rudimentary radio camera having as many picture elements as primary feed antennas.

The fact that the feed point is at ground level completely eliminates the problem of supporting the feed antenna and maintaining its alignment, a problem present in all steerable telescopes. Furthermore there is almost no limitation to the weight and complexity of the equipment placed at the feed point so that feed cable losses are eliminated and low noise amplifiers of the maser and parametric type can be used to best advantage.

At the highest frequency of operation (15 cm wave length) the half power beam width of the telescope antenna will be 0.1° in right ascension by 0.5° in de-

clination. (Initially the beam width in right ascension at 15 cm will be twice this value since only the central 180 ft of the parabola has a reflecting wire spacing of 1 in and only this portion will be useful at 15 cm. The outer portions have a wire spacing of 3 in and at longer wave lengths the entire parabola can be used. However initially only the central 200 ft of the flat reflector will be completed. These modifications which were necessitated by a lack of funds will somewhat hamper initial

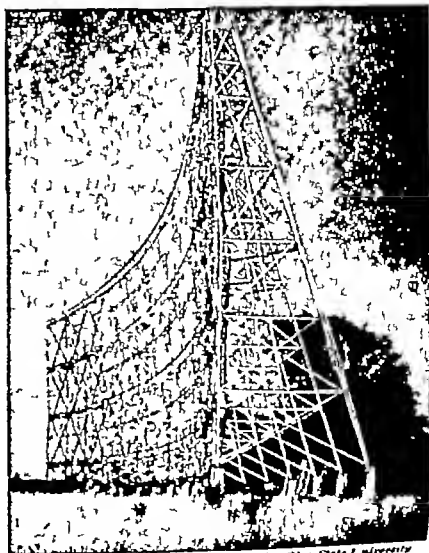


Photo: Dept. of Photography, Ohio State University

Fig. 4 View of the completed 300-ft parabola from the west.

cosmic radiation, against which the steel screen has no effect, is cancelled out by a ring of Geiger counters surrounding the sample counter and connected in anti-coincidence. Other screening precautions which have been shown to be advisable and which are incorporated in the equipment at the Laboratory include a mercury shield, which reduces the background due to traces of radioactivity in the steel screen, and a layer of paraffin wax mixed with boric acid which reduces the component due to neutrons which are in turn induced in the screen by the action of the corpuscular component of cosmic radiation. This neutron flux will also be monitored continuously. Since accurate measurement of these very low disintegration-rates necessarily takes a long time, great emphasis has been placed on the reliable operation of the associated electronic equipment. The instrumentation at the National Physical Laboratory is based on the use, wherever possible, of high-stability circuits as used in computers, and of transistors instead of thermionic valves. The equipment includes a comprehensive system for automatic recording, and a mass spectrometer has also been purchased in order that corrections can be applied for isotopic fractionation effects. The equipment is nearing completion and should be in operation in the near future.

Dr H. Godwin described how the method is being used in the Cambridge Sub-department of Quaternary Research to give an absolute time-scale to the history of events during the Late Quaternary period, that is, the past 35,000 years or so. The apparatus, designed and built by Dr E. H. Willis, consists of a proportional gas counter of about 2-litres volume. It is shielded by 7 tons of zinc and lead and an anti-coincidence array of Geiger tubes. It has a net contemporary count-rate of 28 counts per min and a steady background of 20.7. The equipment was acquired as a result of the generosity of the Nuffield Foundation, but is now maintained by the University of Cambridge.

The oldest sample dated so far was from the Arctic Plant Bed from the Lea Valley. This gives a date of 26,000 B.C. for the time when the mammoth was still alive in Britain. A date from a later horizon in the valley of the Colne, a tributary of the Lea, shows that the full Glacial Period must have persisted until c. 11,500 B.C. After the glaciation, there came a period of climatic oscillation, the so-called Allerød Period. The effects of this change can be recognized in deposits at numerous sites throughout the British Isles. Carbon dating on material from such sites shows that there was a temporary mild

period between 10,000 and 8,800 B.C., followed by a return of cold for about 500 years. These British dates are in excellent agreement with dates from north-west Europe. As a result, British events are now closely tied up with events at the end of the ice age in Europe.

Following the Allerød oscillation came the climatic improvement of the Post Glacial Period. In the past, pollen analysis has provided a relative time-scale for this period since the characteristic changes in forest composition have permitted the establishment of a sequence of pollen zones applicable, with care, to the whole of the British Isles. A series of twelve datings from a site in Cumberland gives a very consistent series of dates for the successive pollen zones. It remains to be seen how far these pollen boundaries are truly synchronous across the British Isles or Western Europe.

The increased temperature at the end of the last glaciation caused melting of the ice sheets and a rapid rise in ocean-level. One effect of this was the flooding of the North Sea and the isolation of Britain from the European mainland. Dates measured in Cambridge on submerged peat-beds from around the coast of Britain, together with those made at other laboratories, show that a rapid eustatic rise of sea-level was in progress between 12,000 and 4,000 B.C. and that the level rose by more than 200 ft.

In the derelict raised bogs of Somerset, several prehistoric wooden trackways have been recorded and excavated. They appear to have been built in the late Bronze Age at a time when increasing wetness of climate induced flooding of bogs and valleys and caused Bronze Age man to construct these wooden causeways. Radiocarbon dating of seven such structures in Somerset and three others in Lancashire, Cambridgeshire and Lincolnshire show that they were built in the period 500-900 B.C.

The picture which emerged from this discussion is a very hopeful one for the future of radiocarbon dating in Britain. Although the method has certain limitations, the work described by Dr Godwin illustrates its great value as a tool for establishing an absolute chronological framework to prehistoric events, and the news that Britain's present limited capacity for radiocarbon dating is to be augmented by the considerable resources of the National Physical Laboratory will be welcomed in many quarters. The dates mentioned in the discussion appear in a paper in the *American Journal of Science* Radiocarbon Supplement, Vol. 1 (1959), the new international organ for the publication of radiocarbon dates.

HAROLD BARKER

MECHANISM OF HORMONE ACTION

By PROF. AARON B. LERNER

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CELLS have specific functions, for example, adrenal cortical cells produce hydrocortisone, nerve cells form noradrenaline, melanocytes make melanin. During their early development cells have in common the capacity to produce substances such as glycogen and protein. The formation of all these end-products depends upon the reaction of specific enzymes with their substrates. Such enzymically

catalysed syntheses usually occur in soluble extracts and homogenates which do not contain intact cells. The formation of cellular end-products also is controlled by hormones that require a high degree of cellular organization in order to function. Although the synthesis of a cell's products is regulated by both enzymic and hormonal reactions, these reactions are not related directly to one another. The hormones

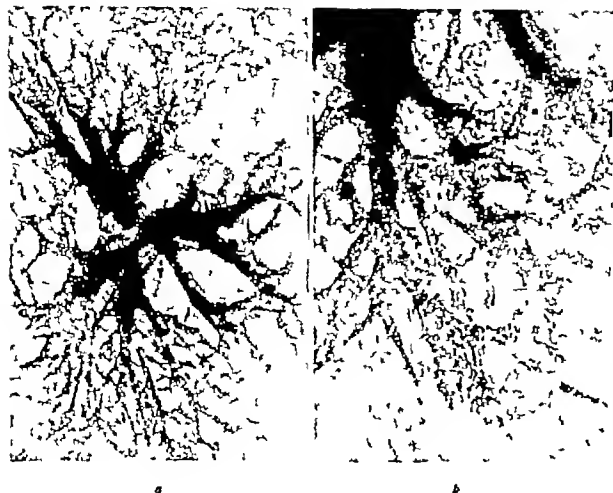


Fig. 1. The pigment granules in a frog's melanocyte can be dispersed throughout the cell as shown above (a $\times c$ 320, b $\times c$ 720) by keeping the cell in solutions of either low osmotic activity low pH or relatively high potassium and low sodium ion concentration. a and b. melanocyte-stimulating hormone and adrenocorticotrophic hormone and caffeine also caused dispersion of granules. While these physical and chemical factors produce the same end effect, namely dispersion of granules within the cell they do so through different mechanisms (see Figs 3 and 4). At \times 720 magnification the melanin granules are seen easily.

react with the intact cell to initiate a series of reactions, none of which need be enzymic that result in a re-location of enzymically active particles. Afterwards the enzymic reactions the formation of various cell products also are affected. The nature of the first reaction of the hormone with the cell is still unknown. It may involve a specific interaction between the hormone, cytoplasmic structural proteins, ions and water to change the colloidal state of parts of the cell.

In this article I wish to show that the melanin pigment forming cell, the melanocyte must be intact if hormones are to affect the rate of melanin synthesis. Initially hormones do not affect the tyrosinase-catalysed conversion of tyrosine to melanin. Instead they produce a change in the location of enzymically active particles which is followed by a change in the rate of enzymic reactions forming melanin. If hormones were added to tissue extracts without intact cells no effect on melanin synthesis would be observed. A similar mechanism may apply to the action of hormones on cells other than melanocytes.

What makes the melanocyte a unique cell in which to study the action of hormones is that it contains enzymic particles made

dark by melanin. Hence these particles are readily visible. Of course it cannot be assumed that a hormone like adrenocorticotrophic hormone acts on the melanocyte in the same way as it does on the fibroblast. Nevertheless the studies with melanocytes are reasonably clear cut and must be acknowledged. Perhaps at a later date techniques will be made available to facilitate similar observations on other cells.

Melanocytes resemble nerve cells. Embryologically they are derived from the neural crest. The pigment melanin is made in the cytoplasm of the melanocyte by the reaction of tyrosine with oxygen and tyrosinase. Ordinarily this reaction occurs on cytoplasmic particles that contain not only tyrosinase activity but that of other enzymes as well. For example the tyrosinase particles from mouse melanoma also possess cytochrome oxidase and succinic dehydrogenase activities. The melanin formed is normally attached to these particles—thus the particles are visible. These particles are called melanin granules or pigment granules and are considered to be mitochondrial structures¹.

It is easy to show that some physical and chemical factors induce clumping of melanin granules about the centre of the cell while others cause dispersion of these granules in the cytoplasm away from the centre.

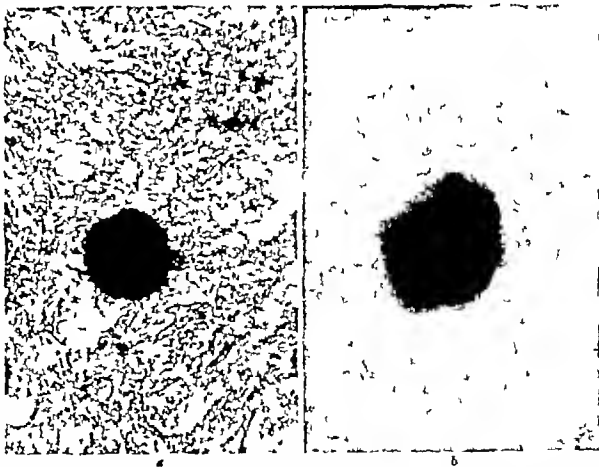


Fig. 2. The pigment cell above is the same kind as that in Fig. 1 except that the cytoplasmic granules are aggregated about the nucleus instead of dispersed throughout the cell (a $\times c$ 320, b $\times c$ 720). The outer borders of the cell, although not shown in this preparation are the same as in Fig. 1. Aggregation of granules can be induced by placing the cell in solutions of either high osmotic activity, high pH or relatively low potassium and high sodium ion concentration. Melatonin, adrenaline, noradrenaline, acetylcholine, hydrocortisone, serotonin and triiodothyronine also produce aggregation of granules. As in the case of dispersion of pigment granules aggregation is achieved by many factors all of which produce the same end result but operate through different mechanisms (see Figs 3 and 4).

of the cell. When frog melanocytes are placed in solutions of low osmotic activity or low pH, the granules disperse.² A similar effect is achieved by changing the cations in the solution from sodium to potassium. A substance like adenosine triphosphate, which may not even enter the cell, also causes dispersion of the granules. Experiments with frog and fish melanocytes indicate that for the dispersion effect to occur the cytoplasm changes from a gel to a sol and oxygen is utilized. One of the most surprising findings associated with this reversible dispersion reaction is that minute quantities of certain hormones can bring it about. The melanocyte stimulating hormones from hog pituitary gland, α - and β -hormones, produce darkening in concentrations of 1×10^{-11} M and 2×10^{-11} M respectively.^{3,4} Hog adrenocorticotrophic hormone is effective at 3×10^{-10} M. These three peptides have related amino acid sequences in their structure.⁵ Other dispersing agents include progesterone, caffeine, marsilid and mesantol. However, when compared with α - and β -melanocyte-stimulating hormones and adrenocorticotrophic hormone, huge quantities are required. Melanocyte stimulating hormone in high concentrations has no effect on the tyrosine-tyrosinase reaction *in vitro*.

Aggregation of pigment granules in frog melanocytes occurs in solutions of high osmotic activity or high pH. Replacing potassium by sodium ions in the solution results in a similar effect. Results of work on frog and fish indicate that for the aggregation reaction to occur the cytoplasm must change from a sol to a gel. Oxygen is not required. Potent aggregating agents for frog melanocytes include melatonin, noradrenaline, adrenaline, acetylcholine, hydrocortisone, triiodothyronine and serotonin.^{6,7} The molar concentrations of these hormones required for the reaction to occur are 5×10^{-12} , 6×10^{-7} , 6×10^{-7} , 4×10^{-7} , 6×10^{-7} , 8×10^{-7} and 3×10^{-6} , respectively.⁸

What happens to the melanocyte when the granules are kept in the dispersed or aggregated state? In the case of melanocytes from hamster melanoma, injection of melanocyte-stimulating hormone into the animal results in an increase in melanin content of the tumour whereas injection of melatonin results in a decrease in melanin content.⁹ Also, injection of melatonin into frogs results in decreased melanin in the skin.⁹ Thus in this case, by dispersing tyrosinase, melanocyte stimulating hormone can bring about more melanin formation. Melatonin, on the other hand, presumably by aggregating the tyrosinase containing particles, decreases the formation of melanin. In both cases the effect of the hormones on melanin formation is indirect, operating through their influence on tyrosinase location and activity. The activity of the enzyme could well be related to its location within the cell. As suggested earlier, the direct reaction between a hormone and

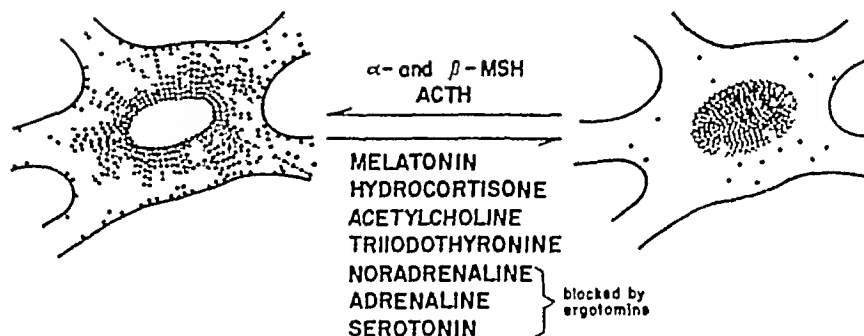


Fig 3 α and β -melanocyte-stimulating hormone and adrenocorticotrophic hormone can produce dispersion of pigment granules in the melanocyte. This action can be reversed by the seven compounds listed above. The action of adrenaline, noradrenaline and serotonin but not that of the other aggregating agents can be blocked by ergotamine.

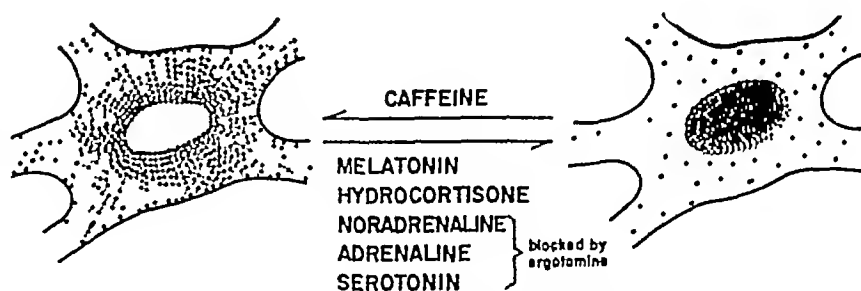


Fig 4 Caffeine like α and β -melanocyte stimulating hormones and adrenocorticotrophic hormone, causes dispersion of granules in the melanocytes. However this effect is reversed by melatonin, adrenaline, noradrenaline and serotonin but not by triiodothyronine, acetylcholine or hydrocortisone. The action of adrenaline, noradrenaline and serotonin but not that of melatonin and hydrocortisone can be reversed by ergotamine. Melatonin and hydrocortisone are the only substances known that not only cause aggregation of granules in cells previously darkened by α and β -melanocyte-stimulating hormone, adrenocorticotrophic hormone or caffeine but also cannot be blocked by ergotamine. However, the action of melatonin and hydrocortisone is not the same. Hydrocortisone acts for only a period of several minutes whereas melatonin has a prolonged action.

the melanocyte may involve only a relatively specific reaction between hormone, cytoplasmic structural proteins, ions and water to change the colloidal state of parts of the cell.¹⁰ This change in colloidal state eventually would affect the tyrosine tyrosinase reaction.

The question arises as to whether or not the effect of hormones on the movement of cytoplasmic particles is peculiar to melanocytes or occurs in other cells as well. In this regard it is of interest that adrenocorticotrophic hormone, cortisone and hydrocortisone affect the structure of mast cells.¹¹ The latter become vacuolated, diminish in size and acquire irregular outlines. Cytoplasmic granules clump together to form aggregates. Cortisone and hydrocortisone induce the formation of cytoplasmic vacuoles in fibroblasts grown in tissue culture. Hydrocortisone also reduces the amount of collagen formed in cultures of fibroblasts.

What I want to emphasize here is that the experiments with melanocytes 'prove' that the intact cell is necessary for the action of a hormone, when action is used in the sense of controlling the end function for which the cell is known, for example, melanin formation in the case of the melanocyte. To change the rate of melanin formation the hormone exerts an indirect effect on the tyrosine-tyrosinase reaction. It is not possible to demonstrate a direct hormonal effect on this reaction. This situation is somewhat analogous to some of the old problems of mathematics. For years attempts had been made to trisect an angle or square a circle with only a pencil, straight edge and compass, or to find a formula to solve equations of the 5th order. However, in fairly

recent times it has been shown clearly that these problems cannot be solved in a strict sense. Only approximations are possible. In biology, unlike mathematics, clear cut proofs are hard to come by. But the experiments carried out by many investigators suggest the conclusion that it is essential for the cell or organized cell unit to be intact in order that a hormone may exert its effect.

¹(a) Woods J W and Hunter J C "Pigment Cell Biology" 455 (Academic Press N Y 1959) (b) Hochstein I *ibid* 456

- ²Lerner A B and Takahashi Y "Recent Progress in Hormone Research" 12 803 (1956)
³Lerner A B and Case J D *J Invest Derm* 32 212 (1940)
⁴Lee T H and Lerner A B *J Biol Chem* 221 943 (1956)
⁵(a) Harris J I and Lerner A B *Nature* 179 1846 (1957) (b) Harris J I *Biochem J* 71 451 (1959)
⁶Lerner A B, Case J D, Takahashi Y, Lee T H and Mori W *J Amer Chem Soc* 80 2587 (1958)
⁷Wright M R and Lerner A B (to be published)
⁸Foster M "Pigment Cell Biology" 301 (Academic Press N Y 1959)
⁹Poster M, Takahashi Y and Mori W (to be published)
¹⁰Klotz I M *Science* 123 815 (1958)
¹¹Ascho-Hansen G *J Agriol Res* 38 440 (1958)

THE NUCLEAR-POWERED SHIP, SAVANNAH

THE marine world has become accustomed to the reality of nuclear powered ships through the widely publicized performances of the American submarines *Nautilus* and *Skate* and the building of the Russian icebreaker *Lenin*. These are specialist craft in which the economics, conveniences and safety precautions pertinent to merchant shipping play no part. To test the possibilities of the application of nuclear power to a vessel normally carrying passengers and a mixed cargo the nuclear powered ship *Savannah*, named after the first steamship to cross the Atlantic is now being built by the New York Shipbuilding Corporation for the U S Atomic Energy Commission and the U S Department of Commerce. She is specifically designed as a test ship, to obtain information on practical construction and operating technology, though it is realized that at the present stage the ship is not an economic proposition.

The *Savannah* is of 22 000 tons displacement when loaded, nearly 800 ft in overall length and draws 20 ft, she has a cargo capacity of 10 000 tons carries 80 passengers, a crew of 110, can cruise at 21 knots, and is expected to be ready for unrestricted operation by summer 1960. Externally, the design appears advanced and pleasingly simple. She has sweeping lines with a well raked stem and cruiser stern. The superstructure incorporating the bridge and sheltered decks is placed well aft, with four holds forward of the bridge. Passenger accommodation is conventionally luxurious, while cargo handling equipment is of the most advanced and fastest type.

The propulsion plant normally develops 20 000 s.h.p. absorbed by a single screw. The pressurized water reactor the type used in the *Nautilus*, is fuelled by uranium oxide with about 4.4 per cent enrichment of uranium 235, clad in stainless steel rods and cooled by light water at a pressure of 1,750 lb/sq in, heat being abstracted from the core by a three-pass flow arrangement. Emphasis has been placed on the necessity for a long lifetime of the core, the design target being 52 000 MW days or 3½ yr under normal operating conditions. A large low-density core is therefore used, while the use of uranium 235 as a fertile material is expected to extend the life of the core through its conversion to plutonium. The variation of power output demanded from the bridge can be met by automatic operation of the boron-stainless steel control rods.

At normal load the inlet temperature of the primary coolant demineralized water flowing through two closed loops, is 404 °F and the outlet temperature 521.3 °F, the coolant being circulated by

four pumps and the heat supplied by the reactor rejected to the secondary circuit steam generators. The primary water is continually purified to remove corrosion, fuel and fission products.

The heat rejected by the primary coolant is used to generate steam in the secondary circuit from two generators which supply dry saturated steam at 490 lb/sq in to high and low pressure De Laval turbines driving the main shaft through a double reduction gear. Two 1,500 kW steam turbine generators provide power for auxiliary services and a low pressure heat exchanger provides steam for hotel services and space heating. For emergency two 750 kW diesel driven generators provide power for removal of reactor heat after shut-down and will supply essential services, including this take home motor coupled to the main shaft.

The installation of nuclear power plants in merchant shipping presents grave problems of ensuring the complete safety not only of both passengers and crew, but also of the inhabitants of the ports of call. It is not sufficient to guard against the hazard of a major explosion. Complete precautions must also be taken against the possibility of irradiation caused by collision or by the sinking of the ship in shallow water. Safety considerations have been elaborated on the *Savannah*. The design of the hull is such that the ship will remain afloat with two of the eleven main compartments flooded. This is not an abnormal requirement but in the *Savannah* elaborate collision bulkheads and collision mats ensure that a ramming ship would have to penetrate 17 ft of stiffened ship structure before the containing vessel of the reactor was affected. The inner bottom below the reactor is also strengthened by transverse and longitudinal members to form an 'egg crate' construction. It is estimated that the reactor compartment is impervious to any collision with all but 1 per cent of the world's mercantile marine. The likelihood of high-speed collision in harbour waters is considered negligible.

The chief radiation sources are the reactor core and the primary coolant. The reactor is shielded by a lead-covered steel tank which surrounds the reactor with an annular water space. It is estimated that the dose rate outside the primary shielding will not exceed 200 mr per hr 30 min after shut down. This rate is low enough to permit approach for inspection and maintenance. The whole of the primary system is further surrounded by a containing vessel, designed to limit the radiation in the holds to 5 r a year and to 0.5 r a year in the passenger spaces. The containing vessel cylindrical in shape 35 ft. in diameter by 50.5 ft long also serves to

prevent spread of radioactivity in the event of any rupture of the primary system. The lower half of this vessel is of concrete surrounded by water tanks, while the upper half is of lead slabs surrounded by polyethylene. Should the ship sink in deep water, two of the manholes will open automatically to equalize pressure and then close to prevent undue leakage of radiation products. Provision is also made in the case of shallow-water sinking to allow purging of the containing vessel or filling it with concrete. The total weight of the containing vessel is about 2,000 tons.

Waste liquids likely to be radioactive are fed to storage tanks and will not be discharged at sea except under the conditions set forth by the Maritime Administration and the Atomic Energy Commission. Radioactive gases are diluted and discharged up the

radio mast after being filtered. Purging of the air of the containing vessel, of which the argon is slightly radioactive, is carried out periodically at sea. Cooling of such components as primary circulating pumps is effected by fresh water cooled by sea water in an intermediate circuit. The sea water does not become radioactive.

Apart from the care taken in the design and construction of the ship, extensive training in nuclear reactor theory and its marine application is being undertaken by the candidates for the posts in the *Savannah*. The longest course taken by engineering-officer candidates occupies fifteen months. A shorter course has also been arranged and is intended for candidates already possessing a science degree and includes seven observers from Britain, Denmark, Holland and Japan.

F. D. ROBINSON

OBITUARY

Sir Alfred Egerton, F.R.S.

ALFRED CHARLES GLYN EGERTON died suddenly on September 7 following a heart attack. He was on holiday at the time at his house at Mouans Sartoux in the south of France, with his wife and son Francis. He was seventy-two, but was in full vigour; his sudden death comes as a great blow to all those in combustion science, in which Sir Alfred has been the acknowledged leader for many years. He had also made many important contributions in engineering, and in scientific administration and education.

He was educated at Eton, where he took the science prize and founded the College Scientific Society, and at University College, London, where he gained first-class honours in chemistry and was later president of the College Chemical and Physical Society. He studied at Nancy and in Berlin with Prof. W. Nernst, and in Sir William Ramsay's private laboratory as his last research student. During 1909-13, he was instructor at the Royal Military College and, during the First World War, carried out research on explosives and had his first contact with chemical engineering.

After the War Egerton went to the Clarendon Laboratory at Oxford and carried out researches on the vapour pressures of metals at high temperatures and, in advance of his time, worked on the separation of zinc isotopes. He was appointed reader in thermodynamics in 1923. During a British Association meeting in Canada, Sir Harry Ricardo and Sir Henry Tizard, with whom his friendship was life-long, aroused his interest in combustion and in the role of the newly discovered 'anti-knock'. He applied his knowledge of physical chemistry to this problem of knock in internal combustion engines and put forward the view that break-down of unstable organic peroxides was responsible for 'pre-sensitizing' the premature detonation. His interest in combustion continued throughout his life, and he and his research group published a steady stream of valuable papers on the role of peroxides in combustion, on peroxide analysis, on slow combustion processes, on gaseous detonation, on limits of inflammability, on burning velocities, and on techniques for these studies, such as the use of absorption spectra and the development of the flat-flame burner.

Egerton also carried out or stimulated work in many fields of applied science. He made measurements of the properties of that important working substance steam, and stressed the value of methane or natural gas as potentially the most efficient fuel for the internal combustion engine, and worked on the combustion, liquefaction and bulk handling of methane. This led to an interest in liquefaction problems, and he was active in founding the Low Temperature Group of the Physical Society, of which he was first chairman in 1946.

He was elected to the Royal Society in 1926, and in 1936 was appointed professor of chemical technology in the Imperial College of Science and Technology (University of London), a position which he held until his retirement in 1952. During his tenure of the chair, he started the undergraduate course in chemical engineering and pioneered the development of this subject in Great Britain. The Department, under his guidance, became a leading centre in both combustion research and chemical engineering.

Egerton was secretary (physical sciences) of the Royal Society during 1938-48, during the important War period, and he was also a member of the Scientific Advisory Committee of the War Cabinet during 1940-45. In 1942, he spent some time in Washington in charge of the British Commonwealth Scientific Office, where he did important work improving Anglo-American co-operation. His membership of numerous committees gave him a tremendous breadth of knowledge of affairs and of people. At various times he was chairman of the following committees: the Heating and Ventilating Committee, the Fuels and Propulsion Committee, Admiralty Scientific Research Department, the Scientific Advisory Council, Ministry of Fuel and Power, the committees reporting to the Government of India on the Indian Institute of Science, and on the sixteen Government of India laboratories, the Scientific Advisory Committee of the British Council, the Combustion and Fuels Committee of the Aeronautical Research Council, and the Royal Society Scientific Information Conference. He had been director of the Salters' Institute of Industrial Chemistry and a manager of the Royal Institution. He was president of the British Section of the Combustion

Institute, editor of *Combustion and Flame*, and formerly of *Fuel*. He was active in work on the dissemination of scientific information (*Science Abstracts Committee*), on the use of scientific manpower (*Barlow Committee*) and on the use of the world's fuel and energy resources. His educational interests are shown by his active membership of the governing bodies of Winchester College and of Charterhouse. Last year, he was responsible for the successful organization of the seventh International Combustion Symposium in Oxford. His recent intense activity had been on the Government Committee of Inquiry into the Fishing Industry, and in research into the characteristics of smouldering for the Tobacco Manufacturers Standing Committee. His work was recognized by a knighthood in 1943 and a number of honorary degrees and medals, including the Rumford Medal of the Royal Society in 1946.

In 1912 he married the Hon. Ruth Crapps, only daughter of the first Baron Parmoor, sister of his close friend at University College the late Sir Stafford Crapps.

As a man we remember his quiet unassuming manner, his unfailing smile of greeting, his tireless work on his many scientific interests, and his delight in his second career as a painter. Somehow despite his many activities, he always had time to spare for everyone. He had the genius for bringing out the best in those with whom he worked and took a fatherly interest in the numerous research students he sponsored, so many of them now in high positions in science and industry. This keen personal interest in his students, colleagues, and indeed in all he did was fully shared by Lady Egerton. His life and work are an example to all those whom he has influenced.

A. G. GAYDON

NEWS and VIEWS

Biochemistry at Birmingham Dr S. V. Perry

THE development of a Department of Biochemistry in the University of Birmingham arising as it does in part from the former Department of Industrial Fermentation needs for guidance a man of scientific ability and vigorous powers of leadership. The appointment of Dr S. V. Perry to be professor of biochemistry has recently been announced. Dr Perry graduated with first-class honours in biochemistry in the University of Liverpool in 1939 and was elected to the Isaac Roberts research scholarship upon graduation. After the Second World War he was elected a Rouse Ball research student of Trinity College, Cambridge, and began his researches on muscle biochemistry in the Department of Biochemistry. He was elected a research fellow of Trinity College, Cambridge in 1947 and a Commonwealth Fund Travelling Fellow in 1948, spending the year 1948-49 in the Department of Physiology of the Medical School of the University of Rochester, New York, investigating the biochemical properties of skeletal muscle. In 1950 he was appointed a lecturer in biochemistry in the University of Cambridge. His researches have been largely concerned with biochemical function in relation to intracellular morphology, with particular reference to the muscle cell. A study of the intracellular components of striated muscle has been pursued in an investigation of the biochemistry of the cell in general, and of the contractile process in particular. These studies are throwing important light on the nature of the association between muscle proteins and the role of their interaction in muscular contraction. Dr Perry has taken part by invitation in a number of international congresses concerned with the biochemistry of muscle and has published many articles on this subject in the *Biochemical Journal* and other scientific periodicals.

Analytical Chemistry at Birmingham

Prof. Ronald Belcher

THE award of the title of professor of analytical chemistry is a tribute to the work Dr Belcher has done at Birmingham in building up the School of Analytical Chemistry, which is unique in Great Britain. The honour comes at an appropriate time, since he is at present the president of the Analytical

Chemistry Section of the International Union of Chemistry and a vice-president of the Union. Prof. Belcher received his early education in Shiffield and gained his first qualifications through the Royal Institute of Chemistry. After carrying out extensive researches since 1928 on coal at the University of Shiffield, he became a lecturer in chemistry in the University of Aberdeen in 1940, moving to Birmingham in 1948. Since that time a constant flow of papers has come from his group and no less than twenty-eight higher degrees have been awarded to graduates in analytical chemistry under his supervision. With pupils and colleagues he has published more than 150 papers and ten well-known books, all in the field of analytical chemistry, and to these and his many editorial and committee activities he owes his world-wide reputation. He gained the Ph.D. and D.Sc. of the University of Birmingham. With the vast extensions of the Chemistry Department at Birmingham nearing completion, Prof. Belcher and his colleagues will have greatly increased facilities for research and the training of analysts at all levels.

Mathematical Physics at Birmingham

Prof. G. E. Brown

THE title of professor of mathematical physics has been conferred on Dr G. E. Brown, at present reader in the Department of Mathematical Physics. Dr Brown, who is a citizen of the United States, studied in South Dakota State College at the Universities of Iowa and Wisconsin, and after war service became a graduate student at Yale in 1947 and obtained his Ph.D. there in 1950. He was awarded the D.Sc. of the University of Birmingham in 1957. He went to Birmingham with a post-doctoral award in 1950, was appointed a research fellow in September 1950 and has been on the teaching staff since 1954, except for a period of study leave from January to September 1958, which was spent in the Institute for Theoretical Physics in Copenhagen. He has published numerous papers on different aspects of quantum theory, particularly on relativistic electron theory including relativistic corrections in atomic problems. More recently he has done important work in nuclear theory including a series of papers with various collaborators on the relation between the nuclear many-body problem and the optical model.

National Science Foundation

Dr David D Keck

THE National Science Foundation has announced that Dr David D Keck has resigned his position at the New York Botanical Garden in order to remain permanently as programme director for systematic biology at the Foundation's Division of Biological and Medical Sciences. The Systematic Biology Programme receives research proposals and administers more than three hundred active grants. In 1950, Dr Keck joined the staff of the New York Botanical Garden as head curator, he became assistant director in 1955 and served as acting director in 1958. From 1926 until 1950 he was on the staff of the Division of Plant Biology of the Carnegie Institution of Washington, at Stanford, California. There he was a member of a research team concerned with pioneer work on the nature of plant species. He is the author of many technical papers and has collaborated with Philip A Munz in writing "A California Flora" that has just come from the University of California Press.

Microbiological Research

IN a written answer in the House of Commons on July 21, Mr H Nicholls, Parliamentary Secretary to the Ministry of Works, stated that since the Council for Scientific and Industrial Research announced last December its intention to encourage university research in microbiology, ten applications had been received for grants for research projects in microbiology not previously supported by the Department of Scientific and Industrial Research and all these applications had been approved.

Zenith Reactor

A QUESTION was asked in the House of Lords on July 15 about the 'Zenith' low-power reactor installed at Winfrith Heath mainly to further the work of the European Nuclear Energy Authority project for research on a high-temperature gas-cooled reactor. In reply, the Minister of Power, Lord Mills, said that the project would pay rent to the Atomic Energy Authority for the use of the reactor. It was hoped that about half the professional staff would be provided from signatory countries other than the United Kingdom. Of the total estimated cost of the project, £10 million would be contributed by the participants, the United Kingdom supplying the balance of £3.6 million and would retain ownership of the reactor and other equipment in Britain when the project was terminated. The work would be carried out by the Atomic Energy Authority, but all participating countries had their say on various matters connected with the project.

Chief Inspector of Nuclear Installations

IN the course of the debate in the House of Commons on July 2, when the Nuclear Installations (Licensing and Insurance) Bill was given its third reading, it was stated that the Minister of Power intended to appoint a chief inspector of nuclear installations who would be responsible for advising on the measures to be taken to carry out the Minister's responsibilities under the Act. The appointment had been offered (pending the Royal Assent) to Major-General S W Joslin, who had accepted it. Major-General Stanley William Joslin was educated at Hackney Downs School, Royal Military Academy, Woolwich, and the University of Cambridge. He

held the appointment of director of mechanical engineering at the War Office, until he joined the United Kingdom Atomic Energy Authority in 1954, and later became deputy director (personnel) of the Industrial Group. As chief inspector, Major-General Joslin will be the head of the inspectorate, and one of his main tasks will be to advise on the organization and build-up of the inspectorate.

Exchanges between Soviet and U.S. Scientists

THE U.S. National Academy of Sciences and the U.S.S.R. Academy of Sciences have announced the signing of a two-year agreement providing for exchange visits by research scientists of each country for periods up to one year. Under the terms of the agreement, each Academy named twenty fields of specialized scientific inquiry in which its scientists wish to observe or conduct research within the host country. In addition, the agreement provides that the two Academies will organize joint symposia dealing with scientific problems of current interest, assist each other in the exchange of scientific information, and on a reciprocal basis exchange invitations to important scientific meetings. Implementation of these provisions will substantially increase the exchange of scientists between the two countries.

Colonial Development

THE annual report of the Colonial Development Corporation for 1958 (London: H.M. Stationery Office, Pp. v+69, 4s. 6d. net) and the last over the signature of Lord Reith, who was succeeded as chairman on March 31 by Sir Nuteombe Huono, records 77 continuing projects compared with 76 the previous year. Four have stopped, and of the five new projects approved, one, Federation Chemicals, Ltd (Trinidad), for the first time associates Corporation money with American technique and finance in a Colonial territory. Much effort has been spent in Nigeria in seeking to bring about joint development companies in partnership with regional Governments, and it is understood that the Corporation's view that such companies have a particular importance as instruments through which Nigerians and the Corporation can share responsibility in investigating and launching development projects will be accepted. Capital approved for new projects and for expansion and completion of existing ones amounted to £3 million compared with £6 million in 1957, and gross new expenditure was £6 million. The report claims that the work of the Corporation has increased Colonial production of rice, citrus, pineapples, bananas, palm oil, cocoa, coffee, tea, margarine, flour, meat and fish, and also of gold, silver, copper, timber, cement, manila, hemp, wattle extract, rubber, hides, tobacco, tung oil, copra, electricity, houses, factories, roads and bridges. Besides assisting in the creation of such productive assets as hydroelectric installations in Dominica, St Vincent, Rhodesia and Kenya, irrigation canals in Swaziland, roads and bridges in Ghana and Nigeria, and in making more than 500,000 acres of idle land productive, direct projects of the Corporation provided employment for more than 16,000 workers.

Lord Reith claims, however, that much more could have been done, and while he stresses the need for first-class management and for trusting the Corporation to use its commercial judgment in the best interests of overseas development and thus of Great Britain itself, he is strongly critical of its relations

with the Government and of consequent frustration and discouragement possibly due to differences of interpretation of the Overseas Resources Development Act. Lord Roth suggests that a rapid review of the working of that Act might be helpful. He comments particularly of the extent to which applications for projects are held up, apparently through disagreement as to the nature of the work the Corporation should do and the degree of control which the Government should exercise over it. He points out that the restrictions imposed upon the future activities of the Corporation in the emergent territories will deny them the full use of its unique facilities and managerial experience at the critical transitional stage of their development, in spite of the obligation for ensuring continuing development finance in such territories which the Government appeared to recognize at the Montreal Conference.

Chinese Scientific Literature

THE Lending Library Unit of the Department of Scientific and Industrial Research is now issuing a list of current periodicals received from China. The first list (July 1959) gives the titles of one hundred periodicals which are being received regularly, and these publications can be borrowed from the Unit by approved borrowers of the Science Museum Library provided Science Museum Library loan requisition forms are used. Twenty-one of the periodicals listed are obtained by exchange and special attention is directed to *Scientia Sinica* (in English) and to *Science Record* (in English, French, German and Russian). The periodicals listed are annotated according to the category of readers for whom they are intended, and whether they include contents lists or abstracts in a Western European language. This first issue also includes a note on the Chinese phonetic alphabet.

Mordell's 'Reflections'

CAMBRIDGE mathematicians have sometimes mitigated the austerity of their scholarship on retirement, and to this wise relaxation we owe Hardy's *Apology*, Littlewood's *Miscellany*, and now Mordell's *'Reflections'* (*'Reflections of a Mathematician'*, by Prof L. J. Mordell. Pp vii + 50. Montreal: Canadian Mathematical Congress, Chemistry Building McGill University or École Polytechnique, 2600 Guevard Avenue, 1959. n.p.). In this collection of short, informal essays the author is primarily interested in explaining the point of view of the professional mathematician to fellow scholars who are not mathematicians. He is not concerned with applications, but with mathematics itself—what it is, the fascination of its aesthetics and its techniques, the difficulties and triumphs of creative work, not without some mild insinuation that the theory of numbers is the crown of mathematics. Two of his points deserve emphasis. The first is that the three cardinal virtues for the young mathematician are faith, hope and curiosity, and that the greatest of these is curiosity. Secondly, he stresses that the mathematician's task is not ended when he has solved his problem: he is under an obligation to his fellow workers to present his results clearly and intelligibly, and must not allow the economic demand for brevity to result in obscurity. The selection of precisely the right number of stops required to support the argument, so that it shall be neither tedious nor obscure, is a matter to which the young mathematician should pay careful attention. Mordell in this connection quotes with

approval Polya's advice: 'if you have two things to say, say them one at a time.'

Museum of Applied Arts and Sciences, Sydney

THE Annual Report of the Trustees of the Museum of Applied Arts and Sciences, Sydney, for 1957 (Pp 20. Sydney: Museum of Applied Arts and Sciences, 1958) stresses the great urgency of allocating a site for a new museum. It points out that a modern science museum requires an extensive area and building not only to preserve and display its national treasures in an appropriate manner, but also to exhibit full-sized engineering exhibits. Within the limits of the resources of the Museum provision was made to show the advance of science during the International Geophysical Year. Also by means of films, diagrams and models visitors were presented with the development of guided missiles and space satellites. The results of research by the staff in the field of essential oil are drawing increasing numbers of inquiries from all over the world. Since the Museum deals principally with applied science it was always necessary to strike a balance between pure and applied research by the staff.

Further Botanical Collectors

THE great tradition of travelling and collecting plants which, among others, we associate particularly with the name of Linnaeus and his followers and adherents is still very much alive in Sweden. A recent issue of the *Arkiv för Botanik* (4 Part 1, 1959, Kungl. Sveriges Vetenskaps-Akademien, Stockholm) is of special interest in this connexion in that it contains many new floristic records based on expeditions to places of such unique interest as the Juan Fernandez Islands. Several of the contributions on *Hepatica* (S. Arnell), *Mosses* (E. B. Bartram), *Uredinales* (I. Jönvall), relate to materials chiefly collected in the course of an expedition by the eminent Swedish botanist, Dr C. Skottsberg, and his wife during 1954-55 to these islands. Some of the records also relate to the Falkland Islands and South America. There is also an account of *Annonaceae* by von Rohd F. Fries based on specimens collected by Dr Eric Asplund during his travels in Ecuador in 1955.

The Ciba Foundation 1949-59

THE Ciba Foundation, founded in 1947 by the Swiss firm Ciba, Ltd., of Basle for the promotion of international co-operation in medical and chemical research, shows in its report for the years 1949-59 a remarkable record of success. Housed at 41 Portland Place, London W.1, in a building designed by the brothers Adam which was built in 1778 and is now scheduled as a building of historical and architectural interest, the Foundation, through its Trustees, Executive Council and International Scientific Advisory Panel, has arranged numerous international conferences, colloquia and discussion meetings on various subjects, as well as the Ciba Foundation annual lectures and scientific film sessions (The Ciba Foundation for the Promotion of International Co-operation in Medical and Chemical Research. Ten Years Report for 1949-1959. Pp 1-64. The Ciba Foundation, 41 Portland Place, London W.1). A feature of the colloquia and conferences is that they are attended for three or four days by experts in various fields of work from various countries who are invited to take part, the number attending being kept low, great importance being attached to free discussion and social contacts.

Table 1 PERFORMANCE OF RATS IN TILTED PLANE TEST DURING ETHANOL INTOXICATION

| Exp. series | Number of animals | | Age of animals weeks | | Performance in test | | Sexes different, $P <$ | Blood alcohol (mgm %) | |
|-------------|-------------------|----|----------------------|----|---------------------|------------|------------------------|-----------------------|----------|
| | M | F | M | F | M | F | | M | F |
| I | 10 | 15 | 20 | 14 | 66.9 ± 4.8 | 74.7 ± 6.1 | 0.005 | 202 ± 11 | 207 ± 16 |
| II | 10 | 10 | 15 | 11 | 68.7 ± 5.0 | 68.7 ± 5.3 | N8 | 202 ± 11 | 106 ± 14 |
| III | 14 | 14 | 14 | 14 | 68.8 ± 6.0 | 75.7 ± 5.1 | 0.001 | 210 ± 16 | 206 ± 14 |
| | 14 | 14 | 18 | 18 | 64.2 ± 6.0 | 60.3 ± 4.4 | 0.01 | | |
| | 14 | 14 | 22 | 22 | 62.0 ± 1.9 | 63.2 ± 4.1 | N8 | | |

The results expressed as per cent of an initial sober value obtained immediately before alcohol injection. The lowest value observed in 10 tests during 90 min. following injection is given. Standard deviation is indicated. In series III the same individuals were tested at three different ages. The means from all 6 tests in one experimental run gave comparable results.

from the tail, immediately after the final testing, for analysis according to the method of Newman and Newman², modified to allow the use of approximately 100 mgm of blood. The results are shown in Table 1. The performance of the animals indicates that the tolerance of females increases transiently when breeding maturity is reached. It returns to the same level as that of the males in about 8 weeks.

The higher tolerance of the females is not due to differences in rate of alcohol oxidation since no significant difference in blood alcohol level was found. Ijiri³ observed that a 1 per cent alcohol solution increased *in vitro* oxygen consumption of unstimulated cerebral cortex and mid brain tissue from normal rats, whereas on a 0.5 per cent solution depressed the oxygen consumption of corresponding tissues from castrated animals. Goldberg and Stortebecker⁴ have reported an anti narcotic effect of oestrone on alcohol intoxication in castrated female rabbits and conclude that the resistance of the central nervous system is related to the hormonal state. Angelucci⁵ has demonstrated a sex difference in rats with respect to morphine tolerance, females being more resistant than males. Female rats tolerate chlorpromazine better than do male rats, and the tolerance of males is reduced with advancing age.⁶

The present observation has obvious relevance for the selection of animals for experiments on the effects of alcohol. Whether a change in the general response to stressors or some specifically nervous mechanism is involved cannot be judged on basis of this material.

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α -Ketoglutaric Acid and Pyruvic Acid in Blood, Cerebrospinal Fluid and Urine

DETERMINATIONS of α -ketoglutaric acid and pyruvic acid in blood, cerebrospinal fluid and urine have been carried out using 2,4-dinitrophenylhydrazono method.¹ The keto acid hydrazones were separated, either by paper electrophoresis or by paper chromatography.

The electrophoretic separation was carried out in 0.05 M sodium bicarbonate at 400–420 V/10–18 m amp for 3 hr. No 1 paper (20 × 20 cm). The separation was per-

formed in *n*-butanol ethanol 1 per cent ammonia mixture (6:1:3 v/v). The amount of hydrazones applied at the start corresponded to 0.5 ml of blood or urine respectively or to 1 ml of cerebrospinal fluid. After separation the hydrazone spots (both isomers in the case of pyruvic acid) were extracted with 1 N sodium carbonate and measured at 390 m μ on the Zeiss spectrophotometer.

Higher values of pyruvic acid in electrophoretic separation (Table I) are due to the fact that together with pyruvic acid other α -keto acids (eventually aldehydic acids) found in traces only in the biological material are determined and their hydrazones travel in the electric field with the same speed as hydrazone of pyruvic acid does. As it was formerly shown in the case of pyruvic acid hydrazone, approximately the same mobility was observed for hydrazones of glyoxylic acid and phenylpyruvic acid (two isomers again) and for α -ketoisocaproic acid by Buerte and Dassooville.² Both hydrazones mentioned above can be separated by chromatography.

Table I VALUES OF α -KETOGLUTARIC ACID AND PYRUVIC ACID IN BLOOD AND CEREbroSPINAL FLUID AS DETERMINED BY ELECTROPHORETIC AND CHROMATOGRAPHIC METHODS

| | The number of cases | Chromatographically mgm/100 ml | | Electrophoretically mgm/100 ml | |
|---------------------|---------------------|-----------------------------------|--------------|-----------------------------------|--------------|
| | | α -keto-glutaric acid | pyruvic acid | α -keto-glutaric acid | pyruvic acid |
| Blood | 12 | 0.15 ± 0.07 | 0.41 ± 0.11 | 0.14 ± 0.04 | 0.60 ± 0.14 |
| Cerebrospinal fluid | 6 | not exceed 10 ⁻⁴ | 0.48 ± 0.12 | not exceed 10 ⁻⁴ | 0.54 ± 0.14 |

In urine of 10 patients confined to bed and suffering from no metabolic disease 14.17 ± 3.20 mgm. of α -ketoglutaric acid and 8.16 ± 1.55 mgm. of pyruvic acid were found on average during 24 hr. Five employees of this institute carrying out their normal duties excreted 18.40 ± 4.05 mgm. of α -ketoglutaric acid and 11.06 ± 4.84 mgm. of pyruvic acid in 24 hr. Both physical and mental strain increase the amount of α -keto acids eliminated in the urine.

Patients confined to bed excreted maximum values of keto acids during the afternoon or evening hours. Women eliminated more α -keto glutaric acid during the night than men.³

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Effects of Methylthiouracil or Thyroidectomy on Activation of Pituitary Acid Phosphatases *in vitro* by Whole Hypothalamic Extract

IN EARLIER experiments¹ it was shown that incubation of whole rat pituitaries *in vitro* in whole aqueous hypothalamic extract increased pituitary acid phosphatase activity. In further experiments^{2,3} evidence has been submitted in support of the view that a relationship exists between activation of pituitary acid phosphatases *in vivo* and formation of the thyrotrophic hormone and that the presumed hypothalamic humoral factor activating pituitary acid phosphatases *in vitro* is related to thyroid-stimulating hormone secretion. The present communication gives the results of experiments investigating the extent to which the influence of hypothalamic extract on acid phosphatases in the rat pituitary *in vitro* can be modified by previous administration of methylthiouracil to hypothalamus donor rats or by previous thyroidectomy of these animals.

In the first experiment 40 fresh pituitaries from albino rats (descendants of the Wistar strain) were divided into five groups and incubated for one hour at $37 \pm 0.1^\circ \text{C}$ in the following media: (1) Krebs-Ringer phosphate with 300 mgm per cent glucose; (2) the same medium plus extract from 2/3 of one control rat hypothalamus/c.c., (3) the same amount of hypothalamic extract from rats to which 0.2 per

cent methylthiouracil was administered in food 16 days before they were killed, (4) hypothalamic extract from rats to which 0.5 per cent dried thyroid ('Thyreoidin' SPOFA) was administered in food for a period of nine days before they were killed, (5) hypothalamic extract from rats to which both methylthiouracil and dried thyroid were administered. The results of biochemical determination of acid phosphatase activity in the individual groups of pituitaries are given in Table 1.

In the second experiment 40 fresh rat pituitaries were again divided into five groups and incubated in the following media: (1) Krebs-Ringer phosphate with 300 mgm per cent glucose, (2) extract of 2/3 control rat hypothalamus/c.c., (3) hypothalamic extract from rats subjected 12 days previously to thyroidectomy, (4) hypothalamic extract from rats to which 0.5 per cent dried thyroid was administered in food for 12 days before they were killed, (5) hypothalamic extract from rats subjected to both treatments (thyroidectomy + 'Thyreoidin'). The results of the determination of acid phosphatase activity are given in Table 2.

The results show that (1) incubation in control hypothalamic extract increases pituitary acid phosphatase activity *in vitro*, (2) previous administration of methylthiouracil to hypothalamus donor rats or previous thyroidectomy of these animals inhibits this increase, (3) the administration of dried thyroid alone does not affect activity under the given conditions, (4) the administration of dried thyroid counteracts the inhibition of activation observed after methylthiouracil or thyroidectomy alone. In our view the above findings are evidence of the existence of a hypothalamic humoral factor activating simultaneously pituitary acid phosphatases and thyroid-stimulating hormone secretion. The decrease which occurs in the concentration of this factor in the hypothalamus after methylthiouracil or thyroidectomy could be due to its being washed out to portal system to increase thyroid-stimulating hormone secretion. The administration of dried thyroid caused no marked change in the activating effect of hypothalamic extract, in other experiments⁴, however, more prolonged administration of dried thyroid slightly enhanced its effect.

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Comparison of individual groups in *t* test: $2.3 = P > 0.01$, $2.5 = P = 0.05-0.02$

TABLE 2

| Group | 1 medium only | 2 control hypothal | 3 hypothal thyroid- ect | 4 hypothal 'Thyre- oidin | 5 hypothal thyroid- ect + 'Thyre- oidin |
|---|---------------------|--------------------------|----------------------------------|-----------------------------------|--|
| No. of pituitaries | 8 | 8 | 8 | 8 | 8 |
| Mean weight of pituitaries (mgm) | 5.7 | 5.2 | 5.8 | 5.4 | 5.4 |
| Mgm of hypothalamic tissue/cc incubations medium | 0 | 100 | 100 | 95 | 100 |
| Mean activity of acid phosphatase in the pituitaries K.A.U./gm $\pm \sigma_M$ | 1.05 ± 0.138 | 2.03 ± 0.205 | 2.11 ± 0.270 | 2.67 ± 0.250 | 2.60 ± 0.121 |

Comparison of groups No. 2 and 3 in *t* test: $P = 0.02$

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Inhibition of Skeletal Formation in the Chick Embryo following Administration of Tetracycline

It has been shown that tetracyclines form complexes with metallic ions^{1,2}, that they become incorporated into bones of young mice³, and also that they are retained in bones of several other species for a considerable period following administration⁴⁻⁵. We have recently demonstrated⁶ that tetracycline inhibits skeletal formation in the sand dollar (*Echinarrachmus parma*) embryo. The above observations prompted us to extend our previous studies and test the effect of the administration of

tetracycline on developing chick embryos with special reference to the formation of the skeleton

Our experiments consisted in brief of injecting tetracycline (achromycin) into the yolk-sac of embryos eight days old in amounts ranging from 0.1 to 2.5 mgm. The embryos were examined two, four, six and eight days afterwards. The presence of tetracycline was identified by its characteristic fluorescence in the presence of ultra violet light.

Administration of 0.5 mgm per embryo is followed by rapid distribution of the drug throughout the embryo. 24 hr later the drug appears exclusively in the calcified portions of the skeleton (Fig. 1). When

supplied by Lederle Division, American Cyanamid Co., Pearl River, N.Y.

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Fig. 1. Photograph of embryo injected on the eighth day with 1 mgm of tetracycline killed and photographed in ultra violet light 24 hr later. Whites area indicate fluorophor in skeleton ($\times 2$)

2.5 mgm of the compound was injected, a pronounced retardation in overall growth occurred which was evident in embryos 10, 12, 14 and 16 days old.

Microscopic examination of the femurs of the treated embryos show several abnormal characteristics. They exhibit a marked bending, the number of trabeculae are reduced and the degree of mineralization is less than half observed in normal bones. In addition, the periosteum is thickened, the development of the hematopoietic elements is arrested and chondrogenesis is retarded. The net result of these several disorders in the growing structure lead to the production of a stunted malformed bone.

Our studies have shown uptake and retention of tetracycline by the growing bones of embryos as previously described^{2, 3} for young adult animals. We have also demonstrated that administration of tetracycline to embryos results in marked inhibition and malformation of the growing bones. Inasmuch as tetracyclines are frequently employed in clinical practice, the results we have reported may be important.

Full details of the experiments performed will be published elsewhere. This study was supported (in part) by Grant No. D-047 U.S. Public Health Service, N.I.D.R. The tetracycline used was generously

Culture of Algae and other Micro-organisms in Deuterium oxide

THERE can be no doubt that algae forced to grow autotrophically in high concentrations of deuterium oxide are confronted with a difficult situation. Nevertheless, recent statements that moderate concentrations of deuterium oxide stop cell division in *Chlorella*, that the growth of *Chlorella* is "extremely slow sporadic and unpredictable" at high concentrations of deuterium oxide and that autotrophic growth of *Chlorella* is "inhibited completely in 90 per cent heavy water" must have only very limited validity. It is in fact entirely feasible to culture several species of algae autotrophically in 99.6 per cent deuterium oxide and at a growth rate such that they become a practical source of fully deuterated compounds⁴.

Algae require a prolonged period for adaptation or acclimatization to deuterium oxide. We have observed that an adaptation time of at least 200 hours is usually necessary before appreciable growth occurs. Such protracted adaptation periods appear to be far longer than those previously employed and this may account for the failure of earlier workers to observe growth in deuterium oxide. Algae from old water cultures appear to adapt faster than young cultures but the factors involved in the adaptation process are still very obscure. Once adaptation does occur subsequent transfers to deuterium oxide produce immediate growth. Although morphological abnormalities are common during the adaptation period, fully adapted organisms cultivated for long periods in deuterium oxide appear quite normal under the microscope.

Three species of green algae have been successfully adapted to growth in 99.6 per cent deuterium oxide. Cultures of *Chlorella vulgaris* and *Chlorella pyrenoidosa* were obtained from the late Dr. Robert Emerson and *Scenedesmus obliquus* from Prof. H. Gaffron. Other cultures of these organisms were obtained from the Algae Collection of Indiana University. For *Scenedesmus obliquus* the following nutrient solution is presently used (gm/l): MgSO_4 , 0.48; $(\text{NH}_4)_2\text{NO}_3$, 0.80; NaH_2PO_4 , 0.20; KH_2PO_4 , 0.20; $\text{Ca(NO}_3)_2$, $4\text{H}_2\text{O}$, 0.40; NaCl , 0.020; FeSO_4 , $7\text{H}_2\text{O}$, 0.030. For *Chlorella vulgaris* and *Chlorella pyrenoidosa* a somewhat different nutrient has been employed (gm/l): KNO_3 , 1.25; Na_2HPO_4 , 1.00; KH_2PO_4 ,

0.25, MgSO_4 , 0.125, $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$, 0.0054, NaCl , 2.00. Both media contain trace elements (in parts per million) B, 0.5, Mn, 0.25, Zn, 0.05, Cu, 0.02, Mo, 0.05. The addition of sodium chloride is found to exercise a markedly beneficial effect on the growth rate of *Chlorella* in deuterium oxide. Carbon dioxide is fed as a mixture of 5 per cent carbon dioxide-95 per cent nitrogen. The temperature is maintained at 26-28°C. The algae are continuously agitated in 200-ml flasks on a rotatory shaker, or are grown in large transparent plastic boxes. Light of an intensity of about 600 ft-candles is supplied by a panel of fluorescent lamps.

Scenedesmus obliquus has shown the fastest growth under our culture conditions. In ordinary water, we have observed a growth rate of 0.55 gm (dry weight) per litre per day. The adapted *Scenedesmus* in deuterium oxide medium, under the same conditions, has a growth rate of 0.30 gm (dry weight) per litre per day. More recently, we have grown *Scenedesmus* on an 8-litre scale in a 'Lucite' box, under these conditions we have observed a growth rate of 0.22 gm (dry weight) per litre per day. The algae were allowed to grow to a concentration of 8 gm (dry weight) per litre, at which time a portion was harvested. A total of several hundred gm (dry weight) of algae has been obtained in this way.

Blue green algae can also grow in 99.6 per cent deuterium oxide. *Gleocapsa* sp and *Oscillatoria* sp have been adapted to growth in deuterium oxide on the nutrient solution used for *Scenedesmus* and under the other conditions given above. We consider it probable on the basis of these observations that other classes of algae will also be adaptable to growth in deuterium oxide.

We have also studied the effects of deuterium on the growth of the bacterium *Escherichia coli*, the yeast *Torulopsis utilis*, and the protozoan *Paramecium caudatum*. *E. coli* is easily grown in 99.6 per cent deuterium oxide using either fully deuterated acetate or fully deuterated glucose (isolated from fully deuterated algae*) as the carbon source. *T. utilis* (American Type Culture, Collection No. 9950) has been grown on fully deuterated glucose, the nutrient solution employed had the composition (gm/l): $(\text{NH}_4)_2\text{HPO}_4$, 1.0, KH_2PO_4 , 0.5; CaCl_2 , 0.2, MgSO_4 , 0.2, NaCl , 0.2, deuterated glucose, 10.0, algae extract, 1.0, and micronutrients as above. Although *T. utilis* ordinarily requires no bios factors for growth, in order to achieve growth in 99.6 per cent deuterium oxide we have found it necessary to add an algae extract prepared from deuterated algae. *P. caudatum* has been cultured in lettuce infusion in 60 per cent deuterium oxide, daily additions of small amounts of fresh lettuce infusions increase the tolerance level to at least 70 per cent deuterium oxide. During adaptation by serial subculture, monster forms of *P. caudatum* were observed, but the organisms now maintained at 60 per cent deuterium oxide are essentially normal in appearance, although they are somewhat smaller than usual.

We conclude that a variety of essentially fully deuterated organisms can be grown. We have already isolated fully deuterated glucose*, and fully deuterated chlorophylls and carotenoids (following communication) from deuterated algae and no doubt these and other organisms will serve as a source of many other fully deuterated compounds.

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Chloroplast Pigments of Deuterated Green Algae

It has recently been found that green algae can be successfully grown in 99.6 per cent deuterium oxide¹. Algae such as *Chlorella vulgaris* and *Scenedesmus obliquus* adapted to deuterium oxide thus provide a source of highly deuterated organic compounds. Since the organisms grow in deuterium oxide with carbon dioxide as the sole carbon source, the cells must be equipped for photosynthetic activity even though their organic matter is constructed with deuterium in place of hydrogen.

To ascertain whether possible modifications in the indispensable, photosynthetically-active pigments of the deuterated organisms have occurred on adaptation we have now isolated the chloroplast pigments of *Chlorella* and *Scenedesmus* and have measured their visible and infra-red absorption spectra. To this end, the pigments were extracted from freshly harvested algae with methanol plus petroleum ether and were separated by column chromatography on powdered sugar. The carotenoids were separated further by chromatography on magnesia-silica columns. In all respects, the chromatographic procedures were those which have been applied to plant pigment studies generally.² The only significant difference was that precautions were taken to minimize contamination of the separated pigments by impurities containing hydrogen from the sugar columns. Each pigment was also crystallized from suitable solvents and dried in vacuum.

As shown by the colour and sequence of the zones in the chromatographic columns, and as indicated by the spectra of the pigments in the visible region, the deuterated chloroplasts contained pigments corresponding to chlorophyll *a*, chlorophyll *b*, α -carotene, β -carotene, lutein (xanthophyll), zeaxanthin, violaxanthin, and neoxanthin, and a xanthophyll characteristic of green algae which is sorbed between violaxanthin and neoxanthin on columns of sugar.² No new bands were found in the chromatograms from the deuterated algae, and none of the usual bands was absent. Chloroplasts of the deuterated green algae thus have the normal complement of pigments.

The absorption spectra of chlorophylls *a* and *b* from deuterated algae and from ordinary spinach, for comparison, were measured in the visible region. Wavelengths and relative intensities of the absorption maxima are summarized in Table I. No significant differences in either position or relative intensities of the absorption maxima are apparent in the chlorophylls from spinach and from the deuterated algae. Similar relationships were found among the spectra of the carotenoids. Possible changes in the magnitude of the extinction coefficients remain to be ascertained.

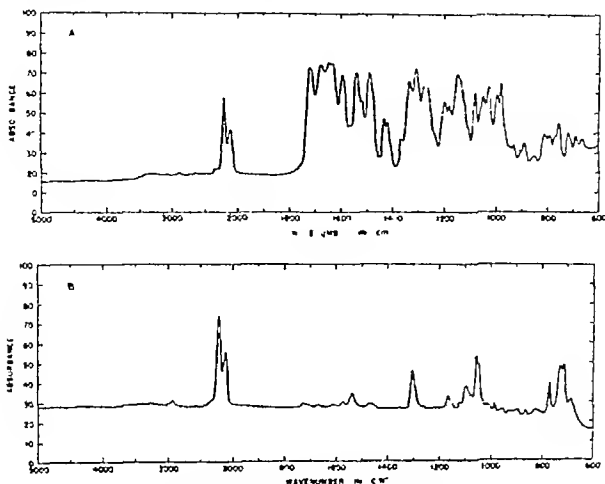


Fig 1 Infra red absorption spectra of thin films of chlorophyll *a* (A) and β -carotene (B)

The infra red absorption spectra of the chloroplast pigments were measured with thin films formed by melting a suitable amount of the compound on a potassium bromide plate. Infra red spectra of ordinary pigments measured in this way agreed well with the respective spectra, of chlorophylls¹ and β -carotene², described in the literature. Infra red spectra of deuterated chlorophyll *a* and β -carotene are reproduced as A and B respectively in Fig 1. In these spectra and in those of the other deuterated pigments the prominent C-H absorption at 2,900 cm^{-1} due to C-H stretching vibrations is essentially absent and is replaced by the C-D absorption at 2,100–2,200 cm^{-1} . As C-H impurities may be introduced from the sugar columns and the solvents, the small amount of C-H absorption apparent in B is probably not significant. In all of the deuterated carotenoid spectra so far examined a characteristic two banded absorption occurs in the 700–800 cm^{-1} region, no corresponding absorptions were noted in the hydrogen prototypes. The band at 902 cm^{-1} characteristic of normal carotenoids is absent in the deuterated forms. We conclude from the infra red spectra that in the pigments obtained from deuterated algae essentially all the hydrogen positions are occupied by deuterium, and the deuterated pigments are effective in photosynthesis.

Table 1 COMPARISON OF ABSORPTION SPECTRA OF CHLOROPHYLLS *a* AND *b* FROM SPINACH AND FROM DEUTERATED ALGAE (SOLVENT, ETHANOL)

| | Absorption maxima (m μ) | | | | Relative intensities of absorption maxima | |
|------------------|------------------------------|---------------|--------------|---------------|---|-----------------------------|
| | Red <i>a</i> | Blue <i>a</i> | Red <i>b</i> | Blue <i>b</i> | Blue max./Red max. <i>a</i> | Blue max./Red max. <i>b</i> |
| Spinach | 660 | 433 | 647 | 472 | 1.00 | 2.88 |
| Deuterated algae | 661 | 432 | 647 | 470 | 1.00 | 2.87 |

We are indebted to Dr Winston M Manning for helpful discussions and support of these investigations, and to Mrs Mary Thomas for measurement of the spectra. A fuller account will be published else

where. This communication is based on work performed under the auspices of the U.S. Atomic Energy Commission.

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Complex Reaction in *Hyoscyamus niger* upon Night Interruption with Red Light

In general, long-day plants form rosettes in short days (in white light), and flower stalks in long days. The dependence on the wave length of radiation of this photoperiodic reaction can be determined in three different ways (a) by growing plants exclusively in light of narrow wave length bands, at high intensity (b) by extending short white days with a coloured light treatment, and (c) by interrupting the long night, in a short-day treatment, with coloured light. Most results on the spectral dependence of the photoperiodic reaction have been obtained with the night interruption technique. These results appear rather clear-cut which is the main reason why the two other possible modes of approach have only been used incidentally. Moreover, the results obtained from the other methods were not taken too seriously if they disagreed with the results of night interruption experiments.

In this communication, some preliminary results are presented which show that results obtained with night interruption may even deviate from the well known scheme, thus warning against a too simple interpretation.

Literature on night interruption with coloured light in *Hyoscyamus niger* is very restricted. Parker et al.¹

reported on the spectral dependence without bringing into account the red-antagonizing activity of near infra-red (that is, far red) radiation. This gap was filled by Piringer *et al.*⁴ and by Downs¹. Stolwijk and Zeevaart⁵, from this laboratory, also reported red light to be most effective. Admixture of near infra-red to the red radiation diminished its activity. Stolwijk and Zeevaart required considerably higher light intensities than the previously mentioned authors^{1,4} to obtain an effect. They suggested that the reason for this difference might be that the basic day-length they used was shorter than that applied by Piringer *et al.* and by Downs. Stolwijk and Zeevaart's results were confirmed in this laboratory⁶. One hour of red radiation (~ 1000 ergs/sec cm^2) was insufficient to cause stem formation within 70 days of treatment⁶. It may be relevant that not only was the day-length different from that applied by the American authors, but also the light quality of the basic radiation period. Sunlight was used by Downs¹, whereas Stolwijk and Zeevaart⁵, and Wassink and Sytsema⁶ used fluorescent light with a much weaker near infra-red admixture.

In the following experiment a basic radiation period of 8 hours white fluorescent light of high intensity ($\sim 20,000$ ergs/sec cm^2) was supplemented with 2 hours of near infra-red at low intensity ($\sim 1,000$ ergs/sec cm^2) and applied as short-day treatment, instead of white light only. The aim was to obtain a reaction more similar to the one with sunlight. The long night was interrupted around the middle with low intensity ($\sim 1,000$ ergs/sec cm^2) red light for 0, 1, 15, 30, 60, or 120 minutes. The numbers of days to the beginning of stem elongation (mean out of 4 plants) are presented in Table 1.

Table 1 Stem elongation in *Hyoscyamus niger*, as influenced by short days (8 hours high intensity fluorescent white (W) supplemented with 2 hours' low intensity near infra-red radiation (I)) in combination with red (low intensity) night interruptions of different durations. High intensity is about 20,000 ergs/sec cm^2 , low intensity is 1,000 ergs/sec cm^2 . Temperature about 20° C. The experiment started on October 17, 1957, and was closed after 78 days. Figures presented are averages of 4 plants each.

| Radiation treatment | | Days to beginning of stem elongation |
|---------------------|--------------------------------------|--------------------------------------|
| Basic | Night interruption (min., red light) | |
| 8 W + 2 I | 120 | 41 |
| 8 W + 2 I | 60 | 55 |
| 8 W + 2 I | 30 | > 78 |
| 8 W + 2 I | 15 | > 78 |
| 8 W + 2 I | 1 | > 78 |
| 8 W + 2 I | 0 | 50 |

Night interruption with low-intensity red light for two or even one hour produces the long-day reaction. Shorter interruptions are ineffective.

However, this description of the results is too simple because the group without any red night interruption also reacted as if it had received a long-day treatment. (This result has been reported earlier²). We must admit that very short night interruptions with red light suppress the long-day reaction, produced by this special short-day treatment, namely, 8 hours white fluorescent light plus 2 hours near infra-red. Longer interruptions are about neutral (1 hour), or are somewhat favourable for stem elongation (2 hours). Thus, in this experiment, the long day plant *Hyoscyamus niger*, treated with short days permitting stem formation, could be kept vegetative with short red interruptions in the middle of a long night. Obviously, near infra-red supplemented to the basic white light period within a short day had converted the long-day plant *Hyoscyamus niger* into a short-day one. This was manifest directly², and also with respect to its reaction upon short interruptions in the middle of the night.

This does not hold for longer night interruptions which restore the original behaviour.

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Isolation of 24-Methylene-cholesterol from Honey Bees (*Apis mellifica* L.)

In connexion with an attempt to isolate pheromone¹ from the queens of the honey bee, *Apis mellifica* L., an examination was carried out on the neutral portion of the extract obtained by perfusion of the powdered whole-bodies of the queens with ethanol and *tert*-butanol. By chromatographing the neutral portion on alumina, or silica gel, a crystalline substance, m.p. 138-145° C. [α]_D²⁵ = $-31.6 \pm 0.6^\circ$ ($c = 0.39$ in chloroform), was obtained, which resembled cholesterol in behaviour and chemical properties. The Liebermann-Burchard reaction gave the same coloration as that obtained with cholesterol and the mixed melting point was the same. However, there were two bands (0.08 μ and 11.33 μ) in the infra-red spectrum of the substance which are not found in the spectrum of cholesterol and its derivatives. The same substance was isolated by similar means from worker bees. The constitution I for the sterol was elucidated from the following. An Oppenauer oxidation using cyclohexanone and aluminium isopropylate in toluene produced a conjugated unsaturated ketone; m.p. 77-84° C., $\lambda_{\text{max}} = 242 \text{ m}\mu$, $\log \epsilon = 4.0$ calculated for $\text{C}_{28}\text{H}_{44}\text{O}$, 396.6. Besides, the double bond of the $\alpha\beta$ -unsaturated ketone function, a second double bond was present as shown by titration with bromine² (1.155 mgm of substance used, in 4 hr. 0.034 mgm bromine which corresponds to 2.01 moles $\text{C}_{28}\text{H}_{44}\text{O}$ by calculation. From the absorption bands at 0.08 μ and 11.33 μ (pressed in potassium bromide) it was inferred that one of the double bonds was present⁴ as a methylene group ($\text{C} = \text{CH}_2$). Similarly 26 per cent of the theoretical yield of formaldehyde was formed on reaction with 10 moles of ozone. Based on these properties we have compared the free sterol and the O-acetyl-compound with 24-methylene-cholesterol and its O-acetyl-derivative⁵ (Table 1).

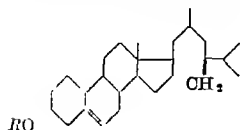
Table 1 COMPARISON OF 24-METHYLENE-CHOLESTEROL FROM DIFFERENT SOURCES

| | Free sterol I | | O-acetyl compound II | |
|--|---------------|---|----------------------|---|
| | m.p. | [α] _D CHCl ₃ | m.p. | [α] _D CHCl ₃ |
| Authentic sample from oysters ⁶ | 143° | -34.5° | 135° | -44.1° |
| From queen bees | 138-145° | -31.6 \pm 0.6° | 131-130° | -42.4 \pm 3° |
| From worker bees | 138-140° | -31.6 \pm 0.2° | 130-134° | -40.35 \pm 4° |

A sample of O-acetyl-24-methylene-cholesterol was shown, by direct comparison, to be identical with the O-acetyl-derivative of the sterol isolated from the bees. This comparison included mixed melting-points, infra-

red spectra in methylene dichloride and in potassium bromide and examination in the mass spectro meter

The X ray powder diagram did not exclude the positive identification. For real proof however, it would have been necessary to recrystallize both samples under the same conditions⁹ but due to the scarcity of the substance this was not possible. The percentage of I amounted to about 0.016 per cent in both the workers and the queens



I R = H m p 143° (-34.8° Chf)

II R = Ac m p 135° (-44.1° Chf)

The full report of this work will be published in *Helvetica Chimica Acta*. We wish to acknowledge the support of the Centro Nazionale de la Recherche Scientifique Paris, and by Ciba Co, Basle. We also wish to thank Prof S Bergström Stockholm, and Prof E Stenholm Uppsala, for doing the mass spectroscopy Prof H Labhardt, Basle for preparing the X ray powder diagram Dr R Chauvin, Station de

RADIOBIOLOGY

Distribution of Radioactive Barium in Eye Tissues

The presence of high concentrations of barium in the pigmented tissues of the eye of many species is now well established.^{1,2} The observations on barium 140 reported here demonstrate that this radioactive isotope of the element is markedly concentrated in the uveal tract of herbivores.

Pure bred Dutch rabbits about 10 weeks old were used. Pairs of animals were injected intravenously with approximately 500 µc of an equilibrium mixture of pile-produced, carrier free barium 140 and lanthanum 140 and were killed by an intravenous injection of Nembutal at intervals of from 30 min to 3 days from the time of injection. The eyes were removed and dissected immediately after death. The left femur, left vastus muscle and a sample of heart blood were also taken for analysis. The tissues were digested with concentrated nitric acid and after standing for 6 days to allow for equilibration between the barium 140 and its lanthanum 140 daughter suitable aliquots of the resulting solutions were assayed in a well type scintillation counter. The results, corrected for radioactive decay, are given in Table 1.

Table 1 DISTRIBUTION OF STABLE BARIUM AND OF INTRAVENOUSLY ADMINISTERED BARIUM 140 IN THE EYES, ETC OF RABBITS

| | Stable Barium (µgm./100 gm. wet weight) | Barium 140 (per cent dose/100 gm. wet-weight of tissue) after | | | | | | | |
|---------------------|---|---|-------|-------|-------|-------|-------|--------|--------|
| | | 30 min | 1 hr | 3 hr | 7 hr | 24 hr | 2 hr | 2 hr | 2 hr |
| Cornea | — | 0.83 | 1.1 | 0.90 | 1.08 | 0.68 | 0.60 | 0.30 | 0.51 |
| Iris and ciliary | — | — | — | — | — | 0.07 | 0.036 | 0.012 | 0.010 |
| Lens | 191 | 2.96 | 3.20 | 3.68 | 4.03 | 3.68 | 4.81 | 3.00 | 4.23 |
| Vitreous body | 6.5 | 0.03 | 0.033 | 0.015 | 0.025 | 0.016 | 0.024 | 0.0007 | 0.0022 |
| Retina | 1.2 | 0.16 | 0.11 | 0.090 | 0.14 | 0.028 | 0.043 | 0.0051 | 0.006 |
| Choroid | 86 | 0.61 | 0.63 | 0.61 | 0.77 | 0.70 | 0.83 | 0.49 | 1.21 |
| Choroid and tapetum | 348 | 10.8 | 9.5 | 9.8 | 15.2 | 8 | 11.0 | 11 | 10 |
| Sclera | — | 1.91 | 3.83 | 3.93 | 4.04 | 2.27 | 2.04 | 1.95 | 1.14 |
| Plasma | — | 2.12 | 1.73 | 1.17 | 0.89 | 0.35 | 0.33 | 0.16 | 0.33 |
| Muscle | — | 0.62 | 0.20 | 0.22 | 0.3 | 0.10 | 0.39 | 0.041 | 0.033 |
| Femur | — | 4.75 | 5.03 | 7.78 | 10.2 | 8.38 | 9.38 | 7.42 | 12.3 |
| | | | | | | | | 8.60 | 8.51 |
| | | | | | | | | 8.40 | — |

Recherches Apicoles Bureau sur Yvetto, France for obtaining the bees M Flury University of Basle for carrying out the bromine titration and Dr D R Idler, Vancouver for sending us a sample of O acetyl 24 methylene-cholesterol

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This table also shows the concentrations of stable barium in the tissues of the pooled eyes of sixteen similar rabbits determined by the method described by Sowden and Stith³

The eyes of two mature cows given approximately 3 me barium 140/lanthanum 140 for another purpose have also been examined. These animals were killed 8 and 25 days after administration of the isotope. The eyes together with the left femur and a piece of the left vastus muscle, were removed immediately after slaughter. The tissues were treated as described above. The distribution of the isotope is shown in Table 2.

Table 2 DISTRIBUTION OF STABLE BARIUM (FROM SOWDEN AND STITH ref. 3), AND OF INTRAVENOUSLY ADMINISTERED BARIUM 140 IN THE EYES, ETC., OF COWS

| Tissue | Stable barium (µgm./100 gm / wet weight) | Barium 140 (per cent dose/ 100 gm. wet weight of tissue) after | | |
|---------------------|--|--|---------|---------|
| | | 8 days | 8 days | 25 days |
| Cornea | — | 0.032 | 0.032 | 0.032 |
| Iris and ciliary | — | — | — | — |
| Lens | 18,700 | 20,600 | 0.35 | 0.17 |
| Vitreous body | 5 | 6 | 0.0002 | 0.0009 |
| Retina | — | — | 0.0001 | 0.0007 |
| Choroid and tapetum | 56 | 129 | 0.002 | 0.002 |
| Sclera | 20,000 | 65,000 | 1.07 | 0.82 |
| Plasma | 1,700 | — | 0.061 | 0.127 |
| Muscle | — | — | 0.00003 | 0.0002 |
| Femur | — | — | 0.001 | 0.001 |
| Proximal end | — | — | 0.017 | 0.016 |
| Distal end | — | — | 0.007 | 0.011 |

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together with, for the purpose of comparison, the stable barium content of cow eye tissue as found by Sowden and Pirie²

The uptake and retention of barium-140 by the different parts of the eye differed several-fold in both species. All parts of the rabbit's eye, except the lens and vitreous body, accumulated barium-140 to a greater extent than the vastus muscle, taken as a representative soft tissue. The highest concentration of the isotope, in both rabbits and cows, was in the pigmented parts of the eye. The concentration in the choroid, on a unit wet-weight basis, was greater than that in the femur, in the rabbit, by a factor of about 1.5, and in the cow, by an order of magnitude. Barium-140 remained at least as firmly fixed in the uveal tract as in the femur but disappeared from other parts of the eye, except the sclera, at approximately the same rate as from striated muscle. The sclera occupied a position intermediate between that of the pigmented tissues and the remainder of the eye.

The relative proportions of barium-140 in the different tissues after 3 days in the rabbit and after 8 and 25 days in the cow were very similar to the relative proportions of stable barium.

The high degree of accumulation of barium-140 in the choroid and iris of the cow may be of significance should it be found necessary to decide on a maximum permissible level for the isotope in this species.

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Effects of Irradiation of Nerve on Muscular Response

THE EFFECTS of gamma- and X-radiation on the excitability and conductivity of the sciatic nerve of the frog have been studied for doses up to 80,000r and an attempt made to correlate these results with the muscular response. Either the whole nerve or a short segment was irradiated. Excitability and conduction velocity of the nerve and the response of the attached gastrocnemius muscle, were recorded both during and after irradiation. Observations were also made of the mechanical activity of the nerves. No stimulation of the nerve by irradiation was observed, but complex and paradoxical effects on the excitability of non-irradiated segments were found.

Isolated sciatic nerve preparations from the common frog (*Rana pipiens*) were mounted on platinum electrodes in a humid 'Plexiglas' chamber similar to that employed by Chailakhian and Iur'ev.¹ The temperature was maintained at 18°—20°C. Stimulation was produced by a 'Tektronix' waveform generator, using 30—40 second bursts of 0.1 msec pulses at 50/sec. Stimulus strengths slightly above maximal were used. Platinum wire electrodes were used for stimulating and recording the action potentials. The nerves were stimulated during irradiation and for periods of several hours after irradiation.

Sciatic nerve-gastrocnemius muscle preparations were made after the method of Kirzon.² Two nerve muscle preparations were placed in the two compartments of a humid 'Plexiglas' chamber. The

nerve of each preparation was mounted on four pairs of platinum wire electrodes for stimulation, one proximal and three distal to an irradiated segment. Stimulation was produced as above, but using 30—40 second bursts of 1 msec pulses. Two different levels of stimulation were applied, threshold and maximal. Muscular responses were registered on a conventional kymograph using an isotonic lever system.

For gamma-irradiation, a cobalt-60 'Teletherapy' unit was used, and for X-irradiation, a conventional X-ray machine with an aluminium filter. For irradiation of isolated sciatic nerve, 250 kVp at 20 mA were used, at a dose-rate of 7,000r/min. In the nerve-muscle experiments, irradiation was limited to a 7-mm segment of the nerve by shielding the rest of the nerve, the control nerve and the muscle with 3 cm lead shielding. For X-irradiation, 50 kVp at 20 mA were used, at a dose-rate of 350–600r/min.

Nerve surface displacements were detected by a micro-interference method, similar to that of Kayushin and Lyudkovskaya.^{3,4} Deflection of an interference fringe in the light reflected from the nerve surface provided a measure of surface movements.

In the isolated sciatic nerves, in non-irradiated controls, conduction velocities averaged 28.5 ± 2 msec. Conduction velocities were unaffected by radiation doses up to 10,000r, in agreement with the results of Gerstner.^{5,6} For doses up to 10,000r and 50,000r, the conduction velocity increased 5 per cent and for doses between 50,000 and 80,000r it decreased 12 per cent and the amplitude of the action potential decreased slightly. In sciatic nerve-gastrocnemius muscle preparations, the irradiation with gamma- or X-rays of the whole nerve trunk, or of a small segment with doses up to 10,000r produced no muscular response, regardless of the dose rate (20—7,000r/min).

Complicated and paradoxical effects on the excitability of the non-irradiated segment of the nerve were found. A decrease in threshold was produced by doses ranging from 1,500r to 20,000r and the magnitude of this effect depended on the dose rate, but it could be more readily detected when employing dose rates ranging from 350 to 600r/min. Paradoxically, the same dose and dose-rate ranges that produced a decrease in threshold, produced a decrease in the muscular response to a maximal stimulus. The results for stimulation of the nerve distal to the irradiated segment are summarized in Fig. 1.

The observation of Kayushin and Lyudkovskaya,^{3,4} indicated the occurrence of a compressional wave passing along the nerve during stimulation. Hill^{6,7} showed that changes during the electrical activity of a nerve fibre were accompanied by changes in optical density. It is possible that there is a correlation between these phenomena. We have been able to confirm the Russian reports using micro-interference measurements and also to show that in nerve irradiated in the same dose range as above these displacements were intensified in the distal segment of the nerve.

Increased excitability in the distal segments of irradiated nerves has been reported by Kirzon.² On the basis of his results, Kirzon has suggested a theory of 'non-impulse effects' in nerve, which may explain the results reported here.

If we assume that the 'displacement' of the surface during electrical stimulation, accompanied by density changes, represent actual transport of substances along the nerve, then the increased displacements

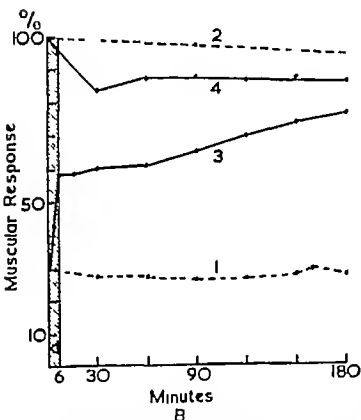
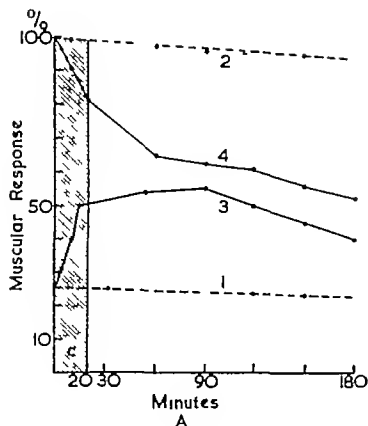


Fig. 1. Results of stimulation of the nerve distal to the irradiated segment. A Muscular responses during and following irradiation with 600r/min. for 20 min. B Muscular responses during the following irradiation with 600r/min. for 6 min. The lined segments 3 and 4 represent the period of irradiation. Abscissae show the time (min.). Ordinates show muscular responses expressed in percentages.

- 1 Muscular response for threshold stimulation (without irradiation)
- 2 Muscular response for maximum stimulation (without irradiation)
- 3 Muscular response for threshold stimulation (with irradiation)
- 4 Muscular response for maximum stimulation (with irradiation)

produced by stimulation which follows irradiation may represent an increase in this transport.

If we further assume that these transported substances include the mediator for neuromuscular transmission then the paradoxical results obtained here could be explained as being due to excessive accumulation of this mediator. Such accumulation would be expected to lead to increased response at low levels of stimulation and decreased response at maximal or saturation levels as actually observed.

To test this concept experiments are being designed which will use isotopically labelled acetylcholine and K 42 to follow their displacements along the nerve

during stimulation, both before and after irradiation. The micro interferometer is being improved so that the surface movements can be analysed with accuracy.

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Latent Period of X-Ray Induced Ageing a Study Based on Mortality Rate and Tumour Incidence

THE increase in age-specific chronic mortality rate that occurs after a single whole-body exposure to ionizing radiation has been commonly used as a parameter of ageing¹. Whether or not the increase occurs immediately or only after a latent period is not known owing to the fact that experiments are customarily initiated with young animals for example, 50 to 125-day-old mice. The mortality rate is then so low that not even a large relative increase can be significantly established in groups of 50 animals.

We therefore designed an experiment to study this point. Groups of BALB/c mice (70-80 males 101-115 females), made up from a single pool served as controls or were irradiated at age 435 days (405-460 days) or at age 635 days (505-560 days). The X-ray exposure dose in soft tissue was 500 r (250 kV, hvl 1.5 mm copper, 45 r/min). This dose was selected to avoid acute killing. The LD 50/30 was estimated to be about 600 r. The animals were exposed and maintained as described previously.²

At age 435 days, 500 r proved to be the LD 3/30 for males and the LD 1/30 for both sexes combined. At age 535 days, 500 r was the LD 40/30 for males and the LD 10/30 for females. Therefore, although the conclusions drawn from the chronic mortality rate data of the 535-day groups may have been in qualitative agreement with those for the 435-day groups, for simplicity and brevity they are not considered here.

For Table 1 the mortality rate q_2 was calculated thus (number dying in 8 week interval beginning at age specified) divided by (number alive at start of interval). To test for significant differences between the control and irradiated groups χ^2 (with Yates correction) was calculated for the pooled data of 2 or 3 successive 8 week intervals.

In the irradiated male, a latent period of 24 weeks (intervals 1-3) elapsed before q_2 rose significantly above the control level. During the remaining 50 weeks (intervals 4-10) q_2 continued at about 2-4 times the control level. In the female the latent period lasted 16 weeks. For the next 48 weeks (intervals 3-8) q_2 usually was 2-3 times the control level after which it fell.

Mimosa pudica was cultivated in the same manner as has been described in the previous papers.^{1,2,3} The material consisted chiefly of those plants which had already received a stimulus. The longitudinal sections were obtained by a cylinder microtome or simply by a hand razor, the petiole being cut 25–30 μ in thickness. Then they were stained with 0.001 per cent aqueous solution of brilliant cresyl blue or 0.003 per cent neutral red, the adequate staining being almost complete after 20–30 min.

The tannin vacuole in the parenchymatous cell is more inflated during the day (10 a.m.–3 p.m.) than during the night (12 midnight–2 a.m.), and the thread-like apparatus is thicker during the day than at night. Furthermore, in the nocturnal condition the chloroplasts have a tendency to form a cluster around the thread-like apparatus (Figs 1 and 2).

Champy's fluid was used for the fixation of the parenchymatous cells. Adequate duration of fixation was about 20 hr. After completion of the fixation they were thoroughly washed in running water for

night the granules as a rule do not appear under this fixation (Fig. 6). But in certain conditions, these particulate black granules are observed in the chloroplast, also at night. These different features of chloroplasts in two cases were also observed in fresh material with vital staining.

From the available data of cytophysiological experiments, it is concluded that the expansion and contraction of the tannin vacuole in parenchyma is connected with the diurnal and nocturnal condition. Concerning this fact, it is advisable to refer to my work⁴ on the changes in motor cells in the diurnal and nocturnal conditions. Full details of this investigation will be published elsewhere.

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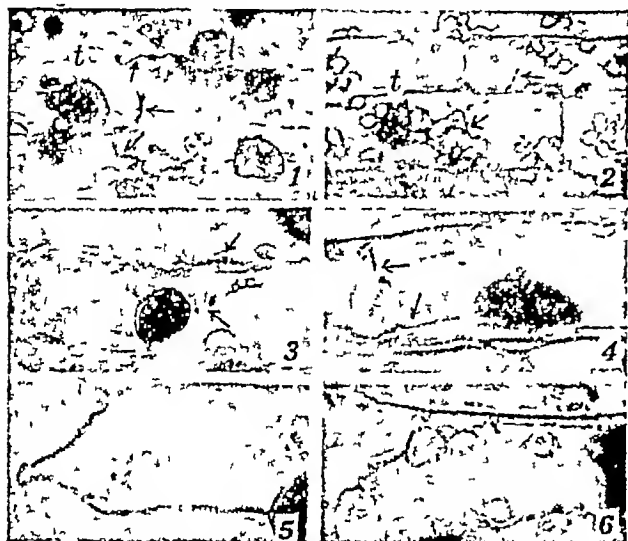
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Figs 1–6 Longitudinal section of parenchyma of *Mimosa* petiole. 1, diurnal condition; 2, nocturnal condition. 1 and 2 are stained with 0.001 per cent brilliant cresyl blue ($\times c 435$). 3, diurnal condition; 4, nocturnal condition ($\times c 530$). 5, chloroplasts and threadlike apparatus in direct ray of sunlight; 6, chloroplasts and threadlike apparatus in nocturnal period. 3–6 are fixed with Champy-Toriyama's method ($\times c 830$). t, tannin vacuole, arrows indicate threadlike apparatus.

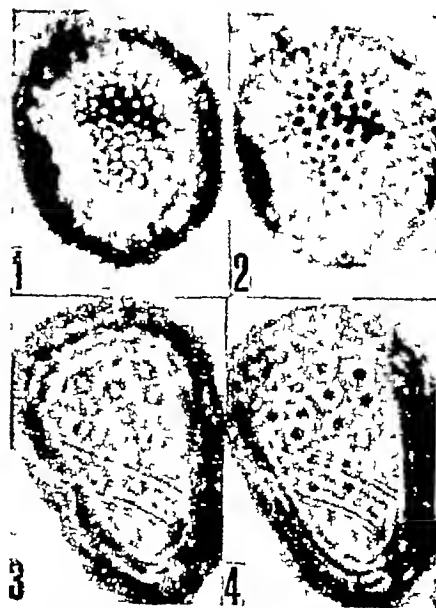
10 hr to remove any trace of the reagents. These materials were cut 25–40 μ thick by means of a hand microtome. The sections were washed in running water, and then in distilled water, changed several times. The sections were mounted in pure glycerin, without any subsequent staining. This technique² was satisfactory in demonstrating the thread-like apparatus, and in fixing the chloroplasts. Generally speaking, osmium tetroxide usually stains the threads and tannin vacuoles black, while the chloroplasts remain colourless.

These results are illustrated in Figs 3 and 4. In the diurnal condition, tannin vacuoles are fixed as a spherical form, and in the nocturnal condition they appear as crushed globes. The thread-like apparatus has a tendency to assume rosary-like features during the day. On the other hand, at night the threads appear uniformly in a thin slender form. When the materials are exposed to sunlight in August, small particulate granules appear in the chloroplast (Fig. 5). By Champy's fixation, these granules and threads are both stained black. On the other hand, at

'LO-Analysis' as an Aid in the Study of Fungal Spore Morphology

ERDTMAN¹ defined LO-analysis as "the different patterns of pollen or spore wall surfaces recorded as they appear at successive adjustments of the microscope".

The usual practice is to select spores in slide mounts which are so oriented that they are seen in surface view. The surface is then examined in two focal planes. In the upper focus of the microscope the raised structures on the spore surface (here rounded warts or pointed spines) are seen as hyaline bodies (Figs 1 and 3), while in the lower focus these same raised structures turn dark (Figs 2 and 4). Figs 1 and 2 show a single urediospore of *Scopella aulica*, and Figs 3 and 4 are of *S. gentilis*. This was termed LO-analysis by Erdtman¹ (L denoting *lux* or lighted areas in the upper focus and O *obscuras* or dark areas in the lower focus). The reverse of this, that is, OL analysis can be attempted where there are



Figs 1 and 2 Urediospore of *S. aulica* at two successive adjustments of microscope (Fig. 1 at high focus, Fig. 2 at low focus, both $\times 5,800$). Figs 3 and 4 Urediospore of *S. gentilis* (Fig. 3 at high focus, Fig. 4 at low focus, both $\times 1,280$).

dopressed areas, holes or concavities present on the spore surface. *OL* analysis is illustrated in Figs 3 and 4. Around the spines (raised structures, hyaline in Fig 3 and dark in Fig 4) there are depressed areas (dark in Fig 3 and hyaline in Fig 4) which following pollen grain terminology, have been designated as 'lumina'. These cavities are bounded by muri which are part of a reticulum enveloping the spore surface.

Erdtman¹ credited H. Welckor as being the discoverer of this optical effect. In an ideal *LO* analysis all the raised structures in the upper focus should appear as bright dots against a black background. This is possible only if the spore surfaces are perfectly flattened. In Figs 1 and 3 because of the convex bulge in the spores, only a few spines are seen in such an ideal condition.

Perhaps, through *LO* analysis some more unsuspected characters might come to light as has happened in the case of urediospores of *Scopella genitilis*. Here the presence of lumina around the spines and of the reticulum around the urediospore surface was first inferred through *LO* analysis. *LO* analysis might even be important where paucity of spore material, for example, in aerobiology or in palaeobotany, might not permit the use of other methods.

This work was performed while I held a research fellowship of the National Institute of Sciences of India to which due acknowledgment is made herewith. I am also grateful to Prof. S. P. Agharkar and Dr. M. J. Thirumalachar for encouragement and valuable suggestions.

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Lepidurus arcticus in the Irish Late-Glacial

THE recent discovery of a fine suite of Late glacial strata near Ballyhalbert on the north-eastern Irish coast in an accessible position has allowed a careful study to be made of the different layers for plant and animal macrofossils. Particularly interesting has been the recovery of numerous characteristic telsons of the freshwater notostracan *Lepidurus arcticus*, a species which was reported recently by Mitchell¹ from Late glacial levels at Ballaugh in the Isle of Man, at Neasham, Co. Durham, and at Mapastown Co. Louth. Records from these Late glacial contexts are significant since the species is not known in the present fauna of the British Isles. Its modern distribution is circumpolar, between 65° and 80° N.

At Ballyhalbert the telsons and mandibles occurred in great numbers in thin streaks of organic material which interrupted a solifluxion deposit of Zone III age. The deposit was a grey, sandy clay, packed with innumerable broken angular fragments of slate. Within this the organic seams were lying horizontally. They yielded numerous leaves of *Salix herbacea* and also identified were *Carex* spp., *Ranunculus accleratus*, *Ranunculus* (Batrachium) spp., *Rumex tenuifolius*, *Viola palustris*, *Hypericum vulgare*, *Menyanthes trifoliata*, *Lycopodium europaeum*, *Selaginella selaginoides*, and *Chara* spp. The large number of aquatics suggests that the organic seams had their origin as small pools. These perhaps formed each summer on top of the spring season's fresh sheets of solifluxion material.

The possibility may also be envisaged that the seams are really fragments of the underlying Allerød or Zone II mud which could have been caught up and rolled into the solifluxion clay as it sludged into position. However, this seems an unlikely explanation since no remains of *Lepidurus* were discovered in the Zone II level. It was clearly restricted to the Zone III clay and did not appear above or below this horizon.

The absence of *Lepidurus arcticus* from the existing British and Irish faunas makes its widespread Late glacial distribution all the more remarkable. Examples of such extinction and retraction of range during Post glacial times are of course more familiar to us in plant kingdom, and Godwin² has documented and discussed the problem in full. It is believed that the plants in question experienced curtailment of their range due to absorption of suitable habitats by the spread of the Post glacial forests. But the factors responsible for the extinction of *Lepidurus* are other wise and are difficult to envisage. Perhaps the problem may be approached constructively once quantitative and systematic studies on the sub fossil micro faunas of Late and Post-glacial lake muds have accumulated to the extent of allowing the different factors in lake evolution³ to be disentangled. Such studies are certainly to be commended since they may lead to a more accurate knowledge also of the duration and character of the important Post glacial Climatic Optimum or Hypsithermal Interval.

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ENTOMOLOGY

Haematopota insidiatrix Austen (Diptera, Tabanidae) in Southern Rhodesia

THE fly round technique has long been used in tsetse fly studies^{1,2}. The procedure is to walk along a pre-determined route collecting those flies attracted to men, to bait animals or to screens carried by men. Recent work in the Wankio National Park, Southern Rhodesia has shown that this method is also effective for the study of *Haematopota insidiatrix* Austen. This insect is frequently a nuisance at Wankio, during the rainy season (November-February), because of its habit of following and entering motor vehicles. It was because of this behaviour that the fly round technique was tried as an aid to their study. A black cloth screen carried by two boys was found to be attractive to the flies. The use of a screen rather than a bait animal allows the technique to be standardized and also to be used in an essentially new way, namely, to study certain aspects of the sensory physiology of this insect.

Portchinsky³ noted that *Haematopota pluvialis* L. is attracted by black surfaces but that it avoids white ones. Curson⁴ states that *Haematopota* sp. alighted on the black part of an animal's coat rather than the white part. In tsetse fly studies Symington⁵ has stressed the usefulness of screens and Lloyd⁶ working with *Glossina swynnertonii* refers to the interference for

Table 1 SIMULTANEOUS COMPARISON OF THE NUMBER OF *H. insidiatrix* CAUGHT ON A BLACK SCREEN AND ON A BLACK AND WHITE SCREEN*

| | | | | | | | | | | |
|-----------------------------------|-----|----|----|-----|----|-----|----|----|-----|----|
| % White in Black and White Screen | 2 | 4 | 9 | 12½ | 18 | 25 | 29 | 33 | 37½ | 50 |
| Total Flies Caught | 101 | 99 | 98 | 101 | 99 | 114 | 91 | 93 | 85 | 61 |
| No. of Black/White Screen | 30 | 34 | 24 | 23 | 21 | 26 | 18 | 14 | 8 | 4 |
| No. on Black Screen | 62 | 65 | 74 | 78 | 78 | 88 | 73 | 79 | 77 | 57 |
| % Flies Caught on Black Screen | 62 | 65 | 75 | 77 | 78 | 77 | 80 | 84 | 90 | 93 |

The catch on the black screen formed a progressively greater proportion of the total catch as the amount of white in the black and white screen increased. The white was added, in each case, as three equally spaced horizontal stripes.

certain colours of screens over others. The present work concerns the importance of the visual sense in the attraction of *Haematopota insidiatrix* towards its host. Two facts prove that the *H. insidiatrix* attracted to the screens were coming to feed. First, all the flies caught were female, the males, which do not suck blood, were not attracted. Secondly, the flies landing on the screens probed the surface with their mouthparts.

Three black screens (24, 16, and 8 sq. ft. in area) were carried in procession. Each screen attracted more flies when carried first in the procession than when carried second and third. The models were rotated so that each occupied the three possible positions an equal number of times. The total number of *H. insidiatrix* caught on the first, second, and third screens was 100, 58, and 60 respectively. The number of flies attracted also varied according to the size of the screen. Ninety-nine flies were caught on the largest screen, 76 on the medium screen, and 43 on the smallest one. However, approximately the same number of flies were caught per sq. ft. of surface (4.12 on the large, 4.75 on the medium, and 5.48 on the smallest screen). It was also found, by comparing two screens simultaneously, that a black screen is much more attractive than a white one of the same size (137 *H. insidiatrix* on the black screen, 5 on the white screen), and that the attractiveness of a black screen is diminished progressively as more white is added to it (Table 1).

Thus decrease in the attractiveness of the screen might be due to the increasing amount of white or to the decreasing amount of black or to both, also, the change in the continuity of the black surface may prove to be involved.

This investigation is to be continued in the wet season of 1959 to 1960, and will be reported in full elsewhere.

I wish to thank Prof. E. B. Edney, Dr. E. Bursell, and Dr. J. S. Weir, for helpful discussion and criticism, Mr. H. Oldroyd of the British Museum for identifying *Haematopota insidiatrix* Austen, and the staff of Wankie National Park for their co-operation.

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Ants and Form Reversal in Aphids

EL-ZIADY and Kennedy¹ found that in colonies of *Aphis fabae* Scop. which were attended by ants there was a higher rate of multiplication and delayed production of winged forms compared with unattended colonies. It has been suggested that the higher rate of multiplication is a result of ant-attendance delaying dispersal of the aphids from the nutritious apical growth of the host plants², and it seemed probable that the delayed production of winged forms may have been due to the same cause. However, ant-attendance does cause a marked increase in the feeding rate of aphids³ and the possibility of it having a more direct inhibitory effect on the development of winged forms was not ruled out. In the present communication such an effect is reported.

When the progeny of apterous parents of *Aphis craccivora* Koch. undergo their development on mature leaves of broad bean (*Vicia faba* L.) which are detached from the plant and kept in tubes of water, a large proportion of them develop into alatae⁴. A series of experiments was carried out to determine whether ant-attendance of the developing nymphs had any influence on their continued development as alatae. Apterous parents were left on leaves until they had deposited the required number of nymphs. They were then removed and the leaves bearing the nymphs were put in a cage close to a nest of small black aphidicolous ants *Paratrachina* (*Nylanderia*) *baveri* Mayr. The ants were denied access to half the leaves by keeping the jars in a shallow tray of water to which a little detergent had been added; they tended the aphids on the other leaves in the manner described by Banks⁵.

The results of four separate experiments are given in Table 1. High percentages of nymphs which had been

Table 1 PERCENTAGES OF APHIDS WHICH DEVELOPED INTO APTERA IN BATCHES OF *A. craccivora* WHICH WERE ANT-ATTENDED AND NOT ANT-ATTENDED AS NYMPHS

| Exp. No. | Period of attendance by ants | Ant attended | | | Not ant attended | | |
|----------|------------------------------|---------------------------|---------------|---------------------|---------------------------|---------------|---------------------|
| | | Mean % of apterous leaves | No. of leaves | Total No. of nymphs | Mean % of apterous leaves | No. of leaves | Total No. of nymphs |
| 1 | Whole of immature stages | 95.5 | 5 | 305 | 27.5 | 5 | 425 |
| 2 | 1st instar only | 88.0 | 5 | 208 | 37.0 | 5 | 193 |
| 3 | 2nd instar only | 100 | 1 | 30 | 10 | 1 | 70 |
| 4 | 3rd and 4th instars | 0 | 5 | 169 | 0 | 5 | 142 |

attended by ants for the whole of their development, for the first instar only, and for the second instar only, developed into normal apterae. A few of them had rudimentary ocelli, but none had wing pads or other alateform structures. Most of the aphids in the control series developed into alatae. Thus it appears that ant-attendance during the early instars resulted in the nymphs being diverted from the alate course of development. Nymphs attended by ants during the third and fourth instars only were not affected and continued to develop into normal alatae.

As aphids imbibe more food when they are attended by ants than when they are unattended, and as apterae can also be produced by allowing first and second instar nymphs to feed on host seedlings⁶, form reversal might be attributable to improved nutrition. But, in the experiments described, the ant-attended aphids did not grow any more rapidly, nor did they attain a larger size, than the controls. Thus nutrition was not a limiting factor in development. If form

reversal was effected through nutrition. It could have been a response to the accumulation of some specific substance. On the other hand, it is probably due ultimately to a change in endocrine activity⁴ and this might well have been brought about independently of nutrition.

Aphids of many species are attended by ants and the influence of ants in causing the suppression of natiiform structures in developing nymphs is undoubtedly of widespread occurrence. But alate aphids are sometimes produced in large numbers, particularly on wilting or dying host plants. On such plants the aphids' rate of feeding and thus excretion are reduced. As a result fewer ants tend the aphids; individual aphids are visited less often and there must come a stage when the effects of infrequent ant attendance are outweighed by the alate-favouring factors of the aphids' environment and the aphids then develop into alatae.

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MICROBIOLOGY

Transaminases in *Shigella*

NUMEROUS investigations have been made of the transaminase system in bacteria and these have been reviewed by Meister¹. The only reference to the transaminase activity in *Shigella* appears to be the one mentioned by Liehstein and Cohen² on a strain of *Shigella dysenteriae* (Shiga).

Using acetone dried cell preparations, the transaminase activity of nine strains of *Shigella* was studied. The strains were chosen from the four serological groups, and were *Shigella dysenteriae* 6, *Shigella dysenteriae* 7, *Shigella boydii* 2, *Shigella boydii* 3, *Shigella boydii* 5, *Shigella flexneri* 1a, *Shigella flexneri* 2a and two strains of *Shigella sonnei*. The strains were grown on nutrient broth³ at 37°C for 18 hr and seeded on to the surface of 1.8 per cent nutrient agar (New Zealand agar) in Roux bottles. Following overnight aerobic incubation at 37°C the growth was washed off with ice-cold sterile double distilled water and an acetone dried cell preparation obtained by the method of Umbrell et al.⁴

Four keto acids α -ketoglutarate, oxaloacetic acid, sodium pyruvate and sodium phenyl pyruvate were used in concentrations of 0.25 M at pH 8.2. The amino acids serving as NH_2 group donor were l-arginine, dl-methionine, dl-histidine, glycine, dl-serine, dl-tryptophan, dl-valine, dl-aspartic acid, dl-phenylalanine, dl-alanine and dl-glutamic acid. dl-tryptophan, l-arginine and glycine were prepared in concentrations of 0.1 M. All other amino acids were in concentrations of 0.2 M. The experiments followed in general the methods described by Gunsalus and Stamer⁵. The reactants were 0.1 ml. M phosphate buffer (pH 8.3), 0.2 ml. of a homogeneous aqueous suspension of acetone-dried cells (30 mgm./ml.), 0.2 ml. pyridoxal phosphate (0.5 mgm./10 ml.) 0.2 ml. amino acid, 0.1 ml. keto acid and water to make up to 1.0 ml.

The reaction of the mixture was adjusted to pH 8.2. The cell suspension boiled at 100°C for 3 min was used as control for each amino acid-keto acid experiment. The tubes were incubated for 60 min at 37°C and the reaction stopped by boiling at 100°C for 5 min. The tubes were centrifuged at 3 000 r.p.m. for 30 min, and approximately 0.002 ml. of the supernatant examined for the presence of the amino acid corresponding to the keto acid used, by qualitative paper chromatography.

With all the strains used the following reversible reactions were shown to occur:

(a) glutamic acid + oxaloacetic acid \rightleftharpoons aspartic acid + ketoglutarate,

(b) glutamic acid + sodium pyruvate \rightleftharpoons alanine + ketoglutarate

(c) glutamic acid + sodium phenyl pyruvate \rightleftharpoons phenylalanine + ketoglutarate.

In addition aspartic acid was formed in the reaction between phenylalanine and oxaloacetic acid with cell preparations of the strains of *Shigella dysenteriae* 6, *Shigella boydii* 3, *Shigella boydii* 5 and one strain of *Shigella sonnei*. Alanine was present in the supernatant of the reaction mixture containing aspartic acid and sodium pyruvate with the strains of *Shigella dysenteriae* 3, *Shigella boydii* 3 and *Shigella boydii* 5. With the strains of *Shigella boydii* 5 and *Shigella dysenteriae* 6 alanine was also formed in the reaction between phenylalanine and sodium pyruvate.

Of the four keto acids α -ketoglutarate was most active and showed reactions with methionine, valine, tryptophan, phenylalanine, alanine and aspartic acid. Phenyl pyruvate showed the lowest activity. Of the two remaining keto acids both of which were poorer amino acceptors than ketoglutarate, oxaloacetic acid was slightly more active than sodium pyruvate. Among the amino donors, glutamic acid showed reaction with the three keto acids and the reaction could be demonstrated with all the strains used. Under conditions of the test, none of the strains was able to show transamination reactions with glycine, serine, histidine and arginine, and any one of the four keto acids.

I am grateful to Prof. P. Collard, Department of Bacteriology, University College, Ibadan for his helpful advice and criticism and to Dr. J. H. Marshall of the Department of Bacteriology, London School of Hygiene and Tropical Medicine for helpful discussions.

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Light-Induced Production of Carotenoid Pigments by *Cephalosporia*

THE pink and orange pigmentation in cultures of various members of the form genus *Cephalosporium* has been noted by several authors¹. Roberts² presents a table including descriptions of the colony colour of a number of *Cephalosporium* species and strains without

S. annua Nutt is an annual species widely distributed in North America. It is reported to act occasionally as a biennial. It has been referred to a separate genus *Poteridium* Spach. It is the first diploid species found in the tribe Sanguisorbeae. As seen from Fig 1 the chromosomes are smaller than in the other species of *Sanguisorba*. This might indicate that *S. annua* is a more distant relative of the other *Sanguisorba* species.

S. alpina Bunge is a perennial species widely distributed in sub alpine meadows in eastern Siberia and the Mongolian Republic. It has chromosomes of the typical *Sanguisorba* type.

S. obtusa Maxim var *amoena* Jess is a perennial native of Japan where it is found at high altitudes. It is very closely related to *S. hakusanensis* Makino which might perhaps be regarded as a variety of *S. obtusa*. In *S. hakusanensis*, $2n = 28$ was found by Sakai⁵, that is, the same number as that found by me in *S. obtusa*.

S. canadense L. is a North American perennial found in swamps from Labrador and Newfoundland to Georgia and Michigan, and as var *japonensis* it is also found in Japan. $2n = 56$ was found in the typical form whereas the Japanese variety has not been examined.

S. tenuifolia Fisch. ex Link is a hybrid between *S. officinalis* L. and *S. parviflora* (Maxim.) Takeda. It has the same distribution as *S. parviflora* and is frequently found among the parents often more predominantly than the pure species, or to quote Hulten⁶ "Sporadically all specimens of the genus *Sanguisorba* in Kamchatka—if we exclude the rare pure *S. officinalis*—form a continuous series between the two species". The chromosome number was found to be $2n = 56$. The same number was found in *S. officinalis* from Hungary, USSR, and Sweden. The present findings indicate that *S. parviflora* also may be considered to be an octoploid species with $2n = 56$.

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SOIL SCIENCE

Occurrence of Microbiological Filaments in Soils

WHILE sieving sands from south-eastern South Australia to determine the particle size distribution, considerable difficulty was experienced in obtaining clean separations. For example it was found that after shaking for 10 min on a mechanical sieving machine 2.2 gm of sand passed the 200-mesh (0.08 mm) screen, whereas an additional 10 min sieving yielded a further 2.4 gm. Thus in this case the true amount of the sand below 0.08 mm equivalent diameter was increased from 10 per cent to a value of 20 per cent of the original sample.

The 8-in. diameter sieve was in good condition, a careful inspection failed to reveal any damaged or irregular apertures. The sand remaining on the sieve was examined under a binocular, stereoscopic microscope, there was no abnormality in size or shape of the quartz grains. However, it was seen that many of the sand grains were held together by fine filaments which adhered to the individual

mineral particles. Some of the finer sand grains were completely enmeshed in a mass of these filaments, while many larger grains were bound to the larger diameter filaments when they divided to form a flat mat adhering to one side of the grain (Fig 1). The soils had been dispersed in the presence of sodium hydroxide and sodium polyphosphate in the standard mechanical dispersion apparatus. The sands were afterwards separated by repeated stirrings and decantation after the appropriate time. The filaments must be quite strong to withstand this treatment. This was confirmed by the difficulty experienced in separating the sand grains mechanically while observing them under the microscope. It would thus appear that the eventual breaking of these filaments during the extended period of sieving freed the finer material enabling it to pass through the screen. Confirmation of this was obtained by screening a sample after prior ignition. Under these conditions practically the whole of the fine material was obtained in the initial period of 10-min sieving.

The filaments appeared to be organic material as they were easily destroyed by ignition. They were somewhat basiphilic, as they stained with aniline blue, and were probably of microbiological origin. Many filaments exhibited a branching form, sometimes with change in diameter. Others which were of larger diameter and more uniform showed well-developed cross walls and less branching. Most filaments were hyaline, some were coloured, usually brown, rarely green or blue.

Afterwards many soils from the collection of the Division of Soils, CSIRO, were examined and it was found that the small aggregates (less than 2mm) from most surface horizons contained similar but usually finer filaments. These filaments formed a strong network within the soil crumbs. Soils examined included samples from Adelaide, Barossa Valley, Mt. Compass and County Robe in South Australia and Lismore in New South Wales.

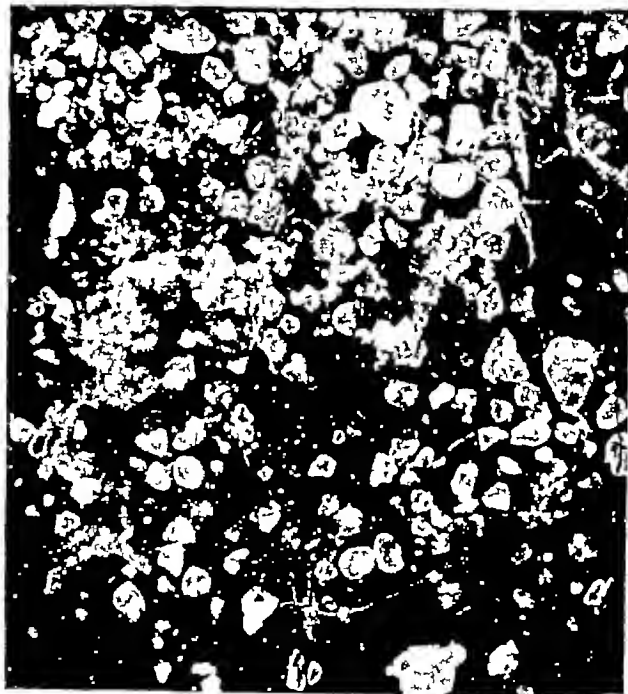


Fig 1. Photomicrograph showing organic filaments in Mount Compass Sand. The aggregate on the left is strongly bound together by very fine filaments, other coarser filaments ramify from it as well as appearing elsewhere in the field ($\times 4$).

These filaments could have a marked strengthening effect on the stability of soil crumbs. Their influence on the structure of soils and the binding of sands is being further examined, the nature of the microorganisms concerned is also being investigated. The persistence of their binding action on sand particles even after considerable mechanical treatment during dispersion of soils stresses the need to ignore all sands prior to detailed sieving for their fractionation.

I am grateful to Mr J. R. Harris for the benefit of discussions with him on the microbiological aspects of these filaments and for taking the photomicrograph used for Fig. 1.

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Titration Curves of Soil Organic Matter

In a previous paper¹ it was claimed that the addition of small amounts of copper sulphate to a suspension of acid washed organic matter resulted in the release of two hydrogen ions for each of added copper. This release was detected by titration of portions of the organic matter with alkali in the presence and absence of copper (ref. 1, Fig. 5). Further experiments with organic matter extracts of peats and podzols have not confirmed a general proton release of this magnitude and are in conformity with the results of Martin and Reeve.² These authors revealed new complications in such experiments, in particular the important association of aluminium with soil organic matter and the difficulty of removing this metal. The purpose of this note is to correct the inaccuracy in my earlier paper and to add further information on the ability of soil organic matter to complex transition metals.

Chelation reactions can occur with for example copper without the demonstrable release of two hydrogen ions per metal atom.³ This fact was not recognized during some previous discussions of chelates in soils^{1,2}, but can be illustrated by titrations of several carboxylic acids. When oxalic acid is titrated with alkali, the addition of even the equivalent amount of copper does not displace the end point of the titration curve. On the acid side of the end point the extra alkali consumed in the presence of copper is less than the stoichiometric amount and differs at different pH values.

Some hydroxy carboxylic acids and salicylic acid show another relationship. The hydrogen of the OH groups becomes titratable with alkali in the presence of metals such as copper which form stable chelate compounds. The titre of these acids increases by an amount proportional to the copper added for additions less than the equivalent of the acid present. The extra alkali consumed at the end point is equivalent to one hydrogen ion per atom of added copper. If excess copper is added, part is precipitated as a basic salt at its usual pH of 'hydroxide' precipitation and this part requires the normal amount of alkali, namely, approximately 1.6 hydroxyl ions per atom of copper. These relationships are exemplified by citric acid with three levels of added copper (Fig. 1). The second level of copper approximates to the maximum amount which can be chelated by the acid present. The highest addition is twice the second and the additional displacement of the end point is about 1.6 times that produced by the second level of copper. The general reaction of α hydroxy acids with copper can be written

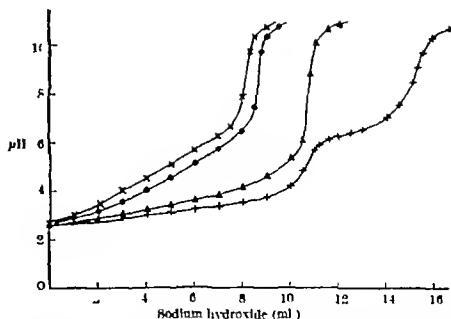
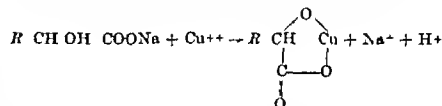


Fig. 1. Titration of 10 ml 0.02 M citric acid with 0.075 N sodium hydroxide: \circ citric acid alone; \bullet +2 ml 0.02 M copper sulphate; \times +10 ml 0.02 M copper sulphate + +20 ml 0.02 M copper sulphate.



Martin and Reeve² have shown the effect of the partial removal of aluminium on the titration curve of podzol organic matter. Their results have confirmed the evidence of Aleksandrov⁴ that iron and aluminium block carboxyl groups on the organic matter. The question remains as to whether other organic groups are simultaneously involved, the metals thereby being chelated.

One difficulty in interpreting titration curves of organic matter in terms of models has been the determination of the end points of the curves. By techniques to be reported elsewhere, Reeve and I have succeeded in preparing organic matter extracts containing only traces of mineral constituents. Titrations of these preparations have given much less ambiguous end points and, when suitable amounts of copper are added, give curves showing the same relationships as those of chelating hydroxy acids. Fig. 2 shows results

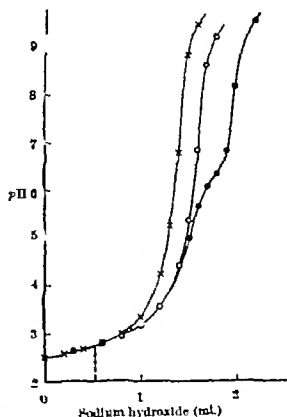


Fig. 2. Titration of 10 ml aliquots of purified organic matter extract from ground-water podzol B horizon with 0.06 N sodium hydroxide: \circ organic matter alone; \bullet +1 ml 0.02 M copper sulphate; \times +2 ml 0.02 M copper sulphate.

obtained with a purified organic matter extracted from the B horizon of a Tasmanian ground-water podzol. Part of the acidity of this preparation (indicated by the dotted line) was due to free hydrochloric acid. Other experiments have shown that the presence of neutral salt in such systems does not alter the displacement of the end-point in the presence of copper.

Although Martin and Reeve² doubted whether chelates were found in any of their organic matter systems, the curves which they obtained with purified podzol humus (ref. 2, Fig. 6) appear to be compatible with the present interpretation. Their other evidence resulted from application of the test of Gregor *et al.*⁵, this test has proved unreliable in application to citric acid systems.

Accumulated evidence leading to the conclusion that transition metals can be chelated by soil organic matter need not be summarized here. However the present evidence appears to provide the first indication of the identity of the binding sites, namely carboxyl and phenolic or hydroxylic groups. Amino- or imino-acids could give titration curves showing the relationship described for hydroxy acids but the amount of copper chelated in these experiments exceeds that which could be bound even by the whole of the nitrogen present. Published figures on the OH content of organic matter are, on the other hand, compatible with the amount of copper bound.

I gratefully acknowledge the benefit of discussions of this problem with both A. E. Martin and R. Reeve. However, the conclusions reached are not necessarily accepted by these workers. I am also indebted to Prof. G. W. Leeper for valuable suggestions during the preparation of this manuscript.

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¹ Beckwith, R. S. *Aust. J. Agric. Res.*, **6**, 655 (1955).

² Martin, A. E., and Reeve, R. *J. Soil Sci.*, **9**, 89 (1958).

³ Quagliano, J. V., and Wilkins, D. H. *The Chemistry of Coordination Compounds*, J. C. Ballar, Editor.

⁴ Aleksandrova, L. N., *J. Sci. Food Agric.*, **6**, Abstracts Pt. 1, 63 (1955).

⁵ Gregor, H. P., Luttlinger, L. B., and Loeb, E. M. *J. Phys. Chem.*, **59**, 34 (1955).

Nitrogen Fixation in a Uganda Swamp Soil

Information about the swamp-soils of Uganda is important since their agricultural potentialities are largely unknown and the swamps cover a large part of the surface of the country. Work on the relationship between the nitrogen status of some tropical soils and the water regime applied to them has given particularly interesting results with a sandy soil from a papyrus swamp at Namulonge, near Kampala.

400-gm samples of soil were placed in 18 shallow jars of thick glass giving a soil layer about 5 cm deep. Distilled water was added to each preparation to give three groups with (1) soil at saturation capacity, (2) soil completely water-logged to the surface and (3) soil flooded under a layer of water 2 cm deep. Each group was divided into two sets (triplicates) where (a) moisture status was maintained by restoration of water loss after daily weighing and (b) water was allowed to evaporate until the soil became completely air-dry as shown by constancy of weight of the

preparation. The latter samples then received distilled water in the original quantity so that a drying and wetting cycle occurred. The experiment ran for nine weeks, the jars being placed on an open flat roof under a stretched polythene sheet excluding dust and insects but not obstructing ventilation. Temperature in the preparations varied between 19° C (8 a.m.) and 36° C (in full sunlight).

Kjeldahl nitrogen determinations were carried out separately (i) on supernatant liquid when it was present and (ii) on the soil plus organisms homogenized by hand grinding. Combined results are given in Table 1. Nitrate-nitrogen determinations by the

Table 1. TRIPPLICATE GROUPS OF KJELDAHL NITROGEN VALUES FOR NAMULONGE SWAMP SOIL IN P.P.M. ON AN OPEN DRY BASIS (105° C)

| Outset | Water status maintained | | | Alternately wetted and dried* | | |
|----------|-------------------------|--------------|---------|-------------------------------|--------------|----------|
| | Saturated | Water logged | Flooded | Saturated | Water logged | Flooded |
| 600 | 445 | 585 | 585 | 585 (4) | 870 (5) | 1100 (3) |
| 710 | 575 | 730 | 540 | 560 (5) | 585 (5) | 1090 (4) |
| 560 | 410 | 505 | 565 | 565 (4) | 540 (4) | 905 (3) |
| Mean 623 | 487 | 637 | 563 | 570 | 665 | 1062 |

* Figures in parentheses show the number of wet/dry cycles undergone by the preparation.

phenoldisulphonic acid method failed because of the presence of organic matter. Ammonium-nitrogen was also determined but did not exceed 3 per cent of the Kjeldahl value.

Considerable increase in nitrogen occurred only where preparations were alternately flooded under 2 cm of water and allowed to dry out. The effect is probably related to that observed by Birch and Friend¹ in which the rate of soil respiration corresponds to cyclic wetting and drying but the influence of the layer of water remains to be explained. The control of the depth and duration of such a layer clearly may be of much importance in crop-production on soils of this type.

In every preparation a luxuriant growth of blue-green algae occurred either as a gelatinous sheet on the surface of the soil or as lobed floating masses in the water layer. *Anabaena* spp. were identified as part of the complex in every case and the nitrogen-fixing properties of *Anabaena* are well known, but the problem remains why they were ineffective in the majority of the preparations.

Preliminary experiments have shown that minute inocula from the jars initiates good growth of blue-green algae (*Anabaena* predominating) in a nitrogen-free liquid medium³. The growth is continued if such cultures are allowed to dry out and particles of the residue transferred to fresh medium.

The situation in this type of swamp soil seems to be similar to that described for the rice-growing soils of parts of India² and the use of some Uganda swamps for agricultural purposes may involve methods similar to the Indian.

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May 11

¹ Birch, H. F., and Friend, M. T., *Nature*, **178**, 500 (1956).

² De, P. K., *Proc. Roy. Soc. B*, **127**, 121 (1939).

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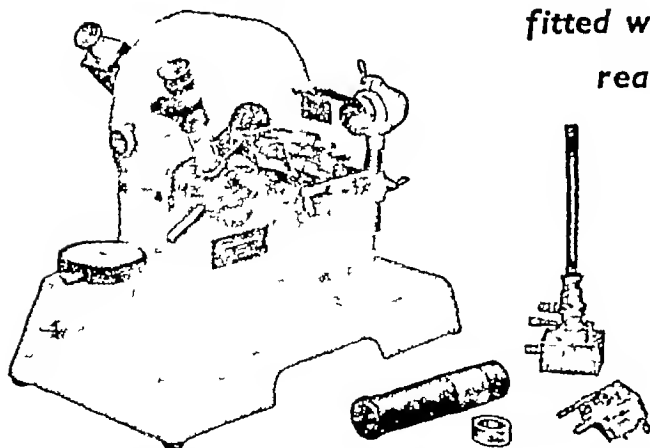
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THE STUDY OF MAN

DESPITE comments during recent years that the British Association for the Advancement of Science appeared to have lost both its bearings and its impetus, it has been generally acknowledged that the presidential address has always been much more than a rallying call at an annual meeting—it has increasingly come to be recognized as a statement by a leading man of science to the nation. In these addresses, each president has considered a theme which often has reflected outstanding interests of men of science at that particular time. In a discipline which daily grows more complex and bewildering Sir Edward Appleton at Liverpool pleaded with men of science to make themselves intelligible to the layman without an informed populace he showed that science could not flourish. At the Dublin meeting, Prof P M S Blackett was concerned with the need for applying science and technology on a world wide front to solve world wide problems of poverty and distribution. With his own travels as background, Prince Philip at Edinburgh discussed international aspects of science and how they could contribute to better understanding between peoples everywhere. Now, in a world where powerful blocs have realized that material strength alone is not enough, this year's president Sir James Gray invites men of science everywhere to pay full regard to moral principles and the social repercussions of their discoveries (see p 36 of this issue).

The address is noteworthy for a number of features. First, because Sir James Gray has looked at science as a whole and has supported his arguments by evidence drawn from a number of the sections which comprise the British Association—he himself has acted as a link between them. Secondly, because he has used the life sciences of biology to show its unifying influence in the overall study of man and, thirdly, because he has used his own wide background to examine defects in the educational system before making suggestions both for spreading and applying knowledge of science and technology throughout the world and for making it part of the general philosophy of man. Like others in this famous series, his address will be long remembered as a contribution to man's general evolutionary progress.

Two of Sir James's general topics will command widespread support. The ever present need to consider the beneficial effects of science on international relationships is made very difficult in a world where science is primarily seen as a manufacturer and distributor of hydrogen bombs. Sir James is emphatic that the primary objective of men of science should be to illuminate the beauty of science its inflexible pursuit of truth, its challenge to courage and tenacity and its power to inspire.

The place of science in a general philosophy of life is equally well put. Like music, science knows no barriers, and the combined efforts of scientists throughout the world are necessary if man is to continue in his efforts to unravel the secrets of

Nature. Where there are political restraints where knowledge is bounded materially and mentally by local and national barriers the man of science can provide a bridge which should encompass the Earth. Misses should be guided not to destroy mankind but to bring fresh delight in making clearer the mysteries of the heavens.

To make wise and humane use of science as Sir James rightly points out something more than statistics or the precise laws of physics and chemistry will be required. The challenge is to the less well defined biological sciences and to the ill-defined social sciences arising from them. These sciences must be vigorously pursued not only to discover more of man himself, but also of his relationships with his fellows everywhere; they must also be more widely taught so that more and more people have better opportunities for understanding themselves and other people. Sir James is right to emphasize that it is in the biological and social sciences that the answer may be found as to whether or not science has real cultural significance. In his address, the new president of the British Association also shows the practical nature of the biological sciences and that man still has much to learn from his evolutionary predecessors. Students of aeronautics, navigation and communications would hasten further discoveries if they paid more attention to biology. It could be added that many students of the humanities and of the physical sciences could considerably reduce the cost of the National Health Service if they would but study some of the general principles of biology, in so doing they would improve their health and, presumably their happiness.

In the field of demography Sir James uses his own arguments to give full support to conclusions put forward by Prof Blackett in Dublin. With evidence drawn from the study of natural evolution he clearly and courageously puts his choice before all civilized beings. Accepting the discipline of voluntary limitation of families, man can direct the course of his own evolution without the evil consequences of over population; if he "behaves like an animal and allows his population to increase while each nation steadily increases the complexity and range of its environment Nature will take her course and the law of the jungle will prevail." Churches throughout the world should examine their doctrines to see whether they are spiritually justified in bringing misery and destitution to so many people, and whether they are indeed helping man to achieve the highest moral and spiritual development of which he is capable. Men, Sir James says really ought to be able to do something better than ants.

In another comparison of man and animals Sir James again shows the practical advantages which deeper study of the biological sciences could bring. Study of the learning process has revealed five basic principles, all of which could be applied to the training of human beings. These principles could be made

techniques well established before 1940. But they are none the worse for that, indeed, it is one of the weaknesses of present-day astrophysics that insufficient effort is being put into basic measurements such as are dealt with in several of these articles, for example, stellar masses and radii from visual and eclipsing binaries, atomic abundances from stellar spectra.

Ch Fehrenbach has given a full account of the classification of normal stellar spectra. P C Keenan has written briefly of stars with peculiar spectra, in a useful although not comprehensive article which contains material not readily obtainable elsewhere, for example, on high-velocity stars. P Swings's contribution on molecular bands in stellar spectra deals with a complicated subject in which much remains to be done and in which there is a scarcity of other publications. Two useful contributions by K Wurm on planetary nebulae are widely separated in the book, although intended to complement each other. I find it difficult to understand why they were not united. J L Greenstein has written an important original paper on white dwarf spectra which is essential reading for anyone working in this field.

P van de Kamp's article on visual binaries is to be commended. It deals with a woefully neglected subject on which there is no modern text-book. There follow accounts of eclipsing binaries by S Gaposchkin and of spectroscopic binaries by O Struve and Su-Shu Huang. Eclipsing binaries are usually also spectroscopic binaries, both classes are very important sources of data for checking theoretical models, but the complications shown by their light curves and spectra have led to speculative ideas for which we have as yet no adequate check.

The article by D Barbier is virtually a short text-book, giving a good systematic exposition of what may be called the conventional theory of stellar atmospheres and its very solid achievements.

The articles are in English, French or German. Each includes a brief general bibliography, in some cases with short comments. Adequate attention has been given to other references also. The index is in three parts: German with an English translation, English with a German translation, and French only for the three articles written in French.

As in every "Handbuch" of this character, the contributions vary a great deal in merit, the better ones are excellent. Present indications are that this is to be one of the cheaper volumes, although its price is more than £8.

R O REDMAN

ELECTRONICS IN BIOLOGY

Electronic Apparatus for Biological Research

By P E K Donaldson. With contributions by Dr J W L Beament, F W Campbell, Dr D W Kennard, Dr R D Keynes, Dr K E Machin and Dr I A Silver. Pp xii+718. (London: Butterworths Scientific Publications, New York: Academic Press, Inc., 1958.) 120s, 20 dollars.

TO be able to use and interpret correctly the results obtained by using electronic apparatus, the biologist requires some understanding of electronics—a secondary subject which may have little direct appeal to him—and for this reason, a book explaining concisely the principles and functions of electronic apparatus used in biological research could

be of great value. The author of the book has had the needs of the biologist primarily in mind and he and his associate contributors, as members of the staff of the Department of Physiology at Cambridge, ought to be well qualified to look after his needs.

The book is divided into four parts. Part 1, principles of electronics (277 pp), Part 2, practical use of components (48 pp), Part 3, articles by specialist contributors on transducers, electrodes, indicators and measurement of temperature, light and radio activity (249 pp), Part 4, complete apparatus (127 pp). The first part is of standard text-book form, with the exclusion of subjects considered to be of little interest to the biologist. The treatment is brief, and in some cases, unfortunately, it is insufficient to permit one to follow applications which are given later. The section on filters is too detailed for the reader wishing to be acquainted with, rather than fully to understand, the subject. On the other hand, the application of the valve as a switching element is covered very briefly, and no mention is made of the pulse response of networks with reference to differentiation and integration. The various sources of noise are analysed, this chapter being particularly useful in quoting orders of magnitude. The graphs here are excellent and self-explanatory but could have been more conveniently placed in relation to the text, as has been done elsewhere. In separating the information on batteries in Part 2 from the section dealing with stabilized power supplies, the opportunity to discuss their relative merits is missed.

There are nine chapters in Part 3 dealing with specific subjects, all of which should prove useful to anyone concerned with biological instrumentation. The theoretical treatment of light sources and detectors is well done, as also is the assay of radioactivity, but circuit applications would have improved both chapters. The articles on electrodes, transducers and the use of relay circuits are valuable contributions, but that on temperature measurement could have been improved by a recapitulation of the physical principles.

The important section of Part 4 dealing with apparatus is unfortunately condensed into only one-sixth of the book. Stimulus artefact is explained very well, as is also the subject of interference, and all readers interested in design would benefit from the author's design procedure. A chapter on transistors gives a useful introduction to the principles but an assessment of their possible future in biological research would have helped to define their importance.

The book is well written, and the practical advice given shows that the author writes from experience. Its value could have been increased by linking the biological specifications to appropriate designs, an important feature of biological instrumentation. The failure to achieve this linkage makes the book of rather limited value to the engineer who is designing apparatus for biologists. However, in helping to satisfy the requirements of the physiologist, the aim of the author has been achieved, albeit at a high price. In the preface the author expresses doubts about the suitability of the title, and since the emphasis is so much on physiological applications, the reviewer is of the opinion that "Electronic Apparatus for Physiological Research" would convey more precisely the nature of the subject matter.

W J PERKINS

HISTORY OF TECHNOLOGY

A History of Technology

Edited by Charles Singer, E J Holmyard, A R Hall and Trevor I Williams. Assisted by Y Peel, J R Petty and M Reeve. Vol 5. The Late Nineteenth Century, c 1850 to c 1900. Pp xxxiii + 888 + 44 plates. (Oxford Clarendon Press. London Oxford University Press 1958) 168s net.

THIS fifth volume of the "History of Technology", covering the approximate period 1850-1900, marks the conclusion of this great work which traces the development of technology from the earliest times to the beginning of the present century. In some fields brief reference is made in the present volume to developments that have taken place so recently as the years following the Second World War.

The book is divided into eight parts. The first deals with primary production, including the management of food and the development of the metal and petroleum industries. The second part concerns itself with stationary and marine steam engines and the internal combustion engine. Part 3 treats of the rise of the electrical industry. Part 4 of the chemical industry. Part 5 deals with transport including rail ways, ships, aircraft, road vehicles and cartography and other aids to navigation. Part 6 is concerned with civil engineering and covers building materials, bridges, tunnels, hydraulic engineering and water supplies. The seventh part discusses manufacturing in general, including textiles, metals, machine tools, ceramics, glass, printing, photography, and rubber. The last part evaluates technological education and the general role of technology and its social consequences in the modern world.

Each of the chapters is written by a competent authority, and the whole volume has been brought together and made into a unified work by its principal editor the eminent Dr Charles Singer and by Dr E J Holmyard and two other distinguished co editors.

Although it could not be expected that every one of the thirty four chapters would delve with equal thoroughness into the mass of technological history behind each subject treated nevertheless the whole presents a most enlightening and valuable summary of progress during the crucial last half of the nineteenth century. For example, two such different stories as the development of machines for the generation of electricity and the discovery of aniline dyes are almost breath taking in their implications for later pure science as well as for technology.

It is certain that many full reviews of this extensive and admirable work will be written in Great Britain. The present American reviewer feels that he should devote special attention to the volume as it may appear to some American eyes. First of all, it is impossible not to be struck by the clarity of exposition of the present work. It is hard to believe that an equal number of American students in this field could be found who could write so well. It is indeed surprising to find authorities in the highly specialized fields of technology who are able to present their subjects so lucidly. The style of the volume will make it attractive even to the layman who is concerned with the full history of our age. Anyone who is interested in reading present day political or social history will also enjoy the style and the content of this volume. Here the reader is not overwhelmed by mathematics or repelled by an unnecessarily techni-

cal vocabulary. It has been possible for the editors to cover the really vast human achievement that is considered in this book only by exercising great verbal restraint. Often a single sentence summarizes a large development that even in an encyclopedia article might have been given a long paragraph. For example Josiah Willard Gibbs, considered by some to be the man who did most for pure science under lying technology in America during this period is described in four words as the formulator of the phase rule.

I could not indeed read many pages of this book without thinking of the fascinating problem of national differences in the approach to scientific and technological history. In recent years the world has noted successive Russian claims that very many of the great inventions and developments of the past really originated in Russia. Similarly, one who walks through the Deutsches Museum in Munich must feel that the tens of thousands of earnest young Germans who go through its admirable halls each year must gain the impression that the full flowering of the industrial revolution took place almost alone in fertile German soil. It is similarly apparent that the present volume quite properly emphasizes British science, technological inventions and developments. This very fact makes the work especially valuable in America. Many new industrial developments in the United States grew out of British beginnings, and this volume clearly portrays this essential background.

Some day a general treatise on detailed technological developments in the United States will be prepared and when it does appear it will be a valuable supplement to the present volume. When such a treatise is written, it will for example give full emphasis to the material contained in the voluminous publications of such organizations as Benjamin Franklin's still very active, learned academy, "The American Philosophical Society, Held at Philadelphia for the Promotion of Useful Knowledge", the National Academy of Sciences of the United States and the Smithsonian Institution. It is indeed a little surprising to find no reference in the index to these American organizations, which were doing so much for world science and technology during this period, in spite of many references to the Royal Society, Royal Institution, and the Science Museum, South Kensington. It is quite understandable, however, that the mass of American material could not be dealt with in a complete way in the present book which is very properly British in its central emphasis.

All five volumes of this great work, nevertheless fill a need long and keenly recognized especially, it may be on the western side of the Atlantic. Americans will long be deeply conscious therefore, of the debt that they owe to the distinguished authors and editors of all five volumes of the work. The book will be read with pleasure and satisfaction by every one in the United States who is professionally concerned with the history of technology and as already suggested, by many others as well. In the years ahead these volumes will be among the reference books most frequently reached for on the working shelf of any student who is concerned with this area of scholarship. An expression of gratitude is also due to the great Imperial Chemical Industries Ltd. which helped to make possible the preparation of these expensive, well illustrated and well printed volumes.

LEONARD CANNON, F.R.S.

The last speaker of the session, Dr Donald H Andrews, B N Baker professor of organic chemistry in Johns Hopkins University, discussed new relationships between art and sciences. He developed an interesting idea on the analysis of form in terms of thermodynamics and entropy on one hand, and of information theory on the other. Citing as an example an unstruck piano string vibrating with overtones set up by its thermal energy, Dr Andrews argued that a statue of marble probably had overtones "which in the harmonic realm are the exact equivalent, homomorphic with the space form". If this statue were cooled to within perhaps a 200,000th of a degree of absolute zero and its heat capacity measured and integrated as it was warmed very slowly, the entropy term would be obtained over the very lowest part of the temperature-range and would bear a direct relationship to the shape of the statue, based on the longest thermal vibrations, with wave-length a function of the shape of the statue.

In theory it should be possible to transmit 'space-form' information defining the statue over a distance via radio waves or telephone signals for reproduction at an appropriate lathe assembly. Developing such new concepts of 'scientific aesthetics', Dr Andrews concluded that perhaps a more faithful algebra of form was needed for many of today's problems, in thermodynamics, in the study of molecules and of molecular aggregates.

The speakers at the third session of the symposium concerned themselves with unifying principles in their respective fields.

Prof P B Medawar, professor of zoology, University College, London, presented a critical account of the various possible theories which might account for the phenomenon of immunological tolerance—the specific immunological unresponsiveness induced by exposure of very young animals to antigens. After making two assumptions (1) that the maintenance of the tolerant state depends on persistence of the antigen, and (2) that any one antibody-forming cell (and its descendant clone) responds to only one antigen at a time, he considered, in turn, a series of mutually exclusive postulates, for example, that immature antibody-forming cells capable of being made tolerant occurred (a) only in embryos or very young animals, or (b) in adults as well. He then went on to discuss the hypotheses one could arrive at by various combinations of postulates, one of which led logically to the view that while some cells in the adult became immunized by exposure to antigen, others must become tolerant.

Dr Francis H C Crick, Cavendish Laboratory, University of Cambridge, spoke on the structure of viruses. He emphasized the multiplicity of factors which govern the aggregation or packing of identical units into a given space. In the simplest case, spherical sub-units are aggregated so as to occupy the smallest possible space. Such an array has certain elements of cubic symmetry. There are five-fold, three-fold and two-fold axes of symmetry. The surfaces of many viruses are polygonal with elements of 2-3, 4-3-2 and 5-3-2 symmetry, in some of these evidence has been obtained of a regular array of sub-units. Apparently, the protein parts of many viruses are made up of roughly spherical sub-units assembled in such a manner as to occupy the least space.

Studies on infectious ribonucleic acid isolated from tobacco mosaic and certain mammalian viruses indicate, according to Dr Crick, that the ribonucleic acid carries, at least in part, the necessary information

to determine the amino acid sequence of the protein sheath of the virus particle. However, since there are no known viruses consisting of less than 70 per cent protein, it is unlikely that the viral nucleic acid carries sufficient genetic information to determine such a large protein shell. The alternative is a large number of small, symmetrically packed, protein sub-units.

Dr H Gobind Khorana, University of British Columbia, showed how advances in our knowledge of organic chemical structures and of organic synthesis had contributed to an understanding of biological processes. He reviewed some of the important accomplishments in protein and peptide chemistry—such as the elucidation of the structure of gramicidin S and of oxytocic hormones. The determination of the total sequence of structural units in adreno corticotrophic hormones and other biologically active materials should soon extend to the sequence in larger molecules such as ribonucleases.

Turning to research on intermediary metabolism, Dr. Khorana discussed the organic chemistry of phosphate esters, with particular emphasis on nucleotide co-enzymes, mentioning his own important work on the synthesis of co-enzyme A. He said that despite the underlying similarity in the structure of nucleotide co-enzymes, it was at present inexplicable and rather exciting that their specificity depends upon the nucleosides that they carry.

On another topic, the sequential analysis of nucleic acids, he emphasized the present need for research. He described the chemical synthesis of a number of oligonucleotides that would be useful in developing enzymatic degradation methods for structural analysis of nucleic acids. One problem which confronted us to day, he concluded, was to match the sequential analyses of nucleic acids with similar analyses of amino-acids in proteins and polypeptides.

A lucid discussion of the mechanism of gene-action was presented by Dr John R Preer, University of Pennsylvania. He said that genes act by influencing the properties of proteins, probably because they are the determinant forms of the templates (usually held to be of ribonucleic acid nature) which direct protein synthesis. He felt that the original Beadle hypothesis of one gene one enzyme should be extended to include protein and template, so that one would have one gene one template one protein.

The many different strain-specific ciliary proteins of *Paramecium* are particularly advantageous materials for the study of gene-protein relations. Many different loci with multiple alleles are involved in the determination of these proteins. Genes at only a single locus affect each type of protein, and a locus determining one type of protein is without effect on any other locus. This complex situation is explicable on the template hypothesis. Studies on the genetic determination of different types of haemoglobin in man, which usually differ with respect to a single amino acid, had furnished beautiful support for gene-amino-acid determination.

Dr George Klein, Karolinska Institutet, Stockholm, gave a lucid analysis of the evolution of tumour cell populations. The change from a normal to a malignant cell was usually the result of a series of successive qualitative steps, known as tumour progression. The various unit characteristics of tumours such as growth-rate, sensitivity to drugs, invasiveness, etc., did not all change together during progression, but re-assorted independently so that each tumour appeared to undergo an evolution of its

own, differing from other tumours on a combinatorial basis. The postulated unit characters were probably not interrelated, but were determined by different cellular mechanisms.

Dr Klein discussed three of the many conceivable mechanisms which might account for progression: (1) the selection, by intrinsic or extrinsic factors, of new variant cell types differing from the original type with respect to one or more unit characters, (2) the loss of ability of cells to respond to homeostatic forces of the organism, and (3) automatic changes in cell population characteristics which might occur merely by virtue of an increase in the population and did not depend on cellular change. Like Lederberg he felt that analysis of the mechanisms of progression should be modelled on techniques derived from microbial genetics.

The closing session of the symposium was devoted to papers presented by members of the scientific staff of the Wistar Institute.

Dr Hilary Koprowski, director of the Institute, spoke of the staff as a group of independent thinkers of widely different backgrounds who approached their scientific problems in individualistic ways but worked together through an "intercommunicating system". The main object of research at the Wistar Institute he said, was the study of cellular biology, or perhaps more accurately, "the study of the biological micro and macro-cosmos and the attempt to bridge the gap between the two". He enlarged on this concept saying that staff members were making quantitative studies at the cellular level and were attempting the difficult and hazardous task of applying knowledge about the cell to studies of the whole organism.

Dr Angus F. Graham discussed general aspects of cell virus relationships and the methodology of their analyses. He had been developing an *in vitro* virus mammalian cell system in fluid suspension, by means of which it might be possible to investigate quantitative aspects of virus infection in a manner analogous to studies with the classic phage bacteria system.

Dr Eberhard Woecker presented evidence that the infectious ribonucleic acid which he extracted by the usual phenol technique at 4°C from cells infected by eastern equine encephalomyelitis or western equine encephalomyelitis was not derived from the virus elementary bodies themselves but from a virus precursor which appeared in the infected cells before the mature virus particles. Although lipid-containing mature virus particles did not yield infectious ribonucleic acid on treatment with phenol at 4°C, Dr Woecker reported a successful extraction at higher temperatures (40–50°C). He concluded by indicating how ability to distinguish between the precursor of ribonucleic acid and the acid itself from mature virus particles might lead to a better understanding of the biosynthesis of viruses within cells.

Continuing the discussion of viral nucleic acids, Dr John S. Colter outlined studies made in collaboration with Dr Kay Ellem. By a modification of the classic Gierer and Schramm phenol extraction technique for ribonucleic acid, in which cells were disrupted in solutions of high instead of physiological ionic strength, the deoxyribonucleic acid was extracted in the aqueous phase while the bulk of the ribonucleic acid was eliminated into the phenol phase. The final product was free from protein and ribonucleic acid, and the yield was quantitative.

By adding sodium desoxycholate, the recovery of infectious ribonucleic acid by Gierer and Schramm's phenol extraction method from Ehrlich ascites cells

infected with Mengo or West Nile viruses was greatly improved—possibly even five-fold. A collateral study of the ribonucleases of normal and malignant murine tissues implicated the pancreas as the source of the enzyme. Because of the existence of a ribonuclease inhibitor the pattern of ribonuclease activity of ascites tumour cells differed markedly from that of a normal tissue. The possible role of the magnesium ion as an inactivator of ribonuclease activity was discussed.

Dr Raymond A. Brown outlined the biophysical properties of the preparations of deoxyribonucleic acid isolated by Dr Colter's new method. The molecular weight was four to five million, and its sedimentation constant and intrinsic viscosity values were lower than those usually quoted for deoxyribonucleic acid.

His own electron microscope studies led Dr Brown to consider cellular ribonucleic acid to be made up of two types of molecules, both 42–43 Å in diameter but differing in length. There was suggestive evidence of a periodicity in the location of the phosphate groups along the axis of the rod. Each rod probably consisted of a tightly coiled single polynucleotide chain. At low ionic strength, the molecule unfolded.

Dr Vittorio Defendi discussed the virus host cell relationships of two tumour inducing viruses: the RPL-12 virus of the lymphomatous tumour of olivine and the polyoma virus in hamsters. He described the necrotic and proliferative lesions of RPL-12 virus infection in tissue cultures, in chick embryos and in hatched chicks, emphasizing particularly the derangement of deoxyribonucleic acid metabolism which occurred during the infection.

He then outlined his findings on the pathogenesis of tumours arising in Syrian hamsters following their inoculation at birth with polyoma (parotid gland) virus. All the tumours were of identical histological type regardless of their location. Preliminary analyses of the infectability of newborn hamsters with the virus suggested that immunological tolerance is involved. For example, inoculation of newborn animals with the virus along with isologous adult lymphoid cells resulted in a greatly decreased proportion of tumour-bearing hamsters, and there was an amelioration of the course of the malignant disease in the minority of animals in which tumours did appear.

Drs. Rupert E. Billingham and Willys K. Silvers described their studies on the tissue transplantation antigen determined by a locus on the Y chromosome in male mice. This antigen was responsible for the rejection of male skin isografts by females in many inbred strains. Female mice of the C57 strain could be made tolerant of subsequent male isografts by inoculation with male cells as late as 17 days after birth, and tolerance in females could also be induced by means of cell free antigenic extracts prepared from isogenic male tissues. Employing the principle of immunological tolerance they were able to show that all male mice, irrespective of their genetic constitution, possessed exactly the same Y chromosome antigen. This conclusion followed from the finding that C57 females injected at birth with cells from males of any other strain are invariably made tolerant of male skin isografts. A Y chromosome antigen was also present in male rats, which preliminary results indicated was exactly the same as in the mouse.

Concluding the symposium, Prof. Sven Gard, Karolinska Institutet, Stockholm, and visiting member of the Wistar Institute (1958–59), gave

warning against the general tendency to over-estimate the potentialities of pure biochemistry. The activities of a living cell as seen under the microscope immediately dispelled any idea that it might be regarded as a bag of enzymes. The fine structure of the cell with its innumerable surfaces and membranes offered

a clue to the fundamental question "Why and how do reactions occur in the right place at the right time?" The multiplicity of interests disclosed by the staff members of the Wistar Institute, and its strong tradition for morphology should guarantee concentric attacks on essential biological problems.

THE AUSTRALIAN ACADEMY OF SCIENCE

ON May 6, the Governor-General of Australia, Field-Marshal Sir William Slim, opened the new building which houses the offices and conference chamber of the Australian Academy of Science. The establishment of the Academy was initiated by a group of Fellows of the Royal Society of London resident in Australia (*Nature*, 170, 549, 1952). With the help of other Australian scientific leaders, they set up a body which received a Royal Charter personally from Her Majesty Queen Elizabeth II during her Australian tour in 1954.

The Australian Academy of Science is the representative body of Australian scientists at the national level, with functions comparable with those of the Royal Society of London, which was itself represented at the opening, on May 6, by its senior vice president, Sir Lindor Brown. The fellowship of the Academy now numbers eighty-seven and up to six new Fellows are elected each year. The president of the Academy since 1957 has been Sir John Eccles, professor of physiology in the Australian National University, Canberra. His predecessor was Sir Mark Oliphant, director of the Research School of Physics in the National University.

In outlining the history of the Academy, Sir John Eccles said that the need for a national scientific body of the highest standing led in 1919 to the formation of the Australian National Research Council, and thanks to the devoted efforts of its leaders, the Council gave most valuable service to Australia. Yet it would be generally agreed that it had failed to achieve the status that was required of a national body with such weighty responsibilities. Various efforts at internal reforms of the Council proved to be impracticable and a more radical proposal emerged from a conference on "Science in Australia" organized by the Australian National University in 1951. At this conference and in the subsequent discussions there was a fairly general agreement that an Academy of Science with much more restricted membership should replace the National Research Council. The Council's executive with great magnanimity agreed to its dissolution in order to make way for the new Academy. This was a fine act of self-sacrifice made in the belief that the new Academy would be better fitted to give leadership in the scientific development of Australia.

The new Academy chose to model itself closely on the Royal Society of London, so taking advantage of three centuries of wisdom. The Academy is also especially indebted to the Royal Society for help in its petitioning for the Royal Charter, and for the gift of a magnificent Signature Book that is a replica of the original Signature Book of the Royal Society.

From the very beginning it has been of prime importance to ensure that the highest standards were maintained in the election to the fellowship, and that it was truly representative of all aspects of pure and

applied science. It could be claimed that it has retained the confidence of the general body of scientists in Australia.

The functions of the Academy are both national and international. At the national level there are certain general responsibilities in the fostering of science and in its publication. However, it is at the international level that the Academy has its principal opportunities and functions. First, it is the body representing Australia at all the international scientific unions as well as at the Pacific Science Congress and the Pan Indian Ocean Congress. Secondly, it undertakes international scientific tasks for Australia. The most notable has been the International Geophysical Year, the Academy being responsible for Australia's fine contribution. From the International Geophysical Year there have developed further important international activities in which again the Academy represents Australia. The Special Committee for Antarctic Research and the Committee for Space Research are of vital interest to Australia, and both have achieved a high status. The third meeting of the Special Committee for Antarctic Research was held in Canberra this year and was generally agreed to be very successful. Among other achievements was the inauguration of the International Antarctic Analysis Centre as an annex to the Bureau of Meteorology in Melbourne. Other international activities are the organization of specialist international scientific meetings in Australia. In August a specialist biochemical meeting on hematin enzymes was held at the Academy. It is a field in which Australia holds a high place, and many of the leaders in other countries went to Australia for the conference. Next year the Academy is arranging for an international conference on the chemistry of natural products, which will be held in Melbourne, Sydney and Canberra.

In all these national and international activities the Academy can count on the devoted service not only of its own fellowship but also of the other scientists of Australia. The aim is to select the scientists best fitted for these special purposes regardless of their affiliation with the Academy. On the Standing and National Committees of the Academy the Fellows are outnumbered, and often scientists who are not Fellows hold key positions.

There will be no relaxation of labour now that a centre for science has been established in Australia. It has fine symbolism with its geometrical form and its great restraint of line and décor. The Academy can now and in the future radiate its influence over Australia and the world and receive from the world for Australia. But every end is a new beginning, and the Academy is now planning to become as well a channel for benefactions for scientific purposes and so to exert its influence not only through expert committees and individually by its Fellows but also

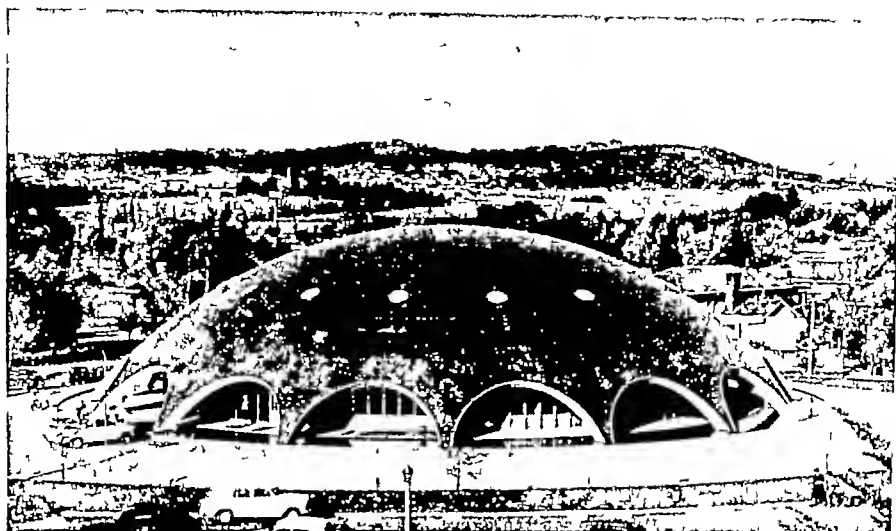


Fig 1 New Building of the Australian Academy of Science in Gordon Street Canberra

by providing the finance for research projects. Benefactors would be secure in the knowledge that their contributions were being administered by the collective scientific wisdom of the Academy rather than by the authority of any one scientist, however eminent.

The copper-sheathed dome of the new Academy building (Fig 1), rising from the waters of a surrounding moat, is backed by the rolling bronze green hills of Australia's national capital, Canberra. Beneath the dome is a central conference chamber, with luxurious seating for 100 and comfortable seating for a further 100, and a ring of offices, council room, and a superb reception room which overlooks an expanse which will within a few years be part of the central lake system of Canberra. The conference chamber will be the venue of the annual meetings of the Academy itself and will be extensively used for meetings of Australian scientific and professional societies as well as for such international symposia as may be held in Australia.

The national responsibilities of the Academy receive material recognition from the Commonwealth Government in the form of an annual grant towards current expenses. The Academy, however, remains autonomous, and indeed the value of its services is derived very largely from its autonomy. It is too young a body to have achieved financial self-sufficiency through endowments, but the creation of the conference chamber and offices has been made possible entirely because of generous contributions to the Academy building fund by Australia's great industrial firms. To these firms, to the architects, and to the vision and energy of the members of its early Councils the Australian Academy of Science, and Australia, owe a debt of gratitude, for they have created one of the most striking and important structures in Canberra and they have provided the Academy with a home of its own which is modern, dignified and of the highest quality.

MERLIN, AN INDUSTRIAL RESEARCH REACTOR

By DR T E ALLIBONE, F.R.S

Research Laboratory, Associated Electrical Industries Ltd., Aldermaston Court, Berkshire

THE Merlin research reactor is situated at the Research Laboratory of Associated Electrical Industries Ltd at Aldermaston Court in Berkshire. It was made critical for the first time on July 16 1959.

The decision to install a reactor for fundamental research at Aldermaston was taken in 1955 and the Associated Electrical Industries—John Thompson Nuclear Energy Co undertook to supply it. The nuclear physics aspects of the reactor and the design of the control system have been the responsibility of the Associated Electrical Industries Research

Laboratory, the mechanical engineering design, the erection and the commissioning of the equipment up to the stage of loading fuel into the reactor have been the responsibility of Associated Electrical Industries—John Thompson. Loading of fuel began on July 6 by the staff of the Laboratory, who are now engaged on the proving trials of the reactor. These trials which involve thermal, mechanical, electrical and physical measurements will extend into 1960 while the reactor power is gradually increased to a maximum of 5 MW.

The original design of the reactor was for a maximum thermal power of 1 MW. However, the shortage of test facilities in research reactors in the United Kingdom was impressed upon Associated Electrical Industries, Ltd, by the Atomic Energy Authority, and inquiries from overseas indicated that a 5 MW reactor was a more likely export, so the design was altered to achieve a power of 5 MW type which is characterized by a large maximum fast *Merlin* is of the light-water-cooled and moderated (> 1 MeV) neutron flux per unit of power. The maximum unperturbed fast flux with 3.4 kgm of uranium-235 in the core is $6 \times 10^{13}/\text{cm}^2/\text{s}$, the average fast flux in the nuclear power reactors being built for the Central Electricity Generating Board is about $10^{12}/\text{cm}^2/\text{s}$. Because it is the fast neutrons which contribute a large portion of any irradiation damage to materials in a reactor, it should be possible to carry out life tests on materials subject to radiation in power reactors. It is believed, therefore, that *Merlin* will be a very useful addition to the research and testing reactors in the United Kingdom.

A view of the reactor as seen from the experimental floor is shown in Fig 1. The reactor has been described in detail elsewhere¹, it is of the pool type, using fuel highly enriched in uranium-235 suspended in a tank of light water. The minimum cold, unpoisoned critical mass of the reactor has been shown in subcritical experiments to be about 2.6 kgm of uranium-235², from which the mass of uranium-235

required to provide a reactivity of 0.055 is calculated to be about 3.4 kgm. With a beryllia reflector, 3 in thick, added around the vertical sides of the core the corresponding masses of uranium 235 are estimated to be 2.18 kgm and 2.87 kgm, respectively. The maximum reactivity of the core has been limited to 0.055 for safety reasons. The maximum unperturbed thermal neutron flux with 3.4 kgm of uranium-235 in the core is $5 \times 10^{13}/\text{cm}^2/\text{s}$, the average thermal flux in the Central Electricity Generating Board power reactors is about $2 \times 10^{13}/\text{cm}^2/\text{s}$.

The reactor is unusual in that the core can be moved vertically to four positions. The top position permits the addition or withdrawal of fuel or experimental apparatus from the core, the moving core structure can be seen in Fig 1 as it appears from the top floor of the reactor building when the core is in its highest position. At two lower positions the core is in the plane of sets of experimental facilities, which can be seen in Fig 2. The lowest position is for storage of the core and is so arranged that the possibility of loss of coolant from the tank in this region is negligible.

The area occupied by the reactor and its associated buildings is close to Aldermaston Lake. The large building contains the reactor and the main experimental area, the reactor control room, the fission-product detector and the ventilation plant for the building. Nearer the lake is the primary coolant pump house, the secondary coolant pump house, a

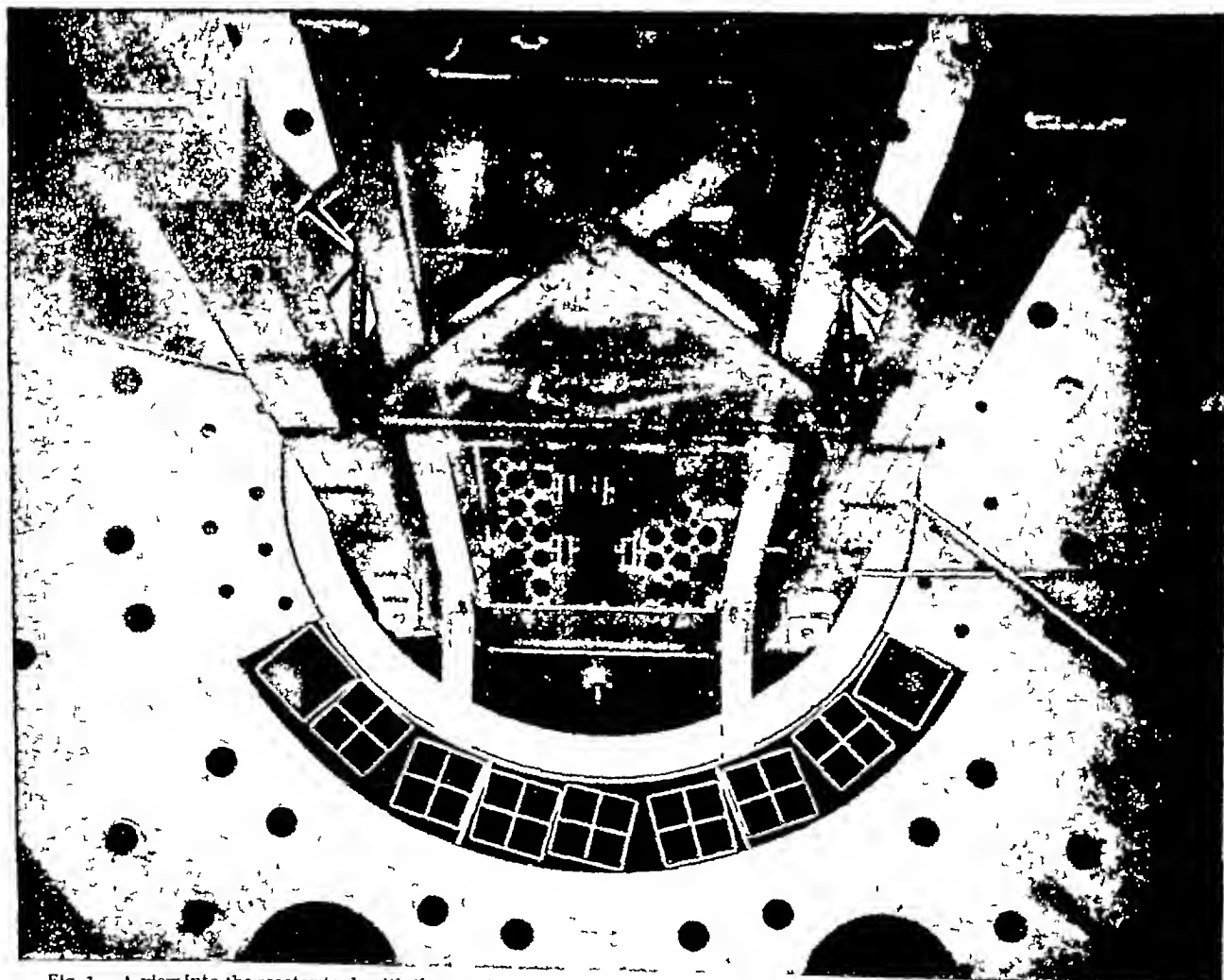


Fig 1 A view into the reactor tank with the core lattice plate at its highest position. Four fuel elements can be seen in position on the lattice plate. The rectangular containers in the foreground, are for temporary storage of active fuel elements.

laboratory for sub-critical studies of the reactor core, an effluent plant for processing liquid effluent by filtration and ion-exchange before disposal and a personnel change room for use when entering and leaving the area in which contamination might occur. Four further small laboratories and offices are between the reactor and the lake. Twenty fixed radiation monitors are situated at positions throughout the buildings and in the effluent discharge system, and a further four monitors are situated approximately symmetrically around the reactor at a distance of several hundred yards, to provide a warning of any undue release of airborne radioactivity.

The proposed research programme for *Merlin* covers both the fundamental and applied aspects of reactor research. Fundamental research being planned includes the provision of nuclear data, the effects of radiation on materials, a study of Čerenkov radiation in reactors, and methods of measuring neutron spectra. The applied aspects of the research, which will certainly involve some fundamental work also include activation analysis, reactor control and safety studies, and the production of short-lived radioactive isotopes.

The Universities of Birmingham, London, Oxford, Reading and Southampton have been invited to consider how they might best use the reactor for the instruction of senior undergraduate and postgraduate students. Members of several university departments and of large polytechnics have spent several weeks with the reactor team, and during this summer a number of postgraduate students from the universities will be working in the laboratory on some research project associated with *Merlin*. University departments have been invited to arrange brief visits to the reactor for final year students in physics, metallurgy and engineering, and longer visits for postgraduate students.

Dr A. J. Salmon is the section leader in charge of the project, and the detailed work in the physics, electrical and mechanical engineering of the reactor

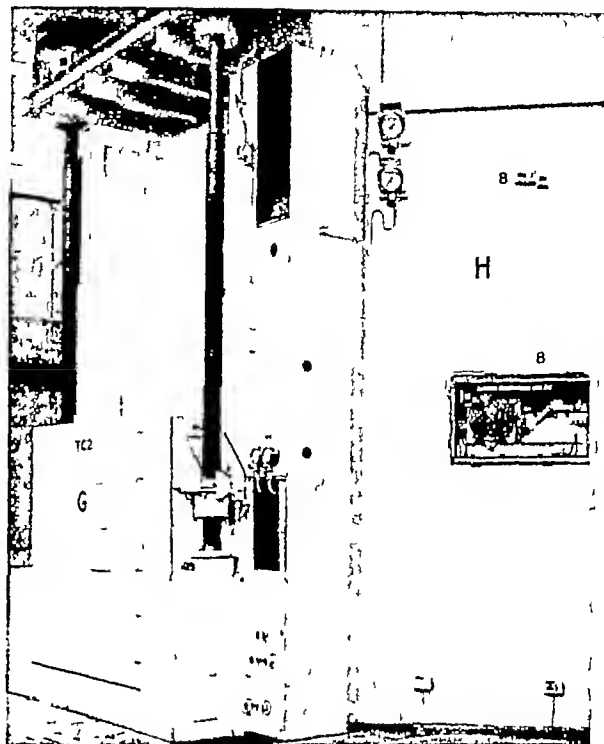


Fig. 2. The reactor and its experimental facilities as seen from the experimental floor.

has been the responsibility of Dr K. Firth, Mr B. Miller and Mr I. Munro, respectively. The Reactor Section together with the Thermonuclear and Nuclear Physics Section, constitute the Nuclear Sciences Group led by Mr D. R. Chalk, who is also responsible for the overall safety from nuclear hazards. Mr J. N. Barnett, the Laboratory supervising engineer, has been responsible for the layout of this site, with Messrs Atkins and Partners acting as consultants.

¹ Allibone, T. R., Chalk, D. R., Firth, K., Miller, B., Munro, I. and Salmon, A. J. *Geneva Conference Paper No. 513* (1955).

² Chalk, D. R., Firth, K., Kerridge, M. and Salmon, A. J. *Nature* 181, 1171 (1955).

NEWS and VIEWS

Sir Owen Wansbrough-Jones, K.B.E., C.B.

At the end of September, Sir Owen Wansbrough-Jones is resigning from the position of chief scientist to the Minister of Supply. After taking his Ph.D. in the Department of Colloid Science at Cambridge, he spent some time with Hahn in Berlin. He returned to Cambridge both to his old department and to his college, Trinity Hall. There were excellent prospects of a brilliant academic career before him but, just as with his brother, he felt the call to the Army.

He succeeded Sir Charles Ellis as scientific adviser to the Army Council. It has been said that the number of civilians who can understand the Army can be counted on the fingers of one hand. Wansbrough was certainly one of them. After some years of close contact with the Army Staff, he realized that he would serve them best by doing his utmost to ensure that the Army gained the weapons that they needed and he consequently moved over to the Ministry of Supply. During Wansbrough-Jones's

period of office there has been a notable growth of the scientific spirit in the Minister's establishments. Under his stimulus the research and development work carried out in the Ministry has proved exceptionally fruitful, and is probably better in spite of national economic conditions than anything like it in the world. His colleagues will miss him greatly in his retirement.

The U.S. National Radio Astronomy Observatory Prof. Otto Struve, For Mem. R.S.

PROF. OTTO STRUVE has been appointed the first director of the National Radio Astronomy Observatory, Green Bank, West Virginia. The Observatory is being constructed and will be operated by Associated Universities, Inc., under contract to the National Science Foundation. Prof. Struve is at present professor of astronomy in the University of California and has been director of the Lick Observatory since 1950. He assumed his duties on July 1. An astronomer of international reputation, he has published approximately a thousand papers concerned with the problems of stellar spectra and other aspects of astrophysics. Although his principal scientific interest has been his important research on the properties of variable stars, his interests have extended more generally over the whole field of astronomy.

The National Radio Astronomy Observatory has been designed to supplement facilities available to research scientists of the universities by making available large and precise radio telescopes not hitherto available to American astronomers. Among these new instruments are the 85-ft. Howard E. Tatel precision radio telescope recently put into operation, the 140-ft. radio telescope now under construction, and a variety of auxiliary devices for radio astronomy. The Observatory is operated by a small permanent staff in co-operation with an increasing number of visiting scientists from various parts of the world.

1964 Olympic Games Prof. Ryotaro Azuma

THAT the 1964 Olympic Games are to be held in Tokyo is largely due to the efforts of Ryotaro Azuma, formerly professor of pharmacology in the University of Tokyo, who was recently elected governor of Tokyo. Azuma, a distinguished member of the Japanese scientific community, has always encouraged the Olympic ideal of friendship and sportsmanship in international relations. He is a keen sportsman himself—he has rowed for the University of Tokyo, he also introduced the 'shell' to Japan from Britain, where he studied at University College, London, during 1922–24. Azuma is a member of the International Olympic Committee and in 1947 he was asked to head the Japan Athletic Federation. He played an important part in organizing the Asian Games which were held in Tokyo in 1958. Under his leadership sports for enjoyment, as opposed to sports as a form of regimentation, have had an immense success in Japan. Azuma sees a very close connexion between sport and Japan's post-war constitution renouncing militarism, but in his own words: "We must still educate the younger generation that it is not a disgrace to lose if you do your best."

Overseas Research Council

THE Overseas Research Council promised at the Commonwealth Trade and Economic Conference at Montreal last September has now been estab-

lished. In a statement in the House of Lords Lord Hailsham said that the Council, of which Dr R. S. Aitken will be chairman, will provide a central point to which Commonwealth Governments and research institutions can refer for advice and information, and it will advise generally on United Kingdom co-operation in scientific research overseas. There are no geographical restrictions in the Council's terms of reference, and matters concerning scientific development in Colonial territories, in Commonwealth countries and in countries outside the Commonwealth, can equally be referred to it. Moreover in promoting such development Lord Hailsham said the Council could look to possible collaboration between Great Britain and other Commonwealth countries, countries outside the Commonwealth, such as the United States, and international agencies, such as those of the United Nations and the charitable foundations. Asked whether the members would be paid, Lord Hailsham said he would require notice before replying in detail but he believed certain officers might be paid. There would be a certain amount of travelling and the members of the Council had been selected largely for their knowledge of overseas territories and connexions with science in them.

The other members of the Council are: Sir Joek Campbell, Sir Charles Dodds, Sir Harold Himsworth, Sir Joseph Hutchinson, Dr R. Lowthwaite, Prof J. McMichael, Sir Harry Melville, Mr E. D. W. Nye, Sir Arnold Plant, Sir William Slater, Dr H. G. Thornton and Sir Solly Zuckerman. The Council will advise the Privy Council Committee on Overseas Research, which consists of the Lord President of the Council and the Secretaries of State for Commonwealth Relations, the Colonies and Foreign Affairs. Its terms of reference comprise advice on the formulation of United Kingdom policy in respect (a) of scientific research undertaken in or for overseas territories within or without the Commonwealth, (b) of methods of making the results of research available in these territories, and (c) of assistance to the scientific services of these territories; on the co-ordination of the activities of United Kingdom Government organizations in the development of science in the civil sphere in overseas territories, and on co-operation within the Commonwealth, with other countries and with international agencies in promoting such development.

National Institute for Research in Nuclear Science

CONTRACTS for more than £430,000 have been placed by the National Institute for Research in Nuclear Science for the manufacture of the magnet coils required to energize the 7,000-ton electromagnet of the 7,000 MeV proton synchrotron. This machine, which has been named *Nimrod*, is being built for the Institute by the United Kingdom Atomic Energy Authority at the Rutherford High Energy Laboratory, Harwell. Contracts have been awarded to British Copper Refiners, Ltd., of Prescott, Lancs., for the supply of more than 300 tons of refined copper (from which the coils are to be made), in the form of cast billets, to James Booth and Co., Ltd., of Birmingham for extrusion of the cast copper into hollow rectangular bars, and to Metropolitan-Vickers Electrical Co., Ltd., of Manchester, for the manufacture of the finished coils from the extruded bars. The Institute has also awarded a substantial contract to Marston Excelsior, Ltd., of Wolverhampton, for the development and supply of the reinforced plastic vacuum chamber in which the protons are

accelerated. This chamber will be one of the largest plastic structures ever made.

Extension to the Chester Beatty Research Institute

On July 16, Sir Chester Beatty laid the foundation stone of an extension to the Chester Beatty Research Institute. The cost of the extension (£200,000) which will double the existing accommodation, is being defrayed from a trust fund deriving from the charitable public, and administered for the benefit of the Institute by the Board of Governors of the Royal Marsden Hospital. A contribution of £40,000 has also been made by the Wellcome Trust, in respect of which the extension will include a Wellcome Laboratory of Pharmacology and Experimental Chemotherapy. The Research Institute of the then Cancer Hospital established in 1909-10 and opened in 1911 by H.R.H. the Duke of Connaught was directed successively by the late Dr Alexander Ffrench, Dr Archibald Leith and Sir Ernest Kennaway. In 1938, Sir Chester Beatty (who was then president of the Hospital) bought equipped and presented the existing building, which thenceforth became the Chester Beatty Research Institute. The Institute is now part of the Institute of Cancer Research, Royal Cancer Hospital which in turn is a school of the University of London, and an institute of the British Postgraduate Medical Federation. The Institute obtains its main support from the Medical Research Council and the British Empire Cancer Campaign, and donations and legacies are received from the public. Generous help has also been given by the U.S. Public Health Service and other American sources such as the Jane Coffin Childs Memorial Fund for Medical Research and the Anna Fuller Fund of New Haven, and the Rosenstiel Foundation of New York City. The new building of which the architects are Messrs Lanchester and Lodge will be formally opened in 1960, when the Institute celebrates its jubilee year.

First Atomic Merchant Ship

The special illustrated supplement to the June 20 issue of *Atoms for Peace Digest* is devoted to a detailed description of the *NS Savannah*, the world's first atomic merchant ship which was launched by Mrs Eisenhower on July 21 at the New York Shipbuilding Company's Yard in Camden, N.J. The *Savannah*, a joint project of the U.S. Maritime Administration and the Atomic Energy Commission, has been built mainly to promote the peaceful uses of atomic energy and will not be commercially competitive. The vessel is named after the *SS Savannah*, the first steam ship to cross the Atlantic, which started her voyage from Savannah, Georgia, to Liverpool on May 22, 1819, and is a combination passenger-cargo vessel 595 ft long, with a beam of 78 ft. She can carry 9,500 tons of cargo and accommodate 60 passengers, and will be manned by a crew of about 100. Her speed is estimated at 20½ knots. The *Savannah's* reactor consists of a system of advanced design using pressurized water as a coolant and moderator and fuel elements with about 4 per cent uranium 235 enrichment. The active core, which is 66 in. high and 62 in. mean diameter, contains the fissile material—7,050 kgm. of uranium oxide in 32 fuel rods, clad in stainless steel. There is a surrounding pressure vessel, primary shield containing vessel and secondary shield of 2,500 tons total gross weight. The reactor will supply 74 MW of heat, providing sufficient power for the vessel to

operate for about three years and to sail 300,000 nautical miles without refuelling. It is being built by Babcock and Wilcox at Lynchburg in Virginia at a cost of about ten million dollars. The total cost of the ship will be about 40 million dollars.

Labour Statistics

The Interdepartmental Committee on Social and Economic Research has recently issued a revised version of its guide to the statistics collected by the Ministry of Labour and National Service (Guides to Official Sources No. 1, Labour Statistics H.M. Stationery Office, London, 1959 5s). The opportunity has been taken to bring the material in the original edition up to date and to include a historical section, showing the development of labour statistics in Britain since the end of the nineteenth century. The topics covered include statistics of employment, unemployment, placements and vacancies, miscellaneous man power statistics, wage rates, earnings and actual hours worked, strikes and industrial disputes, industrial accidents, the cost of living, retail prices and family budgets. Each of the sections is followed by a comprehensive bibliography of official sources.

World Distribution of Atmospheric Water Vapour Pressure

The Meteorological Office is much more than a forecasting institution. It is the public repository of knowledge regarding the weather, and among its many functions is the provision of data on a world wide scale for a variety of users. "World Distribution of Atmospheric Water Vapour Pressure", by G. A. Tunnell (Geophysical Memoirs, No. 100 Pp. 1+61 M.O. 584s London H.M. Stationery Office 1958 10s net) is an atlas of the distribution over the whole world of the daily mean of atmospheric water vapour pressure for the months January, April, July and October, based on records from 3,500 stations. There follows a brief survey of the world distribution of diurnal variation of vapour pressure in different climates. Information concerning atmospheric humidity in all parts of the world is thus available in compact form for industrialists and others who may require it. Mapping is done by means of isopleths. In common with all such maps the distributions so revealed have many interesting features not always readily explained. For example taking account of the characteristics of Russia is the breadth of the patch of higher vapour pressure shown both in January and July near Kazan? The midsummer variations in the mean vapour pressure over South Australia are also noteworthy. An agreeable publication, clearly printed, informative and stimulating in respect of the distribution shown, the policy of the Meteorological Office in producing such memoirs will be widely welcomed.

The Customs and Religion of the Ch'iang

The Ch'iang inhabit a mountainous region in Szechwan in western China and grow maize as the main crop. They speak a Burmese-Tibetan language and are said to have formerly lived in north-eastern China. For some time past, however, they have been losing their own culture and adopting that of the Chinese with whom they were earlier in conflict. We have such meagre information on the non-Chinese population of China that almost any report is of value. Mr D. C. Graham (Smithsonian Miscellaneous Collections, 135 No. 1: The Customs and Religion of the Ch'iang Pp. vii+114+10 plates

polluting substances, of the rate at which the water of a stream will absorb oxygen from the air, and of the effects of aquatic plants and animals on the oxygen balance.

In the field, the only satisfactory method at present available for determining the rate of transfer of oxygen from the air is to reduce the oxygen tension in the water (by adding sulphite and a catalyst), following then the rise in level of oxygen below this point. This method has been used successfully for small streams, but presents obvious difficulties in a large river. Many of the factors involved, however—for example, turbulence, and the presence of substances such as detergents in solution which reduce the rate of oxygen transfer—are being investigated by running water through sloping troughs, 100 ft long, in the grounds of the Laboratory. One question which is often important in Britain—namely, the change in oxygen-level in water when it flows over weirs—has been substantially settled by work in the field and in pilot-scale plant, given the height from which the water falls, and the temperature, the extent to which the oxygen deficit is reduced can be predicted within narrow limits.

In rivers, oxidation and reduction of compounds of nitrogen often play an important part. Oxidation of ammonia and reduction of nitrate, and particularly the effect of concentration of dissolved oxygen on these processes, are being studied in an artificial river in which water passes through a series of tanks fitted with stirrers. In streams containing large numbers of algae or much rooted vegetation, the effects of the bacterial oxidation of polluting matter on oxygen tension may be greatly outweighed by photosynthetic production of oxygen and its consumption by plant respiration. These effects are being studied in a stream near the Laboratory, where continuous recorders are installed. In June and September 1958 there was a net release of 3.8 gm oxygen/m²/day. Estimates are being made of the productivity of different reaches in this stream using cropping techniques assisted by aerial photographs taken by a camera suspended from a meteorological balloon. Consumption of oxygen by respiration of invertebrates is also significant, and this is being determined

in respirometers in which the change in oxygen tension is again recorded continuously.

The Laboratory has a small but well-equipped Microbiological Section in which three main lines of work are in progress. The first is a detailed study of the changes which occur when aqueous solutions of organic compounds (which may be radioactively labelled) are passed over an active microbial film of the type which occurs in percolating filters and on which the purification of sewage by this process depends. The film is built up on the inside of a 'Perspex' cylinder, the long axis of which is inclined and about which it is rotated, the atmosphere in contact with the film is circulated and there are arrangements for withdrawing samples from it and for adding oxygen to replace that used in oxidation. Most of the organic substances present in such materials as sewage are very rapidly oxidized, one object of the work is to identify those which are not.

It is very important, in treating polluting liquids by biological processes, to be able, in the last stage of the process, to remove by sedimentation organic sludge from the liquid—the latter representing, of course, the final effluent from the plant. A large part of the organic matter to be removed consists of bacteria and the quality of the final effluent depends very largely on whether they will or will not agglutinate in the final sedimentation tank. In spite of a good deal of work on the subject, not much is known of the factors which affect flocculation in a treatment plant, these are therefore being studied by the section, using cultures isolated from sewage and sewage effluents.

The third line of work which is being pursued in collaboration with the National Coal Board is on the bacterial treatment of waste waters from coke ovens, in which the chief constituents to be removed are phenols, thiocyanate and ammonia. Rates of assimilation and oxidation of these substances are being studied in continuous-culture apparatus after preliminary trials by the usual Warburg technique.

The Microbiological Section has recently been strengthened by the transfer to it of some of the staff formerly working at the National Chemical Laboratory.

WATER SUPPLY AND DEMAND IN GREAT BRITAIN

THE problem of water supply and demand, the need for improved hydrological knowledge and the necessity for a continuing study of the changing situation in Britain, have received editorial notice in earlier issues of *Nature* (172, 823, 1953, and 176, 1133, 1955). The decision to suspend the Inland Water Survey and disband the Central Advisory Water Committee during the economy measures of 1952 was, from a purely scientific point of view, strongly criticized. Happily this decision was reversed in 1955 when the Central Advisory Water Committee was reconstituted; and in the same year the Inland Water Survey also recommenced its labours and has since published a great deal of information covering the post-war years.

One of the first actions taken by the Central Advisory Water Committee in 1955 was to appoint two subcommittees to investigate information on

water resources and the growing demand for water. Both these subcommittees have recently reported to the Central Committee and the information collected so far has now been published*.

Of the two documents, that of the Subcommittee on Information on Water Resources is perhaps the least controversial and may be considered first. This Subcommittee was appointed with the following terms of reference: (i) to review the current activities which contribute to our knowledge of the nation's water resources, (ii) to define the additional work needed to make a balanced survey of the quantity and quality of surface and underground water available for domestic, industrial and agricultural use, (iii) to advise on ways of collecting and interpreting

* Central Advisory Water Committee. Subcommittee on The Growing Demand for Water—First Report. Pp iv+28. 1s 3d net. Report of the Subcommittee on Information on Water Resources. Pp ii+20. 1s 3d net. (London: H.M. Stationery Office, 1959.)

the necessary information, correlating it with information from other sources and publishing it.

The review of current activities deals with the work of the Meteorological Office (Air Ministry), the Surface Water Survey Centre (Ministry of Housing and Local Government) and the Geological Survey in providing information on rainfall, evaporation, surface water and ground water. It is recommended that the Geological Survey should resume publication of information on ground water; and that all data on rainfall, surface water and ground water should be presented on a common basis of river basin areas. The planned future contents of "British Rainfall" and the "Surface Water Year Book" are endorsed, and the proposed arrangements for the collection and interpretation of hydrological information are considered adequate to meet the known need, although certain extensions of existing activities are recommended. The more frequent inspection of rainfall stations, the more accurate recording of snowfall, additional recording of ground water, the publication of more data on the quality of certain water supplies and the more rapid completion of the network of river gauging stations are all considered desirable.

Although the arrangements for the collection and interpretation of information are considered "broadly [to] meet the known need", the report recognizes the necessity for additional investigation into hydrological relationships and for further inquiry into the use of hydrological information. It is therefore also recommended that work at present being done on hydrological research should be reviewed to determine how such work should be co-ordinated and what extensions or modifications may be desirable. The lack of any central hydrological information and research organization comparable to the Geological Survey or Meteorological Office has already been noted elsewhere*. The publication of this report on information on water resources really arises from the lack of such a body, since data on the hydrological cycle in Great Britain are scattered among such a variety of authorities each of these authorities is only interested in one aspect of the complete cycle. The recommendation that all hydrological results should be presented on a common basis of hydrometric areas is, however, a significant move towards a closer integration of the available data.

The report of the Subcommittee on the Growing Demand for Water is a longer document, although despite three years deliberation and investigation it has appeared as a first and not as a final report for the subcommittee found its terms of reference more exacting than anticipated. These were "To consider the extent to which the demand for water for domestic, industrial, agricultural and other purposes is increasing and is likely to increase, to consider the problems involved in meeting these demands, including, in broad terms, the cost, to consider whether there are any substantial economies in the use or cost of water which could be made without reduction in standards of hygiene or in industrial or agricultural efficiency, and to make recommendations".

The main questions which remain unanswered concern the demand for water for agricultural irrigation and economies in the use of water in industry. The chief difficulty experienced in the investigation was related to the dual character of water supply in Great Britain which is provided by both public water undertakers and obtained privately, and the three fold nature of the demand, which is domestic,

industrial and agricultural. Accurate statistical information on consumption is readily available only from the public water undertakers, but even here the amounts in the various categories of use are not fully known. The subcommittee instituted its own official inquiry among all public water undertakers, the nationalized industries (electricity, coal, gas and transport), and six major industries (brewing, chemicals, iron and steel, leather, paper and textiles) where supplies are largely obtained privately. A large and valuable collection of new statistical data has therefore been accumulated and this together with the unpublished water surveys carried out between 1945 and 1958 by engineers of the Ministry of Housing and Local Government, form the basis of the recommendations accompanying the report.

In the industrial and domestic categories there is clear evidence of a steady nationwide increase in water consumption of between 2 and 3 per cent per annum during the past quarter of a century. This is expected to continue into the future to produce by 1985 something of the order of a 25 per cent increase over the known 1955 consumption figures. As new works under construction or proposed, are scheduled to yield an additional 800 million gallons of water a day by 1985, and this is approximately 40 per cent of the quantity distributed by water undertakers in 1955, the subcommittee concludes that in England and Wales as a whole the rising consumption need not give rise to immediate anxiety. This general statement is, however, immediately qualified with the proviso that "this is not to say that temporary or local shortages will not occur from time to time, quite apart from more general shortages in very dry years (when maximum domestic demand and minimum supply tend to coincide), or that industries seeking new sites will find abundant supplies in any place they care to choose". The estimates also assume that in any particular area the trend of consumption will follow approximately its present course, so that any significant deviation not foreseen at present could upset the balance.

Beyond 1985 the Subcommittee was "unable to obtain any reliable data" and decided not to attempt numerical estimates. The subcommittee is therefore not prepared to commit itself other than to express the opinion that there need be no shortage of water in any part of England and Wales provided that development schemes are prepared well in advance of demand, that the necessary statutory powers and other authorizations are granted, that capital investment is permitted on the requisite scale and the location of industries which require large quantities of water is regulated with the water supply situation in mind.

While acknowledging the great amount of work which has clearly gone into the inquiry, and the valuable new information which the report presents it must be admitted that there are a number of debatable points. In the first instance the Subcommittee has based its arguments upon figures of past consumption which are not necessarily indicative of past demand, and could certainly be misleading so far as future demand is concerned. This is most evident in the agricultural usage of water. Quite apart from the fact that the consumption rises rapidly as soon as piped water becomes available to a farm there is the whole unresolved and rapidly growing problem of agricultural irrigation. The work done at Rothamsted Experimental Station shows, for agriculture, a deficiency of rain in more than five years out

of ten south of a line drawn from the Humber to the Severn, and a deficiency in nine years out of ten in Essex, Suffolk and Kent. The magnitude of the deficiency varies from place to place and from year to year with theoretical values ranging from 1 in to 12 in of rain. The irrigation that would be needed to meet this deficiency would depend on soil moisture retention conditions and plant rooting characteristics, and might amount to a rainfall equivalent in some places of up to 6 in. All the water would be used in transpiration or evaporation, or absorbed by percolation, and would not be capable of re-use. Calculations indicate that a possible demand of some 8,000 million gallons a day might exist in very dry years south of the Humber-Severn line. This amount is more than four times that supplied in 1955 by all the public water undertakers in England and Wales, and it indicates the potential demand which exists and which the subcommittee has ignored in its first report. It is proposed, however, to give further attention to this problem, but the approach appears to be negative as the possibility is mentioned of some form of control over the abstraction of surface water analogous to the existing protection of underground water. If the national policy is to secure the maximum food output from the agricultural industry, farmers in south-east England should be actively encouraged rather than discouraged to irrigate, in which case a more positive approach to the water supply problem and a completely different attitude of mind are then needed.

The reluctance of the Subcommittee to look further ahead than 1965 is also unfortunate, although the difficulties can be fully appreciated. The Ministry of Health Committee on Causes of Increase in Consumption of Water (1949) was prepared to look ahead for a period of some 22 years up to 1970. Past experience clearly shows that water-supply schemes take many years to come into operation and that reliability in supply largely depends on one generation

planning for the next. The blue prints to meet the requirements of the late 1970's should be in process of formulation in the early 1960's if the real needs of agriculture and industry are to be satisfied.

Possible economies in the use of water in industry have also been deferred for future consideration, although the report does direct attention to waste prevention and leak detection, the recommendation is made that all water undertakers should operate an adequate waste prevention service.

There is clearly much food for thought in both of these reports. The rising standard of living of an increasing population in Great Britain has, in the present century, brought water to the forefront as a vital and essential commodity in the life of the nation. Although the natural resources of the country in terms of rainfall are theoretically adequate, Nature has a habit of distributing the precipitation unevenly in both time and place. This situation can only be remedied by care in use and by the conservation of supplies in periods and areas of plenty. Lowland Britain, where consumption is greatest, is also the area where the population is densest, the rainfall least and where local water resources are nearing full utilization. Highland Britain, on the other hand, has a low population, the highest rainfall and a relative over-abundance of water of which only a small proportion has yet been developed. To what extent would the gains from scientific irrigation in agriculture and a guaranteed domestic and industrial supply in lowland Britain outweigh the cost of storage and movement of water from highland Britain? And how far might the conversion of saline water in Great Britain assist in the solution of the water-supply problem? It seems that these are the major questions on water supply that must be answered if the problem is to be approached with vision and concern for the needs of the next generation.

W G V BALCHEN

TEN YEARS OF ERGONOMICS

ERGONOMICS is mainly about 'human factors' in the design and operation of machines, and about the physical environments in which men use their machines. Moreover, it is multidisciplinary. Nobody who attended the tenth anniversary meeting of the Ergonomics Research Society, held in Oxford during April 6-9, could have much doubt on either of these points.

The Postmaster-General, Mr Ernest Marples, apparently less damaged than he should have been by a 400-mile cycling trip in France on what seems to have been a highly unergonomic saddle, opened the conference. He had hard things to say about the word 'ergonomics'. Unlike his chairman, the Master of Balliol, who thought it was splendid because it told us exactly what it meant, Mr Marples thought it was frightful because it did not. However, for ergonomics itself he had nothing but praise. The General Post Office had used it for nine years, and it was his intention to build it into the General Post Office structure so firmly that it could be got out again only by 'positive action'. He pledged his support for everyone, everywhere, including housewives in their kitchens, who moved ergonomically with the times.

Following up a point Mr Marples made about the frequency with which "backroom boys" are either not understood or misunderstood, Sir Frederic Bartlett, formerly—for twenty-one years—professor of experimental psychology in the University of Cambridge, inquired how common difficulties of communication might be overcome, so that proved advances (for example, in the design of altimeters) might be adopted with reasonable rapidity. Mr Marples advised him to get into touch with the top people concerned, or with the Parliamentary and Scientific Committee, or with Mr Marples himself. Sir Frederic looked rather less happy about this than did Mr Marples.

There was more to come from the General Post Office. A paper by Dr R. Conrad, of the Medical Research Council Applied Psychology Unit at Cambridge, dealt with mass communication systems, and a couple by Dr W. F. Floyd, of the Middlesex Hospital Medical School, and Miss June I. Jones, of the General Post Office, covered some problems of lighting, posture, thermal conditions and energy cost of work in telephone exchanges and Post Office factories. These gave a clear indication of what ergonomics amounted to in practice. Dr Conrad told us that to obtain a weather report he had to

dial 96618312274 As this kind of thing was spreading, it had been decided that some General Post Office based studies of immediate memory might pay off. One proved useful in comparing conventional dials with push button arrangements, and another helped in working out the kinds of codes that might be suitable for trunk numbers or postal addresses. Dr Conrad's concern with efficiency was matched by the interest Dr Floyd and Miss Jones displayed in comfort—but Dr Conrad led the other two in his theorizing.

These three early speakers did, in fact, throw up, without explicit formulation of them, problems which were to rear their heads frequently during the conference. What had Dr Conrad in common with Dr Floyd and Miss Jones apart from the General Post Office roof over his head? All he said—and, indeed, all his director, Mr D E Broadbent, said in a later paper—could easily have been labelled 'applied experimental psychology' and all that Dr Floyd and Miss Jones said is usually called 'applied physiology'. Where does ergonomics come in? Does it seek to be regarded as a new science? If so, on what is its claim to independent scientific status founded? Has it any distinctive concepts or methods? Is it, perhaps, mainly a convenient gathering place for people belonging to certain technological wings of certain human sciences, and their agents and users in industry?

As if these puzzles were not enough for us, more were produced by delegates who came from the work study sector of industry. One, Mr A. Graham, of Imperial Chemical Industries, created a small squall after some plain speaking by Mr H Murrell, the founder of the Society. Mr Graham asked scornfully why industry should be expected to prefer the 'toothpick' of ergonomics to the 'pneumatic drill' of work study; and having delivered himself of this broadside he switched on his own pneumatic drill and demanded that work study practitioners should be offered both help and respect. He gave the impression that what was really worrying him was the intrusion of still more outside 'experts'. At this point Mr A T Welford, the editor of *Ergonomics*, deftly applied the oil-can. However, it seems that later in the day at the Society's annual general meeting, Dr E A Müller, of Dortmund, set the cat among the pigeons again by suggesting that meetings between research workers and people from industry were a doubtful blessing and should be only occasional.

It may appear, from all this, that the conference was a bit of a mix up. So indeed it was. But it was probably a healthy one. The physiologists and psychologists, though going their separate and unintegrated ways somehow did battle together with the delegates from industry. True, each side paid tribute to the other and to some extent shared a common cause, but the sparks flew. Perhaps even more would have flown if the meeting had been held in less academic surroundings. The industrial contingent were inclined to be a little shy.

The nature and quality of the papers were as mixed as the audience. Though the title given to the conference as a whole was "Symposium on Ergonomics, its Place in Industry (Past Progress and Future Trends)", only a few of the contributions played up to it. These came mostly at the beginning from Mr Welford and from Dr O G Edholm, of the Medical Research Council Division of Human Physiology, and at the end, from Mr Broadbent

from Dr E H Christensen, of Stockholm, and from Mr L V Green, of Dunlop. The rest were chiefly individual papers. Among them were a description of work done on design problems in E.M.I. Electronics, given by Mr B Shackel, and an account of activities in the Clothing and Stores Experimental Establishment of the Ministry of Supply, given by Dr E T Rembourn and Mr H C Stockbridge. Mr O E Brooks, of Personnel Administration Ltd had some sensible things to say about improving the quality and output of inspectors by systematic re-training, but the information he produced in support of his findings did not carry conviction to everyone nor did it seem to have much to do with ergonomics.

Despite this bitterness a good deal of stimulation was provided. Mr Murrell's own contribution, mentioned earlier, was not what he meant it to be because a midnight argument had made him decide to scrap the original. In the event it turned out to be a usefully provocative statement about what 'ergonomists' could do for industry that methods engineers could not. They could bring to their task knowledge of the capacities and limitations of human beings not to be found in the publications of Shaw Mundel or Barnes. More than that, they could bring to it skill in the conduct of experiments with chips. A methods engineer plus a psychologist or half a physiologist would produce a different outlook on industrial problems. This was the straight from the shoulder stuff that caused offence to Mr Graham. To some others it caused perplexity, for it left unclear the distinguishing characteristics of the ergonomist, the psychologist, and the physiologist. A few among the faithful were dismayed, because although they talk about ergonomics, they do not like the label 'ergonomist'.

In a comment on a paper by Mrs E.M.I. Electronics colleague, Mr J R Arrowsmith, Mr Shackel had a good point to make about the function of machines in relieving the anxieties of skilled men who build up great tension as the possibility of spoiling several days work mounts. So had Mr Broadbent, in the same discussion, when he remarked that in our hopes for the elimination of human error, through the taping of instructions, we must not neglect the risk that the typist typing the tape may err. Earlier, Mr W D Seymour had asked, rather drily, how many of the matters discussed at the conference had not been investigated by industrial psychologists twenty-five years ago.

So some extent, Mr Seymour's question was answered in a later contribution by the present writer, who made comparisons between the first ten years of ergonomics and the first ten years of occupational psychology. The chief differences seemed to be in the wider scope of occupational psychology. It encompassed problems of 'fitting the man to the job' as well as problems of 'fitting the job to the man' and it studied attitudes as well as skills. Dangers arising from narrowing the range of the industrial problems taken into account were illustrated by Dr J J O'Dwyer, of Unilever, who spoke about informal groups in industry, and the importance of perceiving and using them, and by Mr R M McKenzie, of the Social Sciences Research Centre at Edinburgh, who showed—entertainingly—how social factors could keep a worker's output well below his potential.

What of the next ten years? If the members of council of the Ergonomics Research Society have not

yet drawn their conclusions from their experience of the first decade, they might think about covering the following points in their discussions. First, there is perhaps little to be gained by making ergonomics out to be a science. It is a kind of conglomeration—not even a compound—of technologies, and it might be a good thing for it to continue like that. Possibly the Society should be content to serve the same kind of admirable purpose as the British Nuclear Energy Conference, which pulls in people from a number of fields without seeking to detach any of them from their primary allegiances.

Secondly, there is undoubtedly a lot to be said for the running of courses of lectures and practical work for people, from a variety of levels and types of work, who are faced with 'ergonomic' problems. The short Bristol course outlined by Dr S. Griew seems sound in its aim, which is to put across useful facts about the structure and functioning of the human body, to show where more can be found, to explain and demonstrate experimental approaches to problems of equipment design, and to suggest that 'fitting the man to the job' and 'fitting the job to the man' should often be tackled together.

Thirdly, however, there is perhaps room for far more stress on the need to look into, learn about and teach people about, individual differences, especially on the psychological side. Mr Stockbridge's *cri de coeur* ("Individual differences are a frantic nuisance

If only we had a standard man") brought out this need. Some workers in this field are clearly tempted, not merely to wish that there were such a creature, but to assume that there is. Mr Welford seemed almost to succumb when he spoke hopefully

about the discovery of 'standard times' for mental operations, and more particularly when he hinted that one had been run to earth in Antwerp, where telephonists had consistently coped with five bits of information a second. Dr Conrad, commenting on this later, unwittingly challenged Mr Welford by revealing that Norwich girls could manage seven without any trouble.

Discrepancies like this cannot really be met by jocular references to the possible existence of 'national' differences. They must be taken seriously. Could they arise from differences in the kinds of people being guided into and selected for the work in different places or at different times? Or from differences in training arrangements? Or from differences in methods of work adopted? Or from differences in equipment? Or from differences in working conditions of several kinds, including the physical, the social and the financial? All these and other possibilities should be explored.

But here we encounter two important snags. Can exploration of the kind needed be carried out satisfactorily on the tiny, homogeneous, doubtfully relevant groups often used by researchers in the vast field of ergonomics? And can it be tackled adequately by researchers whose devotion to 'precise' measurement is such that they are inclined either to forget or to ignore deliberately the existence of possibly influential factors which lie beyond the reach of their cherished clocks and counters? The state of play in ergonomics ten years from now may depend a good deal on the answers the Council of the Ergonomics Research Society gives to these two questions.

ALEC RODGER

DISTRIBUTION OF SCIENTIFIC PUBLICATIONS IN UNDER-DEVELOPED COUNTRIES

THE Scientific Publications Council, which has recently been formed, includes the editors of twenty scientific journals and the authors of a number of scientific books. It was started by a group of scientists who felt the need for an independent body that could uphold the interests of scientific authors and editors in working for higher standards in the publication and distribution of scientific books and journals. The Council is intended to provide a means for scientific writers and editors to maintain contact with each other and exchange views with others concerned in scientific publication in Great Britain and overseas. It provides a forum for the discussion of matters of mutual interest and a means of obtaining advice in technical and legal matters relating to publication. It is intended that the Council should work to establish good relations between scientific writers and publishers, and co-operate in setting up agreed standards that are acceptable to scientists and publishers alike. The officers of the Council are appointed for a term of three years. Prof G. W. Harris is chairman of the Council and Dr D. Richter, Neuropsychiatric Research Unit, Whitchurch Hospital, Cardiff, is honorary secretary.

At a meeting of the Scientific Publications Council held on April 10 at the Ciba Foundation, London, Mr John Hampden (British Council) opened a discus-

sion on the distributions of scientific publications in the under-developed countries. He described the difficulties experienced in many countries in obtaining British books and periodicals. In Asia and Africa there is rapidly growing up a new literate class which wants to read, but in many places no British publications are available. In some places it is hard to persuade any bookseller to obtain them, as the necessary currency authorization is difficult, expensive or impossible to get, and the profit is small. On the other hand, there is an abundant supply of State-subsidized cheap editions from the U.S.S.R., China and also the United States. The English language is now an international possession. The students wanting books are the scientists, professional men and leaders of the future, and it is bound to affect their future reading and outlook if the only books they can get are not British.

Currency shortages are mainly responsible for the situation in some countries, including Poland, Turkey, Israel, Pakistan and Indonesia. How can people in these countries buy British books and periodicals if they have no sterling to pay for them? Other difficulties in some countries include the shortage of bookshops stocking British books and the lack of libraries where British publications can be seen. The difficulty is especially acute for scientific

and medical books, which are needed by specialists in the Western countries where libraries are largely taken for granted it is hard to realize that in many places a student may have access to very few books which he does not buy for himself, and the cost of one book may be more than a whole month's salary. In many places it is even impossible to get up to date lists of British books and their very existence is in danger of being forgotten.

The Americans have got round the currency restrictions by export schemes in which the publishers are paid directly by the Government, so that the importing countries need no dollars to pay for books. This was originally a British idea (invented by Sir Stanley Unwin) which the Americans have adopted. British text-books have been deservedly popular in Asia and Africa for many years but there is a serious danger that they will soon be swept out of some important markets. Mr Hampden said we are not afraid of fair competition, but British publications cannot compete with exports heavily subsidized by foreign governments. It is a matter of considerable concern to those familiar with the situation that the journals of many British learned societies are not organized as the book publishers are to increase their sales overseas, and it looks as though these journals are getting seriously left behind. It is essential that more information about British scientific books and journals should be made available overseas. The British Council is doing all it can to spread this information abroad.

Dr P. Rosbaud said that the cultural importance of scientific books has only recently been appreciated in Great Britain. The export of scientific and technical books is not only of benefit to the book trade but also has a far reaching influence on education and commerce in general, so that it pays high political dividends as well. One of the main factors influencing distribution abroad is the cost. Why are scientific books so expensive in comparison with other books of similar size and where do all the profits go? For a typical book of 250 pages selling at 30s. the publisher may hope to sell 3,000 copies and break even at 2,400—if he sold less than 2,400 he loses. If more, he gains. For such a book the printer's estimate may be 8s. a copy, including the cost of correction, blocks and paper. There is little to be saved by using paper of cheaper quality. The publisher's overheads might be 2s. 6d., advertising 2s. and the author's royalty at 12½ per cent would be 3s. 9d. Allowing 33 per cent, or

10s. for the bookseller, that left the publisher with only 3s. 9d. as his profit. In any sales in the United States the publisher may need the services of an American distributor who would ask 50–60 per cent of the selling price and the British publisher would also have to pay the additional cost of freight. There is the alternative of selling a small number of books at a high price or a larger number at a lower price, as with text-books. Text books have got to be cheap and this might be achieved by bringing out a large first issue of 5,000 copies without profit and then making a profit on subsequent issues. It was not right that the author should ever be asked to waive his royalty, which was little enough anyway. No reputable publisher would ever ask that. In the publication of scientific journals great patience might be needed before a profit could be made. Sir Richard Gregory had told Dr P. Rosbaud that *Nature* took more than twenty years before the circulation was sufficient for it to make its first profit. Publishing a journal is like cultivating a garden in which one must wait a long time for the harvest. As the circulation increases and the journal gradually becomes more profitable, the publisher can pass some of this on to the consumer by reducing the price or increasing the size. Scientific journals could be made considerably cheaper by including advertising space. Otherwise the only way of reducing the cost is to increase the circulation. Where publishing is a government monopoly, as in the U.S.S.R., books and journals can be produced at a very low cost but there are objections to this practice. Such publications may have plenty of room for the Lysenkos, but not for the Yavilovs and Pasternaks and the results are tragic. There is an urgent need for the British Government to develop an effective export scheme in answer to the floods of cheap State-subsidized publications from other countries.

The chairman Prof G. W. Harris, asked how scientists in Britain could best help in getting scientific books and journals distributed in the countries that need them. Mr Hampden thought that the Scientific Publications Council might help in bringing the problem to the notice of the learned societies. Dr F. N. L. Poynter described the work of the Wellcome Historical Medical Library in collecting scientific books and medical journals and distributing them in under developed countries abroad. He thought it would be helpful if the existence of a voluntary distributing centre of this kind were made more widely known.

MAPPING VEGETATION

AN international symposium on mapping vegetation was held during March 23–26 in Stolzenau/Weser, in the Federal Republic of Germany. This gathering of 112 scientists from sixteen countries, including Japan and the United States of America, was organized by the head of the Bundesanstalt für Vegetationskartierung Prof R. Tixen (Stolzenau), on behalf of the International Association for Plant Geography and Ecology.

The rapid progress of phytosociology (phytoecology) in this century, especially during the past three decades, has made feasible the scientific mapping of vegetation based upon well defined plant

communities. In view of recent advancements in this field, an international meeting to facilitate exchange of views, personal contacts and assessment of new future developments was very timely.

Mapping of vegetation at the Bundesanstalt für Vegetationskartierung (formerly Zentralstelle für Vegetationskartierung des Reiches) began in 1931 for the Nature Conservancy Service in Hanover. Then, as now the mapping of vegetation was preceded by extensive field work on existing plant communities in the respective area by the methods of the Zurich-Montpellier school of phytosociology. In addition to fundamental research on plant communities their

ecology and distribution, a large variety of applied research programmes have been completed which involved mapping actual and potential vegetation for various practical aims in agriculture, forestry, water supply, transport and nature conservancy. At present, a large programme of vegetation mapping has been undertaken for the West Germany railways, in which the vegetation along about 30,000 km of its railway network will be mapped to provide a sound basis for certain practical measures. For some time the Institute has been working on a complex research problem concerning the relationship of a particular plant community to the soil profile, and members of the symposium were much impressed by the exhibition of about 300 large, well-prepared soil profile mounts from north-west Germany. In solving many complex problems on vegetation for Germany, this independent research institute has become indispensable to other neighbouring countries in Europe, which face similar problems of a fundamental or applied nature. It is hoped that recent progress will be maintained and its sound future development preserved.

The papers presented at the conference may be subdivided into three major groups: (a) methods, (b) recent advances, and (c) applications.

(a) *Methods* The importance of fundamental principles, methods and aims is of much concern in any mapping of vegetation. In his introduction, Prof M Schwickerath (Aachen) referred to the significance of 'association diagrams' in mapping, by illustrating this with examples of the *Viola calaminariae* and *Sphagnum* associations. Prof A. W. Kuchler (Kansas) explained the compilation of a small-scale vegetation map of the United States and the various problems involved. Prof A. Scamoni (Ebenswalde) presented the new vegetation map of the East German Republic on a scale of 1:1,000,000 and indicated the principles applied in this work. Prof I. Horvat (Zagreb) referred to the basic considerations in applying higher units of vegetation while outlining the main features of vegetation in Yugoslavia. Prof A. Nierfalsche (Brussels) reviewed the aims and methods used in mapping the vegetation of Belgium, and those for recording marine biocenoses of the sea bottom off the coasts of France were outlined by Dr R. Molnier (Marseilles). On this topic Dr Molnier gave a lecture illustrated by excellent colour slides of underwater scenes taken on various trips in the Mediterranean. Prof H. Gaussen (Toulouse) explained the choice of colours in cartography, illustrated by his excellent bioclimatic maps of Africa and South America. The following five papers from the Bundesanstalt für Vegetationskartierung dealt with the main principles, methods and techniques adopted there: Dr W. Trautmann discussed his field experiences, and Dr W. Lohmeyer assessed the value of aerophotography. Prof R. Tüxen stressed the importance of mapping potential vegetation, which is more advantageous in forestry than the actual vegetation. Dr K. Walter spoke on introductory courses in phytosociology held in Stolzenau, and Dr A. Wenzel explained techniques in cartography employed there.

(b) *Recent advances* The advances made in recent years in phytosociology in various countries and the value of vegetation maps in related fields of science constituted the second topic of the symposium. Dr A. E. Apinis (Nottingham) stressed the relationships of soil micro organisms to higher plants and the value of vegetation maps for the fundamental research in

soil microbiology. Prof F. Major (Davis, California) outlined the basic approach to vegetation necessary for their mapping on a scale of 2 in. to 1 mile, while Mr A. Miyawaki (Yokohama) dealt with the occurrence in Japan of snow-patch communities similar to those of the European mountains. Mr S. Bertovic (Zagreb) described vegetation mapping in Croatia and in other parts of Yugoslavia, while Dr A. O. Horvat (Pécs, Hungary) presented a detailed map of forest phytocenoses of the Mecsek Mountains in southern Hungary, and Dr R. Nollhäusel (Brno) spoke on mapping natural vegetation in Moravia. Mr I. S. Zonneveld (Sleeuwijk, Holland) explained the mapping of both alluvial soils and vegetation in the tidal fresh-water area of the Rhine delta, combining the direct field method with that of aerial photography. Mr D. Kraft (Wageningen) is using physiognomic characteristics in recording the unstable dune vegetation near Harlem. Dr J. Tüxen (Stolzenau) spoke of the application of vegetation maps in solving problems in the historical investigation of rural landscape, while Prof J. Schmitzhusen (Karlsruhe) emphasized the significance of vegetation maps of various scales in phytogeography and other related sciences.

(c) *Applications* The variety of purposes to which the mapping of vegetation may be applied was revealed by the following papers, which were illustrated by a number of excellent large-scale maps. Prof A. Matuszkiewicz (Warsaw) spoke of developments in phytosociological mapping in Poland and its present applications. The possibilities of ecological and phytosociological mapping for applied purposes was discussed by Dr G. Long (Montpellier). Prof P. Fukarek (Sarajevo) outlined the application of vegetation maps in the forestry work of Bosnia and Herzegovina, and Prof M. Wraber (Ljubljana) explained the use of the general map on a scale of 1:100,000 of potential natural vegetation of north-west Yugoslavia as a basis for re-afforestation work on the degraded Karst and Flysch areas. The paper of Mr K. Mraz and Mr V. Samek (Prague) on certain problems on the cartography of vegetation and its applications in forestry was read by Prof R. Tüxen.

The mapping of vegetation is regarded as the best approach to solving problems of water relations in various plant communities. On this aspect Prof H. Wagner (Vienna) reviewed the mapping of vegetation for certain purposes in connexion with hydroelectric works in Austria, while Dr K. Meisel (Stolzenau) spoke on its importance for the assessment of damage to vegetation due to water. Dr P. Seibert (Munich) showed the application of phytosociological mapping of 'Pupplinger Au' near Munich to the water economy service there, and an assessment of damage due to salt water to meadows of the Werra Valley was given and its prevention planned on the basis of a vegetation map described by Dr B. Speidel (Bad Hersfeld). According to Mr Th. A. de Boer (Wageningen) mapping of various grasslands in Holland has been combined with soil mapping to provide an efficient agricultural advisory service in certain areas. Prof L. Steubing (Giessen) found the regular occurrence of certain grassland communities in areas where wind-break hedges are common. The importance and practice of mapping Alpine grasslands in Oberengadin was demonstrated by Dr F. Marschall (Zürich). The two last papers dealt with certain aspects of nature conservancy. Dr E. Preisig (Hanover) reviewed mapping of vegetation in relation to problems of

nature conservancy and landscape, and Mr P Tideman (Doorwerth, Holland) found direct mapping combined with aerial photography very useful in the management of the various protected areas in Holland.

Two decisions of general interest may be briefly mentioned. (1) A permanent commission was formed for the preparation of a vegetation map of Europe, with Prof R Tüxen (Stolzenau) as chairman and the following members: Prof J Braun-Blanquet (Montpellier), Prof L Emborger (Montpellier), Prof I Horvat (Zagreb), Prof A Nourfalise (Brussels) and Prof B Pawlowski (Cracow). (2) The following resolution was adopted for submission to Unesco and all the member Governments concerned: "The vegetation of the Earth represents the vital productive potential upon which all life depends. Therefore the comprehensive study of vegetation is of the utmost importance, and for this purpose the combination

of ecological, phytosociological and cartographical methods are required.

"The present-day methods of mapping vegetation greatly enlarge our fundamental knowledge of plant communities, their development and distribution as well as providing a deep insight into their environments. In applied phytosociology the mapping of vegetation constitutes a solid basis for assessment of habitats, for utilization of vegetation and for the evaluation or even the forecasting of any change or damage to vegetation by erosion, wind, water and other natural or human factors.

"It is suggested that no large-scale technical measures should be planned or carried out which may influence the vegetation or landscape without first mapping the vegetation prior to the respective technical measures being put into effect."

A. E. APINIS

BIOLOGICAL FIBRES

IT is some time since the X-ray Analysis Group of the Institute of Physics has met to consider biological fibres so that the conference in Leeds held during April 17-18, even if only partly devoted to fibres was very welcome. It is however, symptomatic of the present place of specialist techniques (even if they are as well established as X-ray diffraction) in such fields as the study of fibre structure, and perhaps even more of the trend of development of the corresponding specialist groups, that of the seven papers presented on this occasion only two could be classed as predominantly crystallographic in content whereas in two others, which dealt respectively with infra-red absorption and the electron microscope X-rays had no more than a casual mention. That these other techniques are now essential partners with X-ray diffraction in research on fibre structure was emphasized by the part they played in the other three papers. Nevertheless, in this account attention will be confined chiefly to topics which are more closely associated with the nominal activities of the Group.

The successful study of the cellulose fibre by X-ray analysis set a fashion which is evidently even after more than thirty years not yet outmoded. This fibre is still presenting fundamental crystallographic problems for investigation for example it seems still to be possible to argue about whether the cellulose chain molecules are all oriented in the same sense, or form two antiparallel systems. D. W. Jones and his colleagues (British Rayon Research Association) are non-committal about it in their discussion of cellulose I, but favour alternation in cellulose II. Prof R. D. Preston (Leeds) suggests that in cellulose I alternation is unlikely, basing his argument on the idea that growth is by end synthesis. His conclusion was however, criticized in discussion, and also seems impossible to reconcile with the almost universal acceptance of alternation in cellulose II, although whether this is necessary or merely a convenient dogma is not at all clear. It does seem reasonable to expect that, if chain polarity is of any significance at all, the same type of arrangement will be present in both modifications.

Another controversial feature is the type of hydrogen bonding, about which there are two schools of thought respectively accepting or denying the presence of diagonal hydrogen bonds (specifically perpendicular to the [101] normals in the Meyer and Misch cell). The orthodox, among them the British Rayon Research Association team, agree with Meyer and Misch at least on this one point that the hydrogen bonds are parallel to the *a* axis of the unit cell. Both schools have recently adduced infra-red absorption results in favour of their arguments, creating further confusion for the non-specialist.

Agreement does seem to be reached on one point, that there is more than one cellulose I structure, the eucellulose (Preston) or type A cellulose (Marin and Mann) of Valonia must one suppose, be cellulose I proper, rather than the typical type B cellulose is classed with most of the other plant fibres as yielding on hydrolysis, besides glucose, other sugars which are to be regarded as contaminants.

Some fibrillar aspects of the fine structure of cellulose also received attention. Preston believes that the microfibrils retain their identity when surrounded by inclusions in the cell wall, and that their surface structure is in some way responsible for the electron diffraction patterns which he and his colleagues have obtained from metal-cellulose complexes.

The application of X-ray analysis to the problem of the structure of silk fibroin is nearly as old as its application to cellulose, and we have been accustomed for a long time to distinguish between the structures of the two principal silks of commerce, domestic and tussah. It is now clear that these are but two of a family of at least six fibroins produced by various members of the orders Lepidoptera and Araneae, the silks produced by some fifty species were examined by J. O. Warwicker (Slurley Institute, Manchester) to establish this. A disturbing observation is that there appears to be no strict correlation between the crystallographic type of the fibroin and the biological classification of the producing species. Structurally the fibroins differ in the separation of the hydrogen bonded pleated sheets of polypeptide

chains, this distance may be as small as 9.3 Å (*Bombyx mori*) or as large as 15.7 Å (*Nephula senegalensis*). In fibroins with the larger inter-sheet separations amino-acid residues with long side-chains must occur in the crystalline regions. In view of the importance of this idea, which has always been virtually rejected before in theories of fibroin structure, further details of the relevant chemistry would be welcomed.

The cross- β configuration, so extensively studied in the keratin-myelin-elastin-fibroin group of fibrous proteins, has always been something of a puzzle because of the difficulty of obtaining a good X-ray diffraction diagram. That a solution of the problem should now be given in terms of a structure closely allied to a fibroin rather than to keratin is one of those oddities which sometimes arise in fibroin structure research. K. D. Parker and K. M. Rudall (Leeds) have found, in fact, a cross- β fibroin in the egg-stalks of the lacewing fly; it gives a remarkably good X-ray diffraction pattern the interpretation of which leaves no doubt that the fibroin chain-molecules are arranged in long folds transverse to the fibre-axis. From this folded configuration the chains can be brought into the parallel- β state by stretching the material to about six times its initial length. This change is regarded as a true intramolecular transformation like the α - β transformation in keratin, but differs from the latter in that so far no success has followed attempts to reverse the change.

Heavy-metal staining techniques are of great importance in electron microscopy, and are now being successfully employed in studies of the microfibrillar texture of keratin fibres. Work is going on in various centres to correlate such electron microscope observations with the older X-ray results that mercury, for example, can modify the intensities of the equatorial 'reflections' at approximately 80 Å, 45 Å and 27 Å in keratin. H. J. Woods (Leeds) reported that staining with mercuric acetate also affects the wide angle diffraction pattern, when corrections are made for increased absorption due to the metal. In an attempt to account for the small-angle 'reflections' in terms of a model of uniform microfibrils it is found that conventional Fourier transform methods for obtaining the radial distribution of interfibrillar vectors are inapplicable, and the direct method of calculating the intensity from an assumed radial distribution often results in a negative intensity. In the discussion it was suggested that there might be a failure of the conventional theory for systems so nearly close packed as those considered, but it now seems more likely that the difficulty is due to the fact that for such systems the radial distribution must be so nearly determined by geometry that the use of an arbitrary distribution may well be physically unsound. J. Sikorski emphasized that the electron microscope results so far tell us only about the details in paracortical cells, the size and packing of the microfibrils in the orthocortex may well be different. H. J. Woods

THE SMITHSONIAN INSTITUTION

REPORT FOR 1957-58

THE report of the Smithsonian Institution for the year ended June 30, 1958*, covers the 112th year of the Institution and includes the report of the Secretary and the financial report of the Executive Committee of the Board of Regents, together with reports of branches of the Institution and on the library and publications. The Institution has now nearly 51 million catalogued objects in its collections, and visitors to all its branches totalled more than 10.36 million. Field work during the year included the excavation of the Welcoming Mound along the Ohio River in West Virginia, continued field investigations of the bird-life of the Isthmus of Panama, and the mammal survey of Panama, a long-range programme designed to solve the stratigraphic sequence in the Glass Mountains, and extensive palaeontological work in Oklahoma, Texas, New Mexico and Colorado.

Systematic researches by the staff of the Bureau of American Ethnology included Eskimo and Arctic studies, field-work in South Carolina, among the New York Seneca and in Florida, and excavations at Russell Cave, Alabama. The director of the Bureau continued also as director of the River Basin Surveys, which continued its programme for salvage archaeology in areas to be flooded or otherwise destroyed.

* Smithsonian Institution. Report of the Secretary and Financial Report of the Executive Committee of the Board of Regents for the year ended June 30, 1958. Pp. x+232+14 plates. (Washington, D.C. Government Printing Office, 1958.)

by the construction of large dams. By June 30, 1958, 254 surveys and excavations had been made in twenty-nine States and 4,889 archaeological sites located, of which 997 had been recommended for excavation or limited testing, by the end of the year, 388 sites in fifty-two reservoir basins in nineteen States had been partly or extensively dug.

The Smithsonian Astrophysical Observatory continued to work along the four principal lines of solar astrophysics, meteors, the satellite tracking programme and studies of the upper atmosphere, in which methods based on celestial mechanics were developed for inferring the density of the upper atmosphere from the motions of artificial Earth satellites, and a theoretical study of the nature and thickness of the lunar dust layer was completed. Its Division of Radiation and Organisms continued studies on photomechanisms in plants, with special emphasis on growth responses controlled by low levels of red and blue radiant energy. Studies of the interaction of gibberellin, kinetin and cobalt with the photo-process indicate that there is no direct interaction between red irradiance and the added substances, although all these materials modify the final growth response. Studies were continued on the effects of radiant energy on the biosynthesis of protochlorophyll in leaves of higher plants grown in the dark, and in a study of biochemical changes involved in the development and maturation of the chloroplast.

of higher plants, some progress was made in isolating intact proplastids from leaves grown in the dark.

Good progress is reported in locating a site for a new building for the National Air Museum, to which 103 specimens in 52 accessions were added during the year. The National Zoological Park, to which 1,411 animals were added during the year, now totals 2,316 individual specimens, and visitors exceeded 4 million, while those to the Canal Zone Biological Area totalled 570, of whom forty three were scientists, students or observers using the station for scientific work, particularly in wild life

observation, plant and insect studies and photography. The International Exchange Service handled 1,094,708 packages, including 63 full and 43 partial sets of United States official publications in exchange for official publications sent by foreign Governments for deposit in the Library of Congress. The Library received 53,274 publications during the year, and arranged 128 new exchanges. Its holding at the end of the year totalled 974,893, including 580,722 in the Smithsonian Deposit at the Library of Congress. The report includes a list of the 81 new Smithsonian publications issued during the year.

EFFECT OF NITROUS ACID ON TOBACCO MOSAIC VIRUS MUTATION OR SELECTION?

By F. C. BAWDEN F.R.S.

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GIERER and Mundry¹ claim that treating preparations of tobacco mosaic virus or of its nucleic acid with nitrous acid *in vitro* causes mutations. Indeed, they state that their "experiments show that replacement of one single NH₂ group by one OH group *in vitro* can change the genetic character of the whole TMV RNA molecule". The genetical implications of this statement are so great that, before accepting it, there is more than usual need to ensure that their experiments could have no other interpretation. What their results show is that, when tobacco mosaic virus is treated with nitrous acid, its infectivity, as measured by the numbers of local lesions formed in one tobacco variety Xanthi, decreases, while the number of necrotic lesions produced in another variety, Java, increases. Xanthi forms necrotic local lesions with all the usual strains of tobacco mosaic virus, whereas Java forms them with only some and not with the type strain.

These results are readily reproducible. Table 1 shows two experiments with the Rothamsted type culture of tobacco mosaic virus, in one, inoculations were made to Xanthi and Java and in the other to *Nicotiana glutinosa* L. which like Xanthi gives necrotic local lesions with the type strain, and to Judy's Pride, a variety of White Burley, which, like Java, does not. The starting preparation like those used by Gierer and Mundry, produced a few necrotic lesions on Java and Judy's Pride. There is nothing unusual in this, for all bulk preparations of tobacco mosaic virus contain a mixture of strains. However, this being so, it is obviously necessary to consider whether the change in behaviour of the preparations towards the different plants during inactivation by nitrous acid could simply reflect some form of selection from a mixed population of strains. Gierer and Mundry state that this possibility is excluded because the total number of lesions produced on Java increases and not simply the ratio of lesions on Java to those on Xanthi. They therefore conclude that the number of particles able to cause necrotic lesions on Java must have been increased by exposure to nitrite. But must it? Their conclusion rests on the assumption that strains do not interact and that one will always produce its characteristic effects regardless of how much of other strains is present.

Table 1. NUMBERS OF NECROTIC LESIONS PRODUCED BY DIFFERENT *Nicotiana* SPECIES AND VARIETIES WHEN INOCULATED WITH TOBACCO MOSAIC VIRUS TREATED FOR VARIOUS TIMES WITH NITROUS ACID

| Time (hr.) | Numbers of necrotic lesions per leaf | | | |
|------------|--------------------------------------|------|---------------------|--------------|
| | Exp. 1 | | Exp. 2 | |
| | Xanthi | Java | <i>N. glutinosa</i> | Judy's Pride |
| 0-0 | 300 | 0-5 | 350 | 2 |
| 0-5 | 250 | 0 | 300 | 12 |
| 1 | 125 | 24 | 210 | 50 |
| 2 | 95 | 26 | 130 | 55 |
| 4 | 85 | 12 | 60 | 33 |
| 20 | 6 | 0-5 | 10 | 15 |

Tobacco mosaic virus at 4 mgm./ml. was incubated with 1 M sodium nitrite and 0.2 M HCl acetic acid at pH 4.1 for the times stated, when samples were diluted 1/10 in pH 7 phosphate buffer and used as inocula. Xanthi and *N. glutinosa* give necrotic local lesions with the type strain of tobacco mosaic virus. Java and Judy's Pride do not.

Table 2. NUMBERS OF NECROTIC LESIONS PRODUCED BY DIFFERENT *Nicotiana* VARIETIES AND SPECIES WHEN INOCULATED WITH MIXTURES OF TOMATO AUCUBA AND TOBACCO MOSAIC VIRUSES

| Inoculum | Numbers of necrotic lesions per leaf | | | |
|---------------------------|--------------------------------------|------|---------------------|--------------|
| | Exp. 1 | | Exp. 2 | |
| | Xanthi | Java | <i>N. glutinosa</i> | Judy's Pride |
| Aucuba alone | 05 | 240 | 60 | 75 |
| Aucuba in TMV 20 mgm./l. | 130 | 180 | 128 | 90 |
| Aucuba in TMV 200 mgm./l. | 280 | 24 | 350 | 14 |
| Aucuba in TMV 2 gm./l. | 500 | 2 | 400 | 4 |
| TMV 2 gm./l. alone | 500 | 0 | 450 | 2 |

The tomato aucuba mosaic virus was used at 10 mgm./l. With the high concentrations of tobacco mosaic virus (TMV) the lesions on Xanthi and *N. glutinosa* were too many to count accurately.

There is much evidence at variance with this assumption. For example it has long been known that infection of a plant with one strain of tobacco mosaic virus prevents other strains from producing their characteristic effects² and that adding type tobacco mosaic virus to inocula of strains that produce necrotic lesions in Judy's Pride tobacco decreases the number of lesions they produce³. One such strain is tomato aucuba mosaic virus, and Table 2 shows how mixing this with various amounts of tobacco mosaic virus can affect the number of necrotic lesions formed on Java and Judy's Pride. Decreasing the amount of tobacco mosaic virus reproduces the phenomenon which in treatments with nitrite Gierer and Mundry

say can only be attributed to mutations, of decreasing the numbers of lesions produced on Xanthi and *N. glutinosa* while the numbers on Java and Judy's Pride increase. Numbers of necrotic lesions, however, do not tell the whole story, for mixing aucuba mosaic virus with tobacco mosaic virus alters the type of lesion produced, especially on Java. Aucuba mosaic virus alone produces distinctive, reddish-brown circles that may reach a diameter of 0.5 cm. None of the lesions recorded in Table 2 as formed by inocula containing the larger amounts of tobacco mosaic virus was of this type, but all were white spots and flecks of various sizes. With smaller amounts of tobacco mosaic virus, the lesions were more variable, some were all white, but others had small reddish-brown centres, and some approximated to true aucuba type. More of the last type occurred as the concentration of tobacco mosaic virus decreased.

Similarly, when mixtures containing 4 mgm/ml tobacco mosaic viruses and 20 mgm/l aucuba mosaic virus were diluted 1/10 in pH 7 phosphate buffer and inoculated to Java, only white lesions were formed, whereas a range of types was produced after incubation with nitrite. The first brown lesions to appear were small, but as the treatment continued they became more typical of the aucuba type. It is highly unlikely that adding aucuba mosaic virus to the starting preparation directed any mutations caused by nitrite towards characters peculiar to aucuba mosaic virus, and a more reasonable interpretation is that the residual aucuba mosaic virus became increasingly able to make itself evident as the concentration of infective tobacco mosaic virus decreased. This interpretation does not demand that aucuba mosaic virus should be more resistant than tobacco mosaic virus to inactivation by nitrite, for the ability of the latter to obscure the presence of aucuba mosaic virus is not determined only by the proportions of the two. Concentrated tobacco mosaic virus will obscure proportionally more than will dilute virus, for example, whereas 2 gm/l will obscure 20 mgm/l aucuba mosaic virus, 0.2 gm/l will not necessarily mask 2 mgm/l.

The fact that the obscuring ability of tobacco mosaic virus increases with increasing concentration may simply reflect one aspect of the well-known interference phenomenon, that infection by one strain makes cells resist infection by others. The more concentrated the tobacco mosaic virus, the more epidermal cells it will infect at inoculation and the fewer there will be for aucuba mosaic virus to multiply in unhindered. Indeed, the range of local-lesion types in Java produced by mixtures of the two may mean only that, in different parts of the leaf, different proportions of cells contain one or other of the two strains. However, it is equally possible that there are other interactions between the strains as they multiply, leading, perhaps, to genetic recombinations or phenotypic mixing. This could be decided only by isolating the viruses present in different lesions and testing their behaviour when transmitted to a range of plants. Whatever may be the mechanisms of the interaction between strains, there is no doubt that strains able and unable to cause necrotic lesions in Java tobacco do interact and that this interaction affects both the quantity and quality of lesions produced. The experiment recorded in Table 2 shows fewer local lesions on Java when aucuba mosaic virus was mixed with tobacco mosaic virus than when inoculated alone, but the mixtures some-

times produced more lesions, though no lesion was then of the aucuba type and all were white spots, rings or flecks. Obviously the interactions are complex, but the fact that they occur makes the counts of necrotic lesions produced by mixtures of strains valueless for indicating the numbers of particles present that are intrinsically able to cause necrosis in Java. There seems no reason to look further for an explanation of the action of nitrite in increasing the numbers of lesions produced by tobacco mosaic virus in Java than that, as the concentration of particles unable to cause necrosis decreases, so they interact less with those able to cause necrotic lesions.

The phenomena that suggest mutation come from interactions between infective particles, but there is also an interaction between virus inactivated by nitrite and active virus. Inactivation by nitrite is an effect on the nucleic acid, and inactivated virus particles still retain their physical and serological properties, as do those inactivated by ultra-violet radiation. Like virus inactivated by ultra-violet radiation⁵, and like the protein produced when virus particles are disrupted by alkali⁶, nitrite-inactivated virus inhibits infection by active particles, and the presence of 0.4 mgm/ml of such inactivated virus will halve the number of lesions produced by tobacco mosaic or aucuba mosaic virus at 10 mgm/l. This inhibition could affect measurements of inactivation rates, for as the amount of inactivated virus increases so it will increasingly inhibit infections by the residual infective virus, the amount of which will thereby be increasingly under-estimated and preparations will cease to infect while they still contain potentially infective particles. The virus protein is likely to be responsible for the inhibition, so tests with nucleic acid preparations are probably free from this complication, it was with these that Mundry and Gierer² found that inactivation follows first-order kinetics. Their conclusion that changes in single NH_2 -groups cause mutations derives from the observation that the numbers of necrotic lesions produced on Java at first increase linearly with time, but this need mean little more than that the dominating strain in their starting preparation inactivated according to first-order kinetics. That their starting preparation did contain strains already able to cause necrosis in Java is clear, and that these were interacting with other strains is strongly suggested by the fact that, when diluted 1/10, the number of necrotic lesions on Xanthi fell to one fifth whereas the number on Java was only halved.

The isolations Mundry and Gierer² made from single local lesions in Xanthi also show their starting preparation was mixed. Most of the isolates made from 60 lesions produced by nucleic acid after 90-min exposure to nitrous acid differed from type tobacco mosaic virus, whereas only 1 out of 65 isolates made from the starting preparation was obviously different. This fact they advance as further evidence that nitrite caused mutations, but as the treated preparation had lost more than 99 per cent of the initial infectivity, 99 times as many lesions should have been sampled from the untreated as from the treated preparation to make a proper comparison. Had 6,000 lesions been sampled, there is every reason to think that more than 100 isolates differing from tobacco mosaic virus would have been found, for the fact that one was identified for certain from 65 lesions suggests that at least 2 per cent of the particles in the starting material differed from type tobacco mosaic virus.

I have made no tests to see whether different strains differ in the rate at which they are inactivated by nitrite but it is to be expected that they will, for strains have been found to differ in their susceptibility to inactivation by most other treatments. The obvious place to look for resistant strains is among those that survive at the tail end of an inactivating treatment, and all that is needed to explain the preponderance of variants after exposure to nitrite is to postulate that strains differ in their rate of inactivation. That the isolates when propagated continued to show their characteristic differences from type tobacco mosaic virus is interesting but has no relevance to the problem of how they came to be genetically different from the type virus. Mutations no doubt reflect chemical changes in the nucleic acid, and there is no *a priori* reason why changes produced

in vitro should not affect the genetic behaviour of viruses, but to attribute mutations to such changes requires more than demonstrating that the end products of an inactivating treatment differ in behaviour from the bulk of the starting material, it requires demonstrating that chemical changes produced *in vitro* are perpetuated in the progeny of the particles.

I am indebted to Dr A. Gierer for providing me with seeds of the tobacco varieties Xanthi and Java.

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CHARACTERS ASSOCIATED WITH PARASITISM IN GRAM-POSITIVE BACTERIA

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THE concept of parasitism in bacteria has been overshadowed by the more immediate problems of pathogenesis, so that, in standard bacteriological literature, the words parasite and pathogen are treated as if they were synonymous, and harmless parasites are inaccurately designated commensals. Parasitism properly so called, is common among bacteria especially of the Gram positive group, and it is the purpose of this article to indicate certain interesting conclusions that are derived from a consideration of the characters associated with its occurrence.

Many members of the Gram positive group are not, in fact, Gram positive in their staining reactions but nevertheless bear so close a resemblance to the other members of the group in every other respect that they must be considered to have lost this characteristic secondarily. In very many instances, these are parasitic representatives of mainly free-living families. An obvious example is *Neisseria*, a genus consisting of obligate parasites, many of which have lost all trace of Gram positivity, while retaining characters of morphology, metabolism, antibiotic sensitivity, etc., that indicate a relationship with the *Coccaceae*. (Their description as obligate parasites refers to their normal mode of life, and does not exclude the possibility of growth in artificial culture.)

A second important character associated with parasitism is anaerobiosis. So far as I am aware, all truly Gram negative bacteria are aerobic, the so-called Gram negative anaerobes, such as *Veillonella*, *Fusobacterium* or *Bacteroides*, have obvious affiliations with Gram positive families, and these also are obligate parasites. This combination of characters is well known in the facultatively parasitic clostridia, many of which are very weakly Gram positive, whereas the aerobic, sporing bacilli, few of which are parasites, are strongly Gram positive. Anaerobiosis without loss of Gram positivity is found in the parasitic *Actinomyces*. The streptococci would serve as examples in view of their lack of catalase but most species are aerobic by virtue of their insensitivity to hydrogen peroxide.

The third character associated with parasitism in Gram positive bacteria, as indeed in animals and higher plants also, is loss of structural complexity, although the bacteria are exceptional in that they commonly undergo a reduction in the organs of distribution.

Thus, in respect of these various characters, there is quite often found to exist a series of forms connecting a Gram positive aerobic saprophyte of complex morphology, with a Gram negative, anaerobic parasite of simple morphology.

(A) The free living sarcinae are large and strongly Gram positive, they are aerobic, and include representatives which, by virtue of their possession of flagella and spores, attest a recent common origin with the sporing bacilli. The facultatively parasitic micrococci and staphylococci are Gram positive and aerobic, but smaller and devoid of flagella and spores. The parasitic *Neisseria* are aerobic, but Gram variable or negative and the *Veillonella*, in addition to these characters, are anaerobic and very small indeed.

(B) The free living streptomycetes are large and strongly Gram positive, they are aerobic and they branch and sporulate very freely. The large oral leptotrichia are aerobic and Gram positive, they branch freely and form very occasional chains of spores.¹ The classical type of *Leptotrichia buccalis* is microaerophilic and Gram variable, it branches rather rarely and does not appear to form spores.² Fusobacteria resemble *L. buccalis* very closely in general morphology, but are very small, Gram negative, anaerobic and do not branch. All the last three are obligate parasites, but they are progressively more difficult to cultivate, in the order given. The origin of the anaerobic, Gram negative *Bacteroides*, which bears some resemblance to the fusobacteria, is probably similar.

(C) The true *Actinomyces* (a genus of oral parasites typified by *A. bovis*) resemble *Micromonospora* in their main morphological features, but are anaerobic or microaerophilic and structurally degenerate.³

If the conclusions arising from these observations are valid it would appear that the great majority of

parasitic bacteria of the Gram-positive group are descended from more complex, free-living ancestors. This is, of course, a biological commonplace, but systematic bacteriology has not yet fully recovered from the effects of placing a very undue emphasis upon the taxonomic characters of those common pathogens, usually members of parasitic genera, with which the majority of bacteriologists are, or previously were, most closely acquainted, without taking into consideration the possibility of such tendencies as have just been described.

The suggestion that structurally complex Actinomycetes are ancestral to simpler forms, and even to cocci, is not new¹, but former hypotheses of this type have tended to suggest the sort of relationship that exists between the mycelial and oidial fungi, rather than a progressive degeneration of structure, associated with anaerobiosis or loss of Gram-positivity, and sometimes with both.

It is not, however, easy to understand how these bacteria are able to dispense with the production of catalase and of the nucleic acids of the Gram complex², which appear to be essential, or very advantageous, to their free-living counterparts. In the case of the bowel-dwelling forms, it is possible that their environ-

ment protects them against free oxygen, but whereas neither *Clostridium*, *Bacteroides*, *Lactobacillus bifidus* nor *Streptococcus faecalis* produces catalase, the truly Gram-negative intestinal bacteria do so in every case. Nor is the alternative explanation, that the anaerobes of the mouth, for example, live in such close association with large numbers of other bacteria as to profit from their catalase production or oxygen utilization, any more satisfactory, since the oral flora consists very largely of anaerobes or non-catalase-producing aerobes, such as streptococci and lactobacilli. The animal tissues themselves are the only probable source of the enzyme.

The significance of the loss of the Gram-complex in so many parasites is almost beyond speculation, but it is at least possible that it indicates the availability, in an elaborate form, of nutrients, with the synthesis of which from simpler materials these nucleic acids are concerned, under less-favourable conditions.

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DEVELOPMENT OF *TRYPANOSOMA VIVAX* TO THE INFECTIVE STAGE IN TSETSE FLY TISSUE CULTURE

By DR WILLIAM TRAGER

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EARLY in the work on trypanosome diseases of man and animals in Africa, it was found¹ that cultures of trypanosomes could be obtained quite readily in blood agar media inoculated with infected blood and incubated at temperatures of 25–30° C. But at the same time came the disturbing finding that such cultures lost their infectivity as soon as they began to grow^{1,2}. What was happening soon became clear: in the cultures there developed only the so-called midgut forms of the trypanosomes, the same forms which develop in the midgut of an infected tsetse fly and which Bruce³ had shown to be non-infective to the mammalian host. In a suitable tsetse fly, however, the trypanosomes migrate to the salivary glands and proboscis, where they become transformed into infective forms⁴. Recently, Weinman⁵ reported in a preliminary way that he had produced infection in mice with two cultures of *Trypanosoma rhodesiense* maintained in a medium with trehalose (concentration not stated). With this exception, infective forms of the African trypanosomes have not previously been obtained in culture. It seemed possible that these metacyclic forms might develop *in vitro* in the presence of surviving or growing tsetse fly tissue.

The gonads of female lepidopterous larvae are the only insect tissue that has up to now given outgrowths of cells at all comparable to those obtained with vertebrate tissues⁶⁻⁸. Although mosquito tissues survived *in vitro* sufficiently well to support the growth of western equine encephalitis virus⁹, they did not produce cellular outgrowths, nor have such outgrowths been obtained with tissue from other dipterous insects. The cultivation of tsetse fly

tissue was therefore a problem of considerable intrinsic interest, quite apart from its bearing on the developmental cycle of trypanosomes. It is the purpose of the present brief report, however, to relate only the main results of the experiments dealing with the production of infective trypanosomes *in vitro*. The complete details of these experiments, together with full information on the tsetse fly tissue cultures, will be reported elsewhere.

Tissues of the fly *Glossina palpalis* were obtained from pupae or young adults free from extraneous bacteria. Pupae of known age (sent to me from the Kaduna Laboratory of the West African Institute for Trypanosomiasis Research through the kindness of Mr W. MacDonald) were sterilized externally in White's solution (mercuric chloride, 0.25 gm., sodium chloride, 6.5 gm., hydrochloric acid, 1.25 ml., ethanol, 250 ml., distilled water, 750 ml.), rinsed in sterile water and dried on sterile filter paper in a Petri dish. Such pupae, if kept for the required time in sterile vials with sand, produced bacteria-free adults. The pupae or adults were dissected aseptically in a drop of culture medium. Fragments of tissues were explanted either in hanging drops or in a thin layer of fluid (0.3 ml.) on the bottom of a Porter flask closed with a silicone rubber stopper.

The culture medium (Table 1) supported initial outgrowths from, and differentiation of, several kinds of tsetse fly tissue. In one type of outgrowth, mitotic division of the cells was seen. To obtain cultures of trypanosomes, however, tissues were used which lived *in vitro* but showed limited or no outgrowth. These tissues were the alimentary tract and salivary glands of a late pupa or a newly emerged fly. To a

Table 1 PREPARATION OF THE CULTURE MEDIUM

| Solution A* | mgm./100 ml. |
|--|--------------|
| NaCl | 90 |
| KCl | 300 |
| $\text{NaH}_2\text{PO}_4 \cdot \text{H}_2\text{O}$ | 110 |
| $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$ | 370 |
| CaCl_2 | 80 |
| Glucose | 150 |
| Trehalose | 50 |
| 1 M lactic acid | 50 |
| α-Ketoglutaric acid | 25 |
| Succinic acid | 6 |
| Lactalbumin hydrolysate | 1 000 |
| Yeast extract (Difco) | 200 |

* Based in part on work of Wyatt (ref. 7) and Grace (ref. 8). Ingredients were dissolved in water redistilled in a "Pyrex" glass still. pH was adjusted to 6.8 with 1.0 N NaOH. The solution sterilized through a Selas 03 porcelain filter.

| Solution B† | mgm./10 ml. |
|---------------------|-------------|
| Reduced glutathione | 200 |
| Ascorbic acid | 2 |

† Sterilized through alkaline glass filter.

Final mixture. Mix 8 ml of solution A, 2 ml sheep serum, 0.5 ml. solution B. In 1 ml of the above mixture in a centrifuge tube crush gently two sterilized 15-day-old pupae of *G. palpalis*. Centrifuge 15 min. at 2,000 r.p.m. The supernatant with the re-suspended fatty layer at the surface constitutes the culture medium.

hanging-drop culture was added a minute drop of blood or trypanosome concentrate from an infected animal. Continuous culture was achieved of all three species of trypanosomes tried: *Trypanosoma brucei*, *T. congolense* and *T. vivax*.

The most interesting results were obtained with *T. vivax*, a species never before cultured and which, in the tsetse fly, omits the midgut phase and develops directly to the infective forms in the proboscis. A first attempt at cultivation of this species in fly tissue culture, using washed trypanosomes from a heavily infected sheep, gave a negative result. In the second attempt, the only sheep showing trypanosomes on that day was one, infected by fly bites nine months previously, which had survived the acute infection and now occasionally showed small numbers of organisms in the peripheral blood. A concentrate from this blood, in which only one trypanosome could be seen per low power field, was inoculated to fly tissue cultures prepared two days previously. Two days later it was noticed that the temperature of the incubator (set for 28° C) had gone up to 30° C. At this time large synzygotid multiplying forms of trypanosomes were seen in the tissue cultures. From these a strain was established and maintained in tissue culture for three months. It was discontinued only because the work was brought to a close. Soon after its establishment the strain was successfully transferred to blood agar slants and is still being maintained in this way. Later experiments then showed that *T. vivax* could be started in culture only by following the conditions which had occurred quite fortuitously the first time, that is, using blood from the sheep with a long standing chronic infection, inoculating the concentrate of trypanosomes to tissue cultures two days old and—very important—incubating these at 30–32° C, not at 27–29° C. Once started, the cultures can be kept equally well at either the lower or the higher temperature but they have mostly been kept at the higher temperature.

Four strains of *T. vivax* in tissue culture have been begun, three from the original sheep and a fourth from a new infection in a sheep inoculated with blood from the original sheep. The first two culture strains have been studied in some detail. There were present in the cultures numerous forms morphologically indistinguishable from the classical infective

forms of *T. vivax* as seen in the proboscis of the tsetse. But five sheep inoculated repeatedly with such material and followed for more than a month failed to show trypanosomes in the blood. Two of the sheep did have a fever, one on the eighth and the other on the ninth day after intravenous inoculation of culture material, but no trypanosomes could be found.

It was then decided to test the ability of the trypanosomes in fly tissue cultures to survive at body temperature, which is lethal to the usual culture of trypanosomes on blood media. A three-day-old hanging drop subculture of strain 2 of *T. vivax* in culture for six weeks was placed in a jar immersed in a water bath at 38° C. On the following day the culture presented a mass of very active trypanosomes. The material was inoculated intravenously into a sheep. Exactly one week later scanty trypanosomes were present in the blood of this sheep. They were readily identified as *T. vivax*. The sheep was positive again on the following day, with about three trypanosomes per field. This sheep first showed fever (105° F) on the ninth day, the only day of fever it has had. At this time no trypanosomes could be found, and it has since remained negative except for the thirteenth day (1 trypanosome in 150 fields) and the eighteenth day (1 trypanosome in 40 fields). Thus, transmission from culture was accomplished.

Attempts at repetition of this success were immediately instituted. An interesting finding was that whereas some tissue cultures of *T. vivax* showed mostly dead or sluggish organisms after exposure to 38° C, others were very active like the culture which produced infection. A clean sheep raised at the laboratory was inoculated with a culture of *T. vivax* which had numerous active trypanosomes after the one day at 38° C. This sheep showed a positive blood film and had a fever on the seventh day after inoculation.

These two successful transmissions from culture make it certain that a reproducible method is now to hand for obtaining infective *T. vivax* *in vitro*. This makes possible a detailed study of the factors responsible for the acquisition of the infective state by trypanosomes, a matter of significance far beyond its immediate application in the field of trypanosomiasis. The relatively light infections which seem to have followed the inoculation of cultured *T. vivax* suggest the possibility of the development of a practical method for immunization against the parasite, using attenuated but infective cultures. This possibility requires and deserves much further investigation.

The work summarized in the foregoing report was done while I was a visiting investigator at the West African Institute for Trypanosomiasis Research and I thank Dr. T. A. M. Nash, director of the Institute, and Dr. R. S. Desowitz, in charge of protozoology there for their kind invitation to work in their laboratories and for the facilities extended to me by them and their staff. Travel to Africa was made possible by a grant from the Rockefeller Foundation.

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LETTERS TO THE EDITORS

GEOPHYSICS

Disturbance in the Ionospheric F-Region following the Johnston Island Nuclear Explosion

ACCORDING to the newspaper reports, American scientists exploded hydrogen bombs near Johnston Island on August 1 and 12, 1958, at heights of 160 km and 100 km. The Apia magnetic records (Lawrie, J. A., and Gerard, V. B., private communication) give times as 10 50 and 10 30 GMT. Some geophysical aspects of these explosions have been discussed by Cullington¹ and Kellogg *et al.*²

Here we will describe one of the effects on the ionospheric F-region. We have 10 min recordings over the period of the first event and 2-min recordings over the period of the second event.

Prior to both events, ionograms at Rarotonga showed the normal undisturbed night F-region. On August 1, the ionograms 40 min after explosion (zero plus 40 min) showed a great increase in maximum electron density, and 10 min later this had exceeded the recording limit of the machine. In the next 40 min the electron density decreased rapidly and at zero plus one hundred there was no trace of the normal F-region, but above it at a base height of 560 km was seen a layer the maximum electron density of which was roughly one quarter of the normal F-value. The increase at the maximum phase was to at least seven times normal. Another interesting characteristic was the gradual drop of fifty kilometres in height as the ionization decayed. Fig 1 is a schematic diagram deduced from the ionograms.

On August 12, the disturbance in the F-region took longer to reach Rarotonga and was much less severe. A detailed true height analysis of these records confirmed the form deduced for the first event and ensured that no significant phases were missed. We will discuss only the first event.

In order to gain a better picture of the physical process we examined also the ionograms for Christchurch, 44°S, and Campbell Island, 53°S, and, through the courtesy of J. A. Lawrie and V. B. Gerard, the magnetic vectors which they had prepared for Honolulu, Palmyra Island, Fanning Island, Jarvis Island and Apia.

A characteristic movement among the magnetic vectors was identified with the passage of the F-region disturbance. The times of passage of the disturbance at the eight stations were then plotted against distance from the point of explosion (see

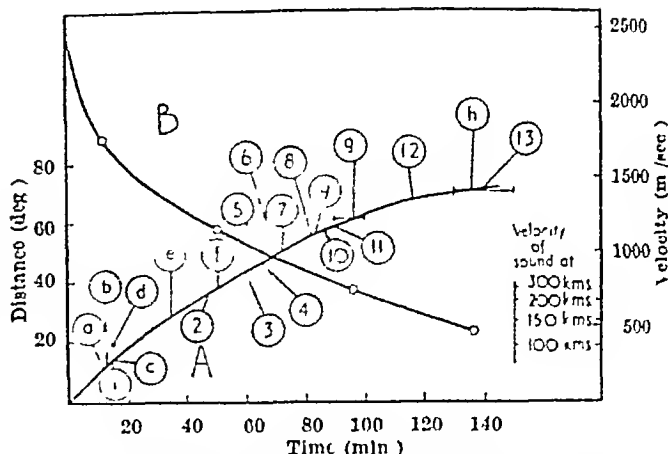


Fig. 2. A, Curve of delay times versus distance in degrees. Observation sites: a, Palmyra Island, b, Honolulu, c, Fanning Island, d, Jarvis Island, e, Apia, f, Rarotonga, g, Christchurch, h, Campbell Island. Places where observations possible: 1, Maui, 2, Adak, 3, Guam, 4, San Francisco, 5, Kokubunji, 6, Akita, 7, Wakkanaï, 8, Townsville, 9, Yamagawa, 10, Brisbane, 11, Okinawa, 12, Baguio, 13, Hobart. B, Deduced velocity curve.

Figure 2 A) The points lie well on the smooth curve except for Jarvis. This Station is on the dip equator, and there is reason for supposing that the time of its vector is advanced by several minutes. The corresponding velocities are shown in Fig. 2 B, values are only approximate because of limited data and time resolution.

The assumption made in drawing this smooth curve is that the velocity of propagation is independent of direction relative to the Earth's magnetic field. Attempts were made to reconcile the time delays with a field dependent velocity but no reasonable pattern emerged. It seems, then, that the ionospheric disturbance is a by-product of a gaseous wave which is propagated at a velocity considerably above that of sound. For convenience we will refer to it as a shock wave.

It is not possible to account for the high value of electron density and its spatial distribution over Rarotonga merely by compression or even by the collection of all the electrons between Johnston Island and Rarotonga. Restraint by the Earth's magnetic field of the motion of charged particles precludes electrons coming from the nuclear event itself. Together with the complete disappearance of electrons after the disturbance, and the general appearance of the ionograms, these facts indicate electron production in the disturbance. We postulate ionization by collision and subsequent removal by

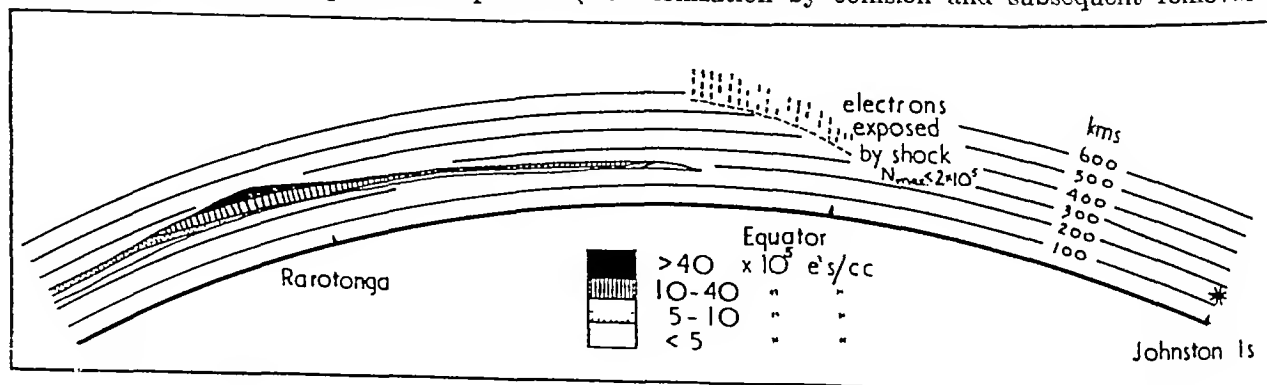


Fig. 1. The spatial form of the ionospheric disturbance as deduced from the Rarotonga ionograms for the event of August 1.

attachment or re combination in a region of relatively high gas pressure

However, it does not seem possible that the main body of the gaseous shock wave travels in the region where the ionospheric disturbance is observed (200-550 km height); for the compression ratios of a shock wave of this velocity are insufficient to produce the observed ionization, and, moreover, there is not enough gas at this level to explain the extended front. The apparent velocity at Campbell Island is below the velocity of sound at F region height, while the characteristic form of the disturbance is maintained (increase in electron density with subsequent decrease in both density and height—no complete electron removal at this distance). Instead of a simple shock, we seem to have a super-sonic surface wave of vortical extent much less than the wave-length, and the very high compression ratios producing the observed ionization are on its upper boundary. We do not feel competent at present to discuss this wave further.

As will be seen from Fig 2 A, many ionospheric stations are in regions where they may have recorded the characteristic movements associated with the wave. Here is an ideal opportunity for international co-operation in an important study on atmospheric properties.

This work will be reported more fully in the *N.Z. Journal of Geology and Geophysics*

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Geomagnetic and Ionospheric Phenomena associated with Nuclear Explosions

NUCLEAR explosions at high altitudes were carried out at Johnston Island (geographically $16^{\circ} 7' N$, $169^{\circ} 42' W$, geomagnetically $14^{\circ} 3' N$, $256^{\circ} 5' E$) at 10:50 G.M.T. on August 1 and at 10:30 G.M.T. on August 12 1958¹. Auroras associated with these explosions were observed on both days at Honolulu² and Apia³. Apia auroras on August 1 have been discussed by Cullington⁴, Fowler *et al.*⁵, Kellogg *et al.*⁶ and Elliot *et al.*⁷. In this communication geomagnetic and ionospheric effects associated with these events are described from the International Geophysical Year obtained at various stations in the Pacific area and the American continent.

Immediately after the explosions, magnetograms showed sudden unusual variations at five stations in the central Pacific—Honolulu, Palmyra Island, Fanning Island, Jarvis Island and Apia. The variation at Honolulu had the form of an intense bay disturbance. The variation at the other four stations was somewhat like an unusually short-period magnetic storm (about 1 hr) with a sudden commencement. Moreover, the sudden commencement at Apia showed an initial short reverse impulse (SSC*) as reported by Cullington⁴. These geomagnetic effects occurred similarly for both events, although the magnetic storm on August 12 was smaller than that on August 1 probably due to the lower explosion height.

These associated geomagnetic storms indicated that counterclockwise circular electric currents were

formed in the vicinity of Johnston Island immediately after the explosion, due to the dynamo effect caused by winds of charged particles which moved radially outward from the centre of the explosion. In other words, if the wind velocity due to the explosion in the 80-100 km level became of the order of 100 m/s and the electrical conductivity increased by the order of 10 times due to high energy particles and X rays, the associated counterclockwise electric currents in the vicinity of Johnston Island would have been sufficient to give the observed magnetic variations even at places 1,800-2,200 km distant, such as Honolulu, Palmyra, Fanning and Jarvis Islands. The geomagnetic effects observed at Apia could have resulted from these circular electric currents and an increase of the electrical conductivities in the 80-100 km level caused by β -decay electrons coming along magnetic lines of force from Johnston Island.

The maximum geomagnetic change at Honolulu occurred around the time at which a shock wave from the explosion arrived at Maui, as mentioned below. It is possible, therefore, that there was an additional effect increasing the intensity of the electric currents just at the moment when the shock wave hit. This could have been caused by a dynamo effect resulting from the shock wave.

At the Maui Ionospheric Station in the Hawaiian Islands a sudden increase of f_{min} (the minimum frequency of the observed radio echo) was observed at 10 50 22 ± 7 G.M.T. on August 1 lasting several minutes, and again at 10 30 37 ± 7 G.M.T. on August 12 for a few minutes. These changes were similar to a solar flare effect. However, since they occurred during local night, they must have resulted from the explosions. Probably they were caused by ionization in the D region by X rays from the blasts.

On August 1 a peculiar oblique echo began at Maui 13 min after the explosion and lasted until 11 12 G.M.T. when it was completely blanketed by increased ionization in the D region. This phenomenon may have been due to a shock wave caused by the explosion. A no echo phenomenon called a 'blackout' began at 11 12 37 ± 7 G.M.T. about 22 min after the explosion, and continued until 13 20 G.M.T. During this time a faint F -echo occasionally appeared. After 13 20 G.M.T. the F_2 layer gradually appeared and recovered to normal.

At Maui, between 10 50 G.M.T. and 10 59 G.M.T. on August 12, both the height and the critical frequency of the F layer decreased abruptly. At 11 03 G.M.T. a stratification appeared in the F layer and showed an unusual sequence of changes. This sequence indicates that an irregular ionization in the F layer, caused by a shock wave from the explosion, was propagated horizontally over Maui from the direction of Johnston Island. The estimated speed of the shock wave is about 0.9 km/s for this event, and 1.3 km/s. for the event on August 1. The wave motion created repeated irregular ionizations in the F layer until a blanketing occurred. A blackout occurred at 10 00 G.M.T., 5 hr 30 min after the explosion, and lasted 2 hr. Even after that time there was severe absorption until 5 00 G.M.T. on August 13. The behaviour of the ionospheric storm of August 12 was in general similar to the ionospheric storm of August 1. On August 12, however, the onset of the blackout was slower and the duration of the radio wave absorption was much longer in spite of a smaller geomagnetic effect. The lower explosion height and the daytime onset of the blackout on August 12 may have been responsible for these differences.

Rarotonga also showed explosion effects in the ionosphere for both events. However, other ionospheric stations—Adak, San Francisco, Washington, White Sands, Huancayo, Godley Head and Okinawa—did not show any certain explosion effects. Accordingly, it is concluded that direct explosion effects on the ionosphere and the geomagnetic field occurred over an area in the central Pacific, roughly the region 170° E– 150° W and 40° N– 22° S. Radio signals from Honolulu (10 and 15 Mc/s) and from San Francisco (13.75 Mc/s) received in Japan showed sudden drops⁷ after both explosions. These were due to radio absorption in that central Pacific region.

From the present study of these geomagnetic and ionospheric effects, the explosion height is estimated as 70–80 km on August 1, and about 40 km on August 12, although the *New York Times* simply reported it as 100 miles on August 1 and lower than that on August 12.

In addition, three other nuclear explosions that occurred in the south Atlantic on August 27, 30 and September 6, 1958, at about the 480-km level, were considered. No remarkable geomagnetic and ionospheric effects directly associated with these blasts could be detected in the normal magnetograms or ionograms.

Full details of this work will be published in the *Journal of Geophysical Research*. I wish to express my thanks to Dr W O Roberts and Mr A H Shapley for their kind help, and to Mr D B Bucknam for his considerable assistance. I am also grateful to the Boulder Laboratories of the National Bureau of Standards for an appointment as guest worker and for extending to me their facilities. I wish to thank the International Geophysical Year Data Centers A for Geomagnetism and the Ionosphere for the use of data. This study was supported by the National Academy of Sciences as part of the International Geophysical Year Programme with assistance from the Ford Foundation.

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Magnetic Effects Resulting from Two High-Altitude Nuclear Explosions

ON August 1 and 12, 1958, two nuclear devices were exploded in the upper atmosphere above Johnston Island in the North Pacific. No exact information is available to us regarding the heights of the explosions, but it is believed that the first explosion was higher than the second. Unusual magnetic effects, mentioned previously by Cullington¹, were recorded after both explosions on magnetographs at Honolulu, Palmyra Island, Fanning Island, Jarvis Island and Apia. Fig 1 shows the location of these observatories.

Vector diagrams of the variations in a horizontal plane are shown in Fig 2a and b. Fig 2a refers to the first explosion, and Fig 2b to the second. The effects at Palmyra, Fanning and Jarvis are very

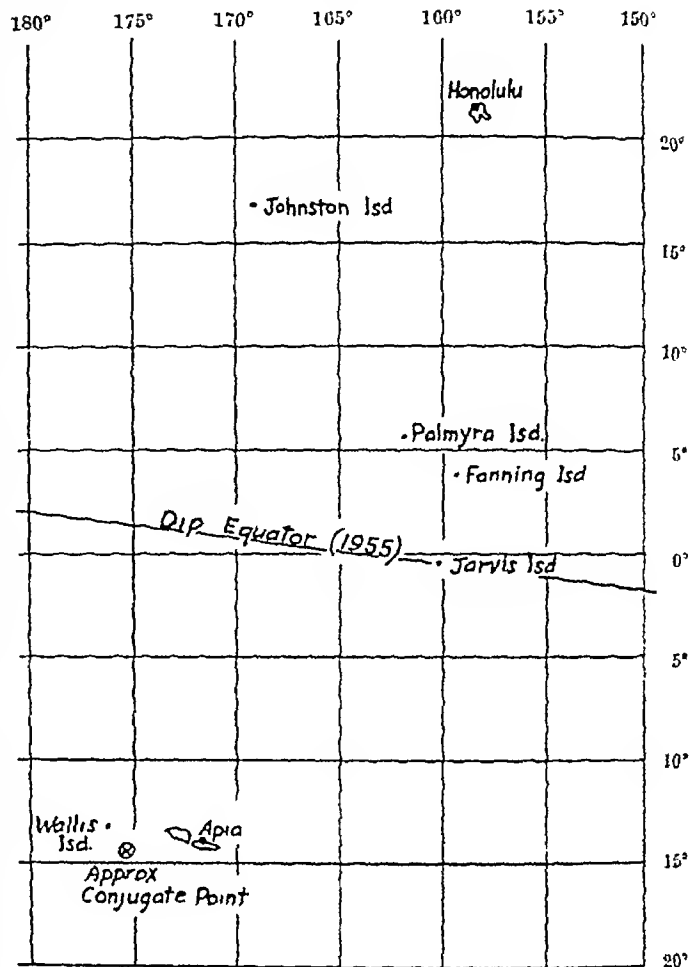


Fig 1 The region of the Pacific showing islands where unusual magnetic effects were recorded

similar, and only the Jarvis Island diagram is presented here. Variations in a vertical plane are not illustrated, since the only important effect they reveal is a marked downwards movement in Z at Apia at about 10.55 GMT, following the second explosion.

An examination of these diagrams has led us to classify the effects into four phases—initial, second, main and final, as labelled in Fig 2a and b.

We suggest the following broad interpretations.

Initial phase A hydromagnetic impulse affected by dispersion, corresponding to the Alfvén wave postulated by Kellogg *et al*.²

The front edge travels faster than 10^8 cm/sec and the time of the maximum corresponds to the speed of a transverse hydromagnetic wave of frequency 1 c/s travelling parallel to the magnetic field³. Across the lines of force, the impulse travels at about the same speed, but suffers greater damping.

Second phase Produced basically by the transport of individual β -particles⁴, photoelectric and Compton electrons, and possibly ions along the line of force from above the point of the explosion to the conjugate point.

As the shock wave and fireball move upwards, more and more individual charged particles can make their escape. Radioactive decay of escaping high energy neutrons probably broadens the region over which the transport occurs.

As well as those magnetic fields due directly to the travelling particles, dynamo effects are caused by

(Continued on page 51)

BRITISH ASSOCIATION MEETING IN YORK

THE PROPER STUDY OF MANKIND IS MAN*

By SIR JAMES GRAY, CBE, FRs

President of the British Association

I

IN the public mind, scientists are largely associated with the study of physical systems and practical problems: they are not directly concerned with moral principles nor are they responsible for the social repercussions of their discoveries. But it is impossible to be a scientist without being a human being and recognizing that social life depends as much on moral principles as on scientific knowledge. So far as science is mainly concerned with our material environment it tends to isolate itself from the main factors which determine human behaviour. So far as the humanities are mainly concerned with Man's reactions to past environments, we cannot be quite sure how far their judgments are relevant to modern life. Such limitations will not be overcome by keeping our own particular type of knowledge in a water-tight compartment; the sciences and humanities should seek common ground. Hence the title of this address.

During the course of years the need for a wider social outlook in science has been reflected by two important extensions in the range of the British Association's interests. It now includes the social as well as the natural and mechanical sciences, and it is more and more concerned with the dissemination of scientific knowledge to the whole community. But the wider the field and the larger the audience, the more difficult the task of presentation becomes. Scientists find it more and more difficult to keep abreast of all the main lines of development within their own subject and almost impossible to know what is happening in other fields; we become more and more specialized and less and less able to see the wood for the trees. It might be said that one of the Association's most important functions is to bridge the gap between its different sections. In addressing the Association, its president has to decide whether he should speak as a specialist and make little or no attempt to relate his theme to wider issues, or whether to stray into unfamiliar fields, and run the risk of scientific, economic or political criticism? Perhaps rashly I have chosen to face these dangers, by trying to look at man from a biological point of view and to suggest how the picture might—here and there—merge into a wider background. But before doing so I would like to touch on two quite general topics.

First one of the most important social aspects of modern science is its repercussion on international relationships. Here there will always be potential

danger and waste of human effort until individual nations can be persuaded to think in terms of the welfare of humanity as a whole. A scientific approach to such problems must be one of dispassionate analysis, but we shall not make much impression on public opinion so long as men's minds are biased by fear and suspicion, frightened or angry politicians like frightened or angry animals, cannot be trusted to react wisely. There is not the slightest doubt however, that the discoveries of physics have frightened mankind and that there are far too many intelligent people looking askance at science and wondering where it is leading them. In trying to link the sciences to the humanities our primary objective should be to depict man's position in the world of Nature as a source not of fear or doubt, but of courage and inspiration. Our second main objective should be to demonstrate the place of science in a general philosophy of life. To be of real value such a philosophy must rest on knowledge and experience which have already proved acceptable over a very wide range of local environments and national interests, and it must at the same time, be closely concerned with problems of everyday life. In these respects science is unique. Except so far as they are subject to political restraint scientists of all nations co-operate in solving Nature's jigsaw puzzles, and as Prof. A. V. Hill said at Belfast, 'The fundamental principle of scientific work is the unbending integrity of thought, following the evidence of fact wherever it may lead within the limits of experimental error and honest mistake.' This attitude of mind is not peculiar to scientists: it is common to all who have a respect for the truth. But in the fields of law, language, history, literature and, above all, politics, our general outlook and our individual range of knowledge depend to a very dangerous extent on local environment and national tradition. By freedom from such limitations science provides ground—perhaps the most solid ground—on which to base a wider range of co-operative effort. But the gap between a scientific and a humanitarian outlook cannot be bridged by the statistical laws of physics and chemistry; we are forced to apply the less precise, but not necessarily less important principles to be derived from the world of living organisms. The challenge is therefore, to the biological sciences, especially those which deal, at the borderline of sociology, with the behaviour of organisms and their relationship to their environment. Can they yield broad principles which are applicable to man or must scientists be content to see the law of the jungle take its course except in so far as it can be restrained by humanitarian effort? The answers to such questions may well decide how far science can claim to be of direct cultural significance.

* Presidential address delivered in York on September 2 and appearing in the September issue of *The Advancement of Science*.

II

Man's position in the world of Nature is brought most sharply into focus by the concept of natural evolution. Cosmic, biological and human evolution can be regarded as phases in a continuous natural process—and, from this point of view, astronomy, geology, biology, archaeology and history form a continuous spectrum of knowledge. To pass from a primeval nebula to a modern man without any sudden break in continuity of thought gives a feeling of intellectual tidiness, but quite apart from this it helps us to visualize man against the background of his past and to regard him as Nature's supreme masterpiece. At the same time, he must not get too big for his biological boots or tend to exaggerate the gap between himself and the rest of the animal kingdom. No animal can manufacture aeroplanes, Asdic or radar, but the prize for aeronautics must go to the shearwater which navigated the Atlantic without compass or chart, while Asdic has an extremely efficient prototype in the vocal cords and ears of bats. By surrounding themselves with an electric field, some fish (for example, *Gymnarchus*) can—in total darkness—detect foreign objects in the surrounding water with very remarkable precision. The weight of the mechanism involved—including the animal's brain—amounts only to a few grams, a man-made instrument of comparable performance would involve at least a ton of highly complex electronic machinery. In fact, as delicate and precise pieces of machinery, man's inventions have not yet reached the standards of those produced during the natural course of biological evolution. No laboratory in the world can compete with the biochemical skill of even the smallest living organism. On the other hand, man can claim that within a few centuries he has produced things for which Nature required many millions of years, but we need not feel in the least ashamed of the older members of our evolutionary family—we have still a great deal to learn from them.

To visualize man's position in the animal world, it may be useful to define his main diagnostic characters. He is a highly gregarious bipedal mammal with unspecialized limbs but a very large brain. He is the only animal which has developed the symbolisms of speech and writing and he may well be the only animal capable of rational thought. He is, therefore, the only organism which can learn on patterns of acquired learning from one generation to another. To these advantages he owes his dominant position in the world to-day. They have enabled him to exploit his environment and increase his numbers and range of distribution far more quickly and far more extensively than any animal of comparable size. He has eliminated some of his competitors and exploited others for his own use, but the time has now come when different races of men are competing with each other within the closed arena of a limited environment, and it is not easy to see where it will end. There is nothing equivalent to this in the inanimate world, but, when a biologist looks at the general trend of events, he is inclined to say, "Where have I seen something like this before, what is it due to, and how does it usually end?"

Of the many points of view from which biologists can study man, three are of particular social interest. First, what is the relationship between the size of a human population and the resources of its environment? Secondly, what are the

factors which influence man's ability to acquire new patterns of behaviour? Thirdly, what is the significance of the gregarious habit?

One of the first attempts to subject social problems to biological analysis was made by Malthus in 1789 when he forecast the fate of a nation the rate of increase of which was greater than that of the resources of its environment. Malthus did not say that war, pestilence and famine were inevitable, he said that they were inevitable unless people, by voluntary control, reduced their rate of reproduction. The theory of animal evolution by natural selection, enunciated just a hundred years ago by Darwin and Wallace, involves the principle of over-population and introduces the concept of randomly produced mutations. Some of these increase an individual's chance of survival whereas others decrease it, those which best adapt the animal to the conditions of life imposed by the environment survive, the rest are eliminated. The course of animal evolution is not directed by the organism itself, but by the external environment, the animal throws the dice but the environment decides the winning numbers. A persistent struggle within an over-populated environment is an essential condition for evolution by means of natural selection, it is the price which Nature demands for progress. There is no evidence that adaptations acquired during the life-time of an individual animal can be handed on to its offspring, each generation has to take an environment as it finds it and make its own way in the world. There is also the danger of over-specialization, a species which has become very highly adapted to a particular environment may be extremely vulnerable if the environment changes relatively suddenly. The course of human evolution is entirely different. Speech and writing enable each generation to modify and control its environment in the light of experience gained by its predecessors and to hand on acquired benefits without bodily specialization. As soon as man learns to discipline himself to the fact that his environment is world-wide, he can begin to direct the course of his own evolution without the discomforts of over-population. If he fails to realize his powers and allows things to drift, his future seems dark, if he really bests himself, there is much less need to be afraid.

Quite apart from any evolutionary significance, there can be no doubt about the validity of Malthus' argument. Western Europe and North America have followed his advice, but, as stressed by Prof P. M. S. Blackett², the density of population in other parts of the world is far higher than can be adequately sustained by the environment. We can, of course, shrug our biological shoulders and say that different races of men live in different environments and are, therefore, subjected to different intensities of struggle, and it would be comforting if we could be quite certain that it is always the fittest which survive. We cannot salve our consciences quite so easily nor will we escape for very long from environmental pressure. Our own population may remain relatively stable, but our environment expands with almost every new major scientific discovery, and the greater the overlap of the environments of different nations the fiercer is the competition. The result is substantially the same as that of an expanding animal population within a limited environment. These problems lie within the field of Section F (Economics), but they are fundamentally similar to those which arise in animal ecology, it seems just as unrealistic to regard

one race of man as an isolated unit as to study the population of one member of a biological food chain without reference to those of all the others. The writing on the wall is tolerably clear: if man behaves like an animal and allows his population to increase while each nation steadily increases the complexity and range of its environment, Nature will take her course and the law of the jungle prevail.

To see this law in action, it is useful to remember that Nature has made, not one but two, great experiments in the design of social animals. The first was carried out in Mesozoic times when man's mammalian ancestors were beginning to emerge from reptiles. The results of this experiment are represented to-day by the social insects—notably the ants. There are a very large number of different species of ants, none of which interbreed, among them is found a range of complexity of social behaviour which is not only unique in the animal kingdom but which also forms a very remarkable parallel to different races of human beings. At one extreme are species forming small communities, restricted to localized or specialized environments and exhibiting relatively little sub-division of labour between individuals. At the other extreme are large and often aggressive communities with marked differentiation of structure between different grades of individuals, populations of this type display high levels of co-operative effort involving, in some cases, the rudiments of agriculture and husbandry. In all cases, however, ant societies are organized on a straightforward totalitarian basis for the contribution made by each individual towards the welfare of the community is determined from the time of birth: each grade of individual is structurally adapted for predetermined tasks. How far ants can communicate with each other may be doubtful, but it is tolerably certain that members of the same community recognize each other by a characteristic smell, and as the brain of an ant is about the size of the head of a pin, it is perhaps not surprising that ants should attack or kill an individual from another colony with a smell slightly different to their own. It is much less easy to understand why a man, with a brain of an entirely different order of complexity should at times, react almost equally violently to skin pigments slightly different to his own.

But it is not only in respect to individual relationships that the study of ants is relevant to man. Ants are the only organisms which—apart from man—indulge in organized warfare, raiding the nests of other species and incorporating captives into their own society. But perhaps the most striking facts relate to species which have changed their habits and distribution within recent times. Two instances of territorial expansion are known to have occurred in the past 150 years. Early in the nineteenth century an Eastern species (*Pheidole mesocephala*), having spread rapidly over North Africa and South Europe managed to reach the islands of Madeira and Bermuda: in both places it exterminated the smaller native races. Meanwhile, a similar policy had been carried out by another species (*Tridomyrmex humilis*) from the Argentine which, having landed at New Orleans, very rapidly overran the southern United States, in due course it too reached Bermuda, where it proceeded to eliminate *Pheidole*. In the world of ants there is no place for small peaceful communities unless they can isolate themselves effectively from larger and more powerful neighbours, nor does there seem any lasting peace between large aggressive communities. Solo

mon's advice has, I suspect, been misinterpreted. It should read "Consider the ants, and, if you use your intelligence, you will see how *not* to deal with international problems."

Having designed the ants, Nature waited for about 150 million years before embarking on her second or human experiment. She waited, in fact, until it could be carried out with a species in which an individual's contribution to society was no longer based on inherited structural characters but on the power of intercommunication with other individuals. In other words, until man's brain had reached a level of development which enabled him to control his environment, and to deal rationally with the sub-division of labour between individuals and with the distribution of natural resources between different groups of individuals. At the same time she arranged that such groups should not be physiologically isolated from each other. Different races of men can interbreed or they can, if they wish, come to mutual agreement about the distribution of world resources between different nations. The first policy would seem to lead to a World State with uniformity of social pattern and of material interests: the second policy involves territorial limitations and economic agreements. Both, as we know only too well, involve great practical difficulties. All the same, men really ought to be able to do something better than ants.

The second basis of comparison between man and animals concerns the factors which control his behaviour. The past fifty years have produced a very great increase in our knowledge of animal behaviour and about the factors which control the acquisition of new patterns of response. For present purposes, however, attention may be focused on two problems: the extent to which animals can profit from extraneous instruction and the extent to which they are able to learn for themselves. The first of these fields is explored by means of the conditioned reflex technique, whereby an animal learns to associate a specific visual, or other sensory stimulus with forthcoming food or impending danger. In order to establish this result it is necessary to conform with five basic principles, all of which have their counterpart in the training of human beings:

(i) The response expected from the animal must not be unduly complex: the animal must be able to reach the food or escape the danger by making reasonably simple movements. In other words the problem must not be too difficult. (ii) The lesson must be presented to the animal under conditions which ensure freedom from extraneous disturbance. It will not learn if its attention is constantly diverted by other changes in its environment. (iii) The problem must be presented to the animal on an adequate number of occasions: the more frequent the lesson, the fewer the mistakes become. (iv) There must be an 'incentive to learn'—a 'reward' for success or a punishment for failure. Further the 'reward' must be related to the needs of the animal. (v) Finally, the experimenter must possess adequate skill and patience. The ability of an animal to learn depends to a very large extent on the personality and enthusiasm of the teacher.

These five principles apply equally well to the education of human beings if we make suitable allowances for increase in complexity of the lesson to be learned and in the nature of the incentive to learn. But we can go a little further for, as with men, different individuals of the same animal species learn at very different rates. On the other hand

there does not seem to be any clear correlation between an animal's ability to learn and its position on the evolutionary tree. It is possible to trace the structural evolution of the human brain through each of the main classes of vertebrate animals, the large paired homispheres arose in the Devonian lung-fishes and the cerebral cortex in the early Permian reptiles. It would be very convenient if step by step with an increase in size and complexity of the brain it were possible to trace a corresponding increase in complexity of behaviour and in ability to learn. Unfortunately this is not the case, some fish, without hemispheres or cortex, exhibit behaviour patterns which seem just as complex as those of reptiles or even of some mammals. In due course this difficulty will be resolved but for the time being one can only say that there seems to be one feature common to all species which learn easily, namely, a vivacious but not unduly excitable temperament—fish, rats, monkeys and children are all interested in their surroundings, they have a natural tendency to explore their environment and they are interested in anything new or strange, they are all, perhaps, potentially good scientific observers.

But the value of the instruction given to human beings by a teacher is largely judged by the extent to which it enables a pupil to make use of his acquired knowledge and to go on to learn more by himself. Within the animal world there is very little evidence to suggest that experience acquired from one pattern of environment or from one problem can be readily applied to subsequent ones of somewhat different nature. An animal's own approach to a problem, like that of a very young child, is very largely one of random exploration, having found the solution by chance the number of ineffective responses on future occasions becomes less and less until the correct response is stabilized.

How far animals display evidence of the higher levels of mental analysis associated with 'intelligence' in human beings is not too clear, for it is extremely difficult to subject intelligence to an agreed standard of measurement. When judged by human standards, the I.Q.'s of all animals are, undoubtedly, very low, but it may be that we are not always setting them quite the right type of examination.

Although it is difficult to detect an increasing capacity to learn with an increase in size and complexity of the brain throughout the main classes of vertebrates, it seems clear that there is a substantial increase in learning ability as soon as an animal's brain reaches a level of structural complexity comparable with that of man. The young chimpanzee, like a human baby, is typically a friendly playful creature dependent on, and with an affection for, its mother. But as it grows up, it begins to show marked signs of individuality, some become morose, unfriendly and vicious, others retain a friendly disposition towards their neighbours and a co-operative attitude towards human teachers. The ability to respond to training shown by the latter type of individual is, of course, very remarkable, but when left to itself, a chimpanzee seems to rely on an initial process of trial and error. Like many other mammals, it can give audible and visible signs of fear, anger or pain, but there is no evidence that a chimpanzee can make audible or visible signs which other individuals associate with specific material objects, the mental development of the adult ape seems roughly equivalent to that of a human baby before the latter has learnt to speak. Nothing can disguise

the enormous difference between an adult ape and an adult man in ability to learn and to control their environments, but it might be argued that a relative test of the brains of an adult ape and of an adult man, as computing instruments, should be conducted on the basis that neither pupil nor teacher should be allowed to speak, read or write, the gap between animals and men might narrow very appreciably.

The third and perhaps most important biological aspect of man's behaviour concerns the gregarious habit. Here again the distribution among vertebrate animals is curiously unrelated to their evolutionary history, it is well marked in certain species of fish, birds and mammals, but absent in others. In some cases the existence of a herd or flock is clearly of survival value, a pack of wolves has a wider choice of food than an individual operating by itself. But, it is not always clear why one species should be more gregarious than another to which it is closely related. In the present state of knowledge, it may be safer to say that some animals are restless or uneasy unless in close proximity to individuals of the same species—that they have, in fact, a deep-rooted antipathy to isolation or loneliness. The resultant grouping establishes the herd as a unit which responds as a whole to an external stimulus applied to one or a few individuals. The response is most clearly defined when the stimulus evokes an emotional reaction of fear or anger in the individuals directly concerned, and one of the most distinctive features of herd behaviour is the speed at which these emotions spread throughout the community. If certain individuals are more highly susceptible than others to external stimuli, the response of the group is determined by the most timorous or the most belligerent members of the community. The majority of the herd subjugate their own individual behaviour to that of a few, and in the long run individuals benefit by greater security from predators or greater certainty of obtaining food. If an individual is unduly insensitive to emotional stimulation by its neighbours, it is likely to be eliminated by natural selection—the sheep that walks by itself gets eaten and the solitary wolf may starve. These principles were applied to the analysis of human behaviour by Wilfrid Trotter⁵. In order to avoid physical or mental isolation, men are prepared to subjugate their own immediate needs or predilections to those of society as a whole. Anti-social activity is kept in check by fear of intellectual or physical isolation, feelings of increased security and greater freedom from personal doubts and fears are set off against loss of individual freedom of action. How far psychologists have developed or rejected Trotter's suggestions I do not know, but there can be little doubt that they opened up a useful biological approach to sociology by suggesting that our instinctive reaction to something new or strange is, as in animals, to conform with our neighbours, and that, at moments of crisis, it is better to follow a leader than rely on personal judgments. These and allied problems belong to Section J (Psychology). All I wish to stress is that the phenomena of mass psychology in man, like other aspects of his behaviour, have their roots far down in his evolutionary history.

Perhaps the most striking difference between the social habits of man and those of animals is the existence of a hierarchy or grading within human society. Only in a very few cases does this appear to exist within the animal kingdom. The nearest

approach seems to occur in birds, a flock of jackdaws feeding in a restricted area resolves itself into a well marked order of feeding priority. Lorentz has recently reported that if a high ranking male decides to mate with a low ranking female, the latter rises in social status and feeds with her husband, all this sounds reasonably familiar to human ears.

This is perhaps as far as a zoologist ought to go in trying to view mankind through biological spectacles. But one does not need to be a professional biologist to appreciate that the rates of change in the pattern of human behaviour and in the nature of our environment have, during the past five thousand years, been incomparably greater than those of any other organism at any period of its history: our clothes, houses, habits and social organization change with successive generations. In fact, if one were forced to select the organism which best displays the phenomenon of persistent evolution one would undoubtedly choose man. I have tried to show that the broad principles which relate the size of human populations to the resources of their environments and those which govern an individual's ability to learn from personal experience and so adapt himself to his environment are qualitatively similar to those which apply to animals. On the other hand, man is—as I have said—unique in that he is—or can be—the master and not the slave of his environment, and the story of his later evolution is told in terms of social and economic history.

In suggesting further points at which biological principles seem to be applicable to the evolution of human society a zoologist can only look towards Section H (Archaeology and Anthropology) and hope that his spectacles are not completely out of focus. In its very early stages human society must have been organized into quite small units each dependent on the natural resources of a small circumscribed environment. The discovery of fire and development of agriculture must have increased the range of the environment and the optimum size of the population required for its exploitation, while the stability of the group would become more and more dependent on the maintenance of an effective sub-division of labour. The larger the population and the greater the degree of specialization the greater the limitations necessarily imposed on individual freedom of action. A now and very important integrating factor seems to have come into action when natural phenomena became linked with supernatural concepts—fear of isolation or reprisals from fellow men being reinforced by fear of a superhuman agency and a sense of greater security inspired by reliance on supernatural support. Such beliefs had no material basis but they would be the cement which held society together and, as such, be of immense survival value. But it is difficult to avoid the conclusion that such beliefs like scientific theories, must undergo change as man's knowledge increases and his environment alters. From this point of view, it is not easy to regard any one belief as an expression of absolute and unchanging truth. It may be argued that such things lie outside the orbit of the British Association but if science is to be of direct cultural significance, it cannot shut itself off from one of the main factors which have influenced men's attitude to social problems. A recent issue of *Nature* contained a leading article on the proceedings of the last Lambeth Conference, it must have been a very long time since an Archbishop of York addressed such a Conference in language which scientists could so readily understand. Against such a background,

the sciences and the humanities ought to be able to find something in common.

III

It is easy to say that science should be welded to the humanities, but much less easy to suggest how this should be done. Each of us has different views according to his own particular interests. I confess that my own approach is based on personal experience. About fifty years ago I chose to specialize in biology and from time to time I have been asked, 'If you had known that you would spend a good deal of your later life studying the movements of animals, what subject apart from biology would you have read at school and at the University?' The answer is simple. I would have read physics, chemistry, mathematics and mechanical engineering. The moral is that no young scientist should be allowed to forget that new discoveries tend to arise from the borderland between different subjects where the discipline of one is applied to another. Had I appreciated this I would have been a much better biologist, but whether I would have been a better human being is another matter. If I am asked the 64 thousand dollar question, 'Had you known that you would have had to adjust yourself to a rapidly changing and somewhat uneasy world, what additional training would you like to have had?' I think my answer would be that I would like to have been trained to think dispassionately about social and political affairs in the light of experience drawn from the past and to have been taught to appreciate beautiful things. But could I have acquired this knowledge while training as a scientist? Perhaps not but I still think that I could have been shown a wider picture. Having been taught to visualize the spectrum in terms of the wave lengths of light, could not I have been encouraged to learn a little about colour as a source of aesthetic pleasure? Why did I learn about the properties of iron and carbon without reference to the industrial revolution? I might even have developed a taste for the classics if I had known that Aristotle had written a very good text book of zoology. Perhaps I expected too much in hoping to appreciate an artist's view of Nature from the point of view of the scientist. But I am not completely convinced. A scientist's attitude towards his observations does not seem to me to be so very different from that of a poet towards his words or a painter towards his colours, isolated observations have no more value than single words, it is only when they fit into a satisfying pattern that the scientist feels he has achieved his end. This analogy may be unconvincing, and if it still seems difficult to combine the vision of the artist with the outlook of a scientist. I can only suggest that Leonardo de Vinci and Sir Christopher Wren seem to have had pretty good shots at it. It would be very interesting to know the sort of training they had in early life.

But a plea for a wider outlook in the teaching of science is nothing new. It was largely the background against which Section J (Education) came into being and it was urged again and again by Sir Richard Gregory. Since then there has been much discussion and many reports. In 1933 the declared aim of the London County Council was that they "wished their pupils to obtain a broad view of nature, to study Mankind and his environment from various standpoints more particularly from the point of view of both the biological and physical Sciences. In 1946 the Advisory Council for

Secondary Education in Scotland was even more explicit "During the earlier secondary years at least, the study of man in his world, like the study of science, is a unity which should not be broken by any sharp division into 'subjects' the theme must be one" Only last year (1958) a Committee of the Science Masters' Association urged that "The schools have the duty of presenting Science as part of our common cultural and humanistic heritage, it should be taught in harmony with and not in opposition to the various Arts subjects" It seems fair to assume that this is a goal towards which we would all wish to strive, but when we try to approach it the road proves extremely hard and most of us, in practice, fall by the wayside

We cannot shut our eyes to the fact that our national economy depends on our ability to make and exploit new scientific discoveries If we wish to maintain or extend our standards of material comfort, we must have more professional scientists and highly trained technicians, and we must be prepared to devote an adequate fraction of our educational effort to get them But highly trained specialists form only a very small proportion of the population, and we may be paying for them in very hard currency if we have to deny to a very much larger fraction of the community a reasonable chance of "seeing life steadily and as a whole" A democratic society has to decide how much of its total educational effort should be devoted to an ever-increasing standard of living, and how much to raising the intellectual standards whereby the majority of the population forms its judgments on matters which are susceptible to personal prejudice or political propaganda It is not easy to assess the factors which mould public opinion, but a recent inquiry sponsored by the Nuffield Foundation and the B B C indicates relatively clearly that the attitude of mind of an individual towards a changing environment is directly related to the nature and extent of his full-time education and that it is this training which largely determines, in later life, his response to other potential sources of education—such as libraries and broadcasts If we wish to awaken a widespread interest in science, or—still more—wish to contribute toward the formation of an enlightened public opinion, we must sow our seeds in the schools and in organized centres of adult education In the latter field, the Area Organizations of the British Association are of fundamental importance as authoritative and coherent sources of information for an increasing fraction of the community By working with other organizations they can make a very definite impact not only on the scientific but also on all aspects of public opinion

But the key to the main problem lies in the schools, and the responsibility resting on school teachers can scarcely be exaggerated Too many are asked to do two jobs at once—to provide a training for potential specialists, and at the same time give a training which will best equip the average boy or girl for later life If we are to pay more than lip service to the belief that a good all-round education is the best means of raising the intellectual level of the community, we must recognize that our most urgent need is for good general practitioners in the art of education Really inspired teachers working with adequate but simple equipment will achieve more for general education than specialists in highly equipped laboratories But the scales have been heavily weighted in favour of specialization Almost exclusively, our universities are producing specialists

Some of these return to the schools, where they in turn teach on a specialized front So the spiral of specialization has gone on It is only natural that able teachers should get an intellectual stimulus by preparing boys and girls for scholarship examinations and so providing recruits for fields of research in which they themselves are interested, but it is by no means clear that their work is necessarily more important, or more difficult, than that of those whose primary object is to persuade people that they cannot live by bread alone If we really believe in general education, we must produce and encourage the right type of teacher No man or woman in their senses enters the school-teaching profession for financial gain, but a community which rates thirty inspired school teachers as equivalent to one high-grade comedian or film star may well deserve a very unhappy fate A benevolent dictator would make school-teaching the most highly respected and the most highly paid of all professions, and the Ministers of Education the most important officers of government; but, in both cases, he would demand a very high level of performance We must do the best we can without him

The value of an educational system can perhaps be judged by the extent to which it leaves people with a desire to know more about the world at large and a feeling that this can be satisfied, at least in part, by personal effort To meet a constantly changing environment the general pattern of teaching must be constantly under review If a curriculum is allowed to degenerate into a series of isolated subjects with little or no immediate bearing on everyday life, the result can, perhaps, best be described in words which I think the president of Section L (Education) will recognize "When far too many boys and girls will carry away from school little more than gobbets of ill-digested knowledge and a distaste for what has yielded so little"

But, as I have said, it is easy to talk and to criticize, it is much harder to plan for action So far as science is concerned, the British Association might approach the problem of general education in the three familiar stages of research, development and production The first step would involve an assessment of the evidence if the Association's judgment were given in favour of a wider, and perhaps more biological, outlook on education, it should do all it can to see that it is put into practice on a limited front and—in the light of experience—allowed to spread gradually into full-scale production All this would involve very far reaching reorganization of schools and universities While Oxford and Cambridge shiver on the brink of optional Latin, the University College of North Staffordshire is swimming the Hellespont by insisting that all students should, during their first year, survey the whole field of knowledge as a coherent picture before proceeding in three subsequent years to specialized training This is, in my opinion, one of the most important and courageous educational experiments in our times for, if it succeeds, a great number of our major difficulties will be resolved

On the other hand, if 'general education' and 'general science' are condemned as 'smatterings of everything and a knowledge of nothing', and if the concept of a central theme around which all parts of a syllabus would revolve be found to be illusory, it is high time we stopped talking about the broad cultural value of science and concentrated our efforts on widening the interests of specialists during or

after their technical training. Much can be done by relatively formal teaching but—if I may judge from personal experience—more depends on the extent to which students are given the time and opportunity to educate themselves by contact with men and women with entirely different interests and outlook from themselves. This is the great strength of the older residential universities, but, here again, they may have something to learn from North Staffordshire.

But the older we get the less inclined we are to go back to school. If we want every member of the population to keep in touch with what is going on in the scientific world and to realize its impact on their lives, we must rely on the Press and on the broadcasting authorities. Neither of these is primarily an educational medium, in both cases the main objective is to put science across in a form that readers and listeners find interesting. In respect to music, the BBC has been outstandingly successful; other fields of broadcasting may be less amenable, and it is not altogether easy to know how far an increase in factual knowledge concerning a number of isolated

fields of science enables listeners to appreciate the broad social and international implications of science as a whole.

But when all is said and done, science can only play its full part in furthering the welfare of mankind if it is used at a very early stage of education as a means of encouraging a dispassionate but optimistic attitude towards all aspects of human affairs. To move from national traditions and aspirations to others based on international welfare may prove less painful if we are prepared to look on men and all his problems as a phase in the evolution of the universe and if we have the courage to believe and to teach that he can be by means of his intellect control and direct his own evolution and destiny.

¹ See Blackett P M S *Advancement of Science* 15 36¹ (1959)

² Presidential address to the British Association (1952)

³ Presidential address to the British Association (Dublin 1957)

⁴ Hacking C P *Of Ants and Men* (1945)

⁵ *The Hard Instinct in Peace and War*

⁶ *Nature* 152 955 (1958)

⁷ Thirteenth Report of the Nuffield Foundation 65 (1958)

⁸ Proc. B.A. Conference "Science in Schools" (1958)

⁹ Report of the Advisory Council for Secondary Education in Scotland 25 (1948)

SUMMARIES OF ADDRESSES OF PRESIDENTS OF SECTIONS

THE VISUALIZATION OF MAGNETIC PROCESSES

IN delivering the presidential address to Section A (Mathematics and Physics), Prof. L. F. Bates prefaces his remarks with a brief outline of the ferromagnetic domain concept. He then describes the several ways in which the boundaries and surfaces of such domains in single crystal and in polycrystalline materials may be manifested. He shows how the original Bitter figure technique has given results of great value concerning main domain and closure domain configurations. It has provided considerable support for the ideas of Néel and others as applied to the magnetization processes which occur when single crystal specimens of appropriate shape are exposed to magnetizing fields, and has given visual proof of the important effects of inclusions, defects and strains on magnetization phenomena.

The technique has recently been much extended first by Craik's development of a detachable colloid film carrying with it a record of domain configuration which can be examined optically and also in a commercial form of electron microscope. Craik and Griffiths have shown that the film technique can be successfully used to examine fine domain structures on ferrite surfaces prepared by the simple cleavage of single crystal specimens. By using films of over decreasing colloid concentration, Craik found the minimum thickness of a continuous deposit above a 180° domain wall on a cobalt crystal to be 10⁻⁴ cm.

The colloid film techniques restrict the experiments to static observation and to limited ranges of temperature and recently attempts have been made to develop dynamic methods. Perhaps the most successful is the polarized light technique of Lee, Callaby and Lynch, which has been applied to the motion of a domain wall in a thin sheet of polycrystalline

Perminvar, an alloy of approximate constitution Ni₄₀Fe₄₀Co₂₀, which has been magnetically annealed by cooling it in a magnetic field. Davis has followed the motion of such a wall by pick up in a search coil wound on the specimen. Lee, Callaby and Lynch have used the transverse Kerr effect. The specimen is illuminated by a beam of plane polarized light, which forms a small strip on the specimen surface roughly parallel to the wall, and which acts as a light probe. The reflected light is collected by a microscope passes through a Polaroid¹ and is thrown upon the cathode of a photomultiplier. As a domain wall moves across the beam, the intensity of the collected light changes, the change being made periodic by the application of a weak alternating field to the specimen. The current from the photomultiplier is amplified and a signal displayed on a cathode ray oscillograph. By using two light probes a domain wall can be made to move through each in turn so that the velocity of wall movement can be followed. It is found that the velocity is fixed almost entirely by the eddy currents in the specimen.

An electron microscope has been directly applied by M. Blackman and others to examine the stray fields at the edges of ferromagnetic specimens, and in this way it has been shown that the domains in hematite are unexpectedly large. Spivak and his collaborators in Moscow have obtained direct photographs using the secondary electrons released by a primary beam on the specimen surface. They have also used an electron mirror method. Káczér in Prague has used a thin Permalloy probe vibrating above the surface of a specimen to map domains. However, all these methods have to date been less informative than the colloid method and may more readily manifest surface imperfections and inhomogeneities than domain walls, but they may of course be greatly improved in future.

MEDICAL ASPECTS OF COMPLEX CARBOHYDRATES

PROF M STACEY points out in his presidential address to Section B (Chemistry) that carbohydrates play an essential part in the vital processes of all living cells. Their simplest forms, the monosaccharides, are synthesized from carbon dioxide and water in the leaves of living plants by the agency of sunlight and chlorophyll. The chemistry of these photosynthetic processes, including sugar inter-conversions, phosphate transfer and the enzymes involved therein, is now being worked out. Likewise, the mechanisms of the build-up and breakdown of the complex carbohydrates, the polysaccharides, is now well established.

Microbial and animal cells, devoid of photosynthetic pigments, must use the simple sugars as material and energy sources for their own metabolic cycles. The proper carrying out of these cycles is necessary for the healthy condition of every living cell, and in the animal the blood sugar (glucose) balance must always be maintained. For the growth and reproduction of cells and tissue, complex polysaccharides must be built up, for example, to form cell membranes, structure and storage material and colloidal fluids, while the pentose sugars form a part of the genes and chromosomes.

Some of the important processes in which both simple and complex carbohydrates are involved are discussed by Prof Stacey.

(a) *General metabolic processes* These involve digestion of foods and the absorption of glucose and other sugars, they involve the metabolic cycles and the function of enzymes concerned with them. They concern the synthesis and breakdown of glycogen, the conversion of sugar to fat, the biochemistry of muscle action, formation of milk, etc. The hormones insulin and epinephrine are involved in glycolysis. The great medical value of insulin in controlling diabetic conditions is well known. In this field synthetic substitutes for use in diabetes are being actively studied.

(b) *Detoxication mechanisms* Frequently the body needs to get rid of excess toxic substances such as drugs, and it can do this by oxidation processes, coupling up with the sugar acid D-glucuronic acid and then excreting the complex D-Glucuronic acid as an important tissue component.

(c) *Structural components of the body* It is with these substances that we can expect to see great advances in the future, for complex carbohydrates known as mucoproteins and mucopolysaccharides form a large part of components such as bone and cartilage tissue, cell membranes, connective tissue, skin and its ground substance, joint fluids, synovial fluid, eye tissues and fluids, gastric and intestinal mucosa, etc.

These complex polysaccharides have as their building units nitrogen-containing or 'amino'-sugars, hexuronic acids and hexoses, and often, too, acetyl and sulphate residues are present. Associated with the carbohydrate protein complexes is a novel group of 'nine carbon' sugars, the nonulosaminic acids, known as sialic and neuraminic acids. Detailed work on the chemistry and biological importance of these acids is not yet well advanced. Generally, the mucopolysaccharides are concerned with movement of parts of the animal body and thus are important in conditions of arthritis, rheumatism, etc., and with general ageing processes.

(d) *Blood components* Many components of blood contain complex carbohydrates, the red cell surface contains mucoproteins, white cells contain nucleic acids, while serum contains a wide range of mucous substances.

Furthermore, many tissues and fluids of the body such as gastric mucosa, saliva, etc., contain the so-called blood-group factors, which are polysaccharide-amino acid complexes. One of the most important medical developments has been with blood plasma substitutes, where the bacterial polysaccharide dextran has become established as an excellent expander of blood volume. The clotting of blood in the body is inhibited by heparin, a complex polysaccharide sulphate, the action of which can be imitated by other polysaccharide sulphates.

(e) In many other directions carbohydrates are becoming of increasing importance. In the antibiotic field, streptomycin is an important complex carbohydrate, while many others such as puromycin, magnamycin and kanamycin contain amino sugars.

In disease-producing agents, the complex surface carbohydrates play a significant part in immunity studies, and there is a close relationship between carbohydrate structure and immunological specificity. Pyrogens or fever-producing agents from bacteria are also carbohydrates. Mucous substances and the enzymes which destroy them are important in fertilization processes, but little is known at present about the carbohydrates of eggs.

A new branch of carbohydrate chemistry is developing in the virus field, and the necrosis of some tumours by bacterial polysaccharides has yet to be studied in detail.

RECENT DEVELOPMENTS AND TRENDS IN PALÆONTOLOGY

THE past two or three decades have witnessed a remarkable increase in the output of palaeontological research. Most of this has been of a purely descriptive character, often related to the needs of the stratigraphical palaeontologist, but much has been of more general interest, particularly in the borderline fields of taxonomy and evolutionary theory. Prof O M B Bulman attempts in his presidential address to Section C (Geology) to give a non-technical account of palaeontological activities in some of these directions.

Chance plays a large part in the preservation and discovery of fossils, and modes of preservation limit the techniques which can be applied. Hence from the nature of his material, the palaeontologist has less freedom than the neontologist in planning his research, and is often unable to follow some otherwise desirable line of investigation. New material is, however, constantly being obtained, and the scale on which effective techniques are being devised and applied is a distinctive feature of modern palaeontology. Particularly characteristic of the immediately post-war years also have been the many attempts at constructive syntheses of palaeontology and allied sciences.

Palaeontology provides a general and imperfect, though steadily improving, record of most groups of organisms, and in supplying a few true evolutionary series it has given a fourth dimension to the concept of the species. Applying the results of absolute rather than merely relative dating of rocks, it is

beginning to contribute some tentative calculations of evolutionary rates in various groups, particularly among vertebrate animals, and the establishment wherever possible of invertebrate phylogenies will have rewarding results here as in other fields. The problem of evolutionary mechanism is a purely zoological one, but the ultimate proof or disproof of evolutionary theories involving phylogeny, such as protogenesis recapitulation and orthogenesis, also lies fairly within the field of palaeontology.

The major contributions in palaeontology have been made where its limitations have been frankly recognized and its unique assets most fully exploited. These are, of course, the time factor and the historical record of evolution. To bring palaeontological evidence into the evolutionary picture, however, involves a synthesis with genetics, taxonomy and zoology from which is now emerging a new 'science of four dimensional biology'. In such studies, the emphasis has tended to shift from the individual to the population, with the consequent need for statistical treatment, and successful generalizations will call for accurate quantitative as well as qualitative methods of research, but Prof Bulman emphasizes in this address the primary importance of the most detailed and exact morphological investigations which contemporary techniques can provide.

MAN AND THE WORLD'S FAUNA

DR L. HARRISON MATTHEWS, in his presidential address to Section D (Zoology) points out that man has continually preyed on the fauna of the world. The increase in the human population and man's technical skills have enabled him to exploit the fauna with ever increasing destructiveness. It was not until the populations of animals were reduced below the danger point that man realized that they were not inexhaustible. Destruction of particular species has also been due to man's destruction of the environments to which the fauna has been adapted. Human settlement of land and the development of agriculture have caused many animals to be banished from their natural environments.

Man now realizes that breeding fauna in captivity will not alone maintain its existence. He has introduced legislation prohibiting or limiting the killing of certain species and has provided sanctuaries in the form of reserves. It is essential, however, that the conservation be not only applied to the fauna but also to the environments. Basically it is a problem of land management and development, vital to man as a means of producing energy—food and other useful products.

For the conservation of animals specifically for commercial purposes Dr Harrison Matthews gives examples of the recoveries for the fur-seal and the elephant-seal, and how extinction in the Antarctic was prevented by the intervention of the Falkland Islands Government. He also mentions the not so satisfactory history of the whaling industry—the only thing that regulations gained here was to reduce the rate of extermination. In general, the sea fishing industries of the world present many complications so far as conservation is concerned especially the question of replacement of the life giving plankton. On land over grazing is often a serious threat to animals, however, some scientists hold the theory

that in some cases artificial control is unnecessary, stating that it is effected by natural causes in the long run.

Dr Harrison Matthews refers to the population dynamics of certain classes of mammals and gives an account of the catastrophic 'crash' that in variously arrives after a peak in numbers has been reached, especially in vole-plagues. The over crowding of the immediate environment that occurs tends to result in psychological tension which eventually causes dysfunction of the adrenal gland; the breakdown of adrenal function causes the rapid death of the animals.

A recent inquiry shows that in 1958 the world population increased by 47 millions, at this rate, in forty years time the human population would double. It is unlikely, however, that this will occur as the growth of the human population tends to become slower and reach a stable level with the increasing standards of living. If we compare the present build up of population with the cyclic build up of the population of small mammals, it would seem that we are rapidly approaching the peak and the catastrophic crash. Other factors are also likely to control the growth of population, such as atomic war and its radioactive contamination of the atmosphere, social control by inhibiting fertility in either sex or the emergence of new epidemic diseases.

Dr Harrison Matthews points out that the conservation of the world's fauna must be planned on a world wide scale. It must be decided what parts are to be developed for human occupation and what parts are suitable for conserving fauna, already a number of national and international bodies interested in conservation exist, however, as such there has been only little action. He sums up by advising all zoologists to study any aspects of biology of the larger animals before it is too late.

TRENDS IN URBAN EXPANSION

LARGE-SCALE urban growth which was a feature of nineteenth century industrial development in western Europe and eastern North America is the theme of the presidential address to Section E (Geography) by Prof K. C. Edwards. It has continued to the present day, affecting almost all parts of the inhabited world. Recent decades, however, have witnessed a sharp acceleration of the process and urban expansion is now going on at an unprecedented rate. While industrialization remains a primary factor it has come to play a relatively less important part in the crowding of people into cities.

Owing to the lack of a common definition among different countries as to what constitutes an urban population precise measurement of the rate of urban growth for the world as a whole is impracticable. Some idea of its magnitude over the past half century so far as large towns are concerned—that is those of 100,000 inhabitants or more, can be obtained from the figures in Table 1.

Table 1

| | No of towns of 100,000 inhab or more | Size groups (population in thousands) | | | | |
|---------|--------------------------------------|---------------------------------------|---------|---------|-----------|---------------------|
| | | 100-250 | 250-500 | 500-750 | 750-1,000 | More than 1 million |
| 1910-13 | 322 | 200 | 63 | 23 | 4 | 18 |
| 1950-53 | 1,071 | 611 | 209 | 67 | 32 | 62 |

Not only has the number of large towns more than trebled, but also a marked upward trend in their mean size has occurred. The most spectacular evidence of urban growth is afforded by the millionaire cities. There are now about ninety of these vast agglomerations, of which London and Paris were the only examples a century ago, and their number increases yearly. Some 200 million people now live in these huge cities, and the day is not far off when they will shelter one-tenth of all mankind.

Yet the mammoth cities and existing conurbations do not represent the ultimate stage in the process of urban accretion, for in certain instances groups of these tend to coalesce, forming vast continuous urban areas to which the term 'megalopolis' has been given. The outstanding example is the virtually continuous urban belt stretching for 400 miles from Boston to Washington, D C, containing more than 30 million people.

Whether in the older regions of settlement or in those of newer development, the expansion of cities is mainly due to the movement of people from rural areas and from the smaller to the larger towns. The townward drift is primarily the expression of a desire for improved conditions of life. In the process no new equilibrium between rural and urban populations is discernible, for food production, despite a dwindling labour force (except in south-east Asia), is increasingly dependent upon technical advances in agriculture. To-day the essential relationship is that between urban demands and agricultural productivity.

The latest phase of urban expansion has had significant effects upon the individual city. The rising importance of service functions of all kinds has substantially altered the structure of urban employment, the growth of administrative and other non-productive activities has intensified the use of the central business quarter, the demand for office accommodation in particular has increased the pressure on building sites, leading to an acceptance of the tall building for such purposes, often in defiance of tradition, retail services have become hampered through traffic congestion and competition for space, resulting in an increased emphasis upon secondary shopping centres in residential districts. In connexion with these and other changes, the controlling factor is motor transport. Its effects are both centrifugal and centripetal, and the capacity of the city to discharge its functions satisfactorily will increasingly depend upon the solution of problems to which this form of transport gives rise.

HOW MUCH SCIENCE ?

THE recent campaign in Great Britain for increasing the proportion of our human and material resources engaged in science, in all its forms, has been supported by a wide range of arguments, some of which are of doubtful validity. What tests can be applied to determine if and when there is a shortage of scientists? It is with this question that Prof J Jewkes commences his presidential address to Section F (Economics). To the economist the term 'shortage' has an exact meaning. There is a shortage when, at the existing price, the demand is greater than the supply. Although the evidence is scrappy, the indications are that there is no shortage of scientists, in this specific sense, in Great Britain at present. For the salaries of scientists are not at a level nor moving in a direction which suggests

shortage, nor do the latest estimates of probable supply and demand indicate any serious gap between the two.

It is frequently suggested that there is, nevertheless, an 'unmet need', implying that those who exercise the demand for scientists are not sufficiently conscious of their value to the community. Unmet need is an elusive concept, but four reasons have been given for believing that it exists. First, it is said that Britain is lagging behind the United States and the United States behind the U S S R. These international comparisons, when they include the U S S R, are for the most part hazardous statistical exercises with non-comparable material. Even in the comparisons between Great Britain and the United States many obstacles exist, both as to method and materials. It seems to be a reasonable assumption, however, that having regard to their populations, there is no great disparity between the two countries. Secondly, efforts have been made to establish correlations between the rate of change of industrial output and of the number of scientists and technologists in industry. But the statistical material employed here and the deductions based on it both seem to be unsatisfactory. Thirdly, it is sometimes suggested that since some industries spend on research and development relatively more than others, this proves that the second group is lagging. Fourthly, attempts have been made to measure the net gains arising out of expenditure on research and development, the results obtained in this way are interesting but do not support any very spectacular conclusions.

The scale of scientific activities in the community is determined by a very puzzling combination of public and private views, public and private actions and, in the last resort, the striking of the right balance will inevitably be a matter of informed guesswork and of intuition. At the moment the final judgment is probably being distorted by the tendency to exaggerate the part that science has played in raising the standard of living in the past, to over-stress the potential material benefits of the more spectacular recent scientific discoveries, and to belittle the contribution made to economic expansion by skills and capacities non-scientific in character.

THE CRITICAL IMPORTANCE OF TRANSPORT AND COMMUNICATIONS

IN the modern world, transport affects the citizen and the engineer at every turn. In Britain, about 25 per cent of the gross national product is accounted for by transport and communications. Not only is the modern State utterly dependent for its daily bread on transport, but also its competitive power depends largely on its efficiency in operation. Moreover, it is one of the most easily observed aspects of a country's organization and achievement, and it has a psychological as well as a material impact. The subject bristles with technical, economic and political problems, but the aim of Sir Ewart Smith's presidential address to Section G (Engineering) is to express some very general thoughts as a challenge to our sense of urgency.

In the mid-nineteenth century, Britain had the best transport system in the world, this was largely the creation of engineers, who not only invented, designed and constructed in the technical sense but also often organized the business sides of the ventures

they had conceived. When to day, we compare land transport at home and abroad, we must admit that we have not applied either the technology or the money necessary to keep up with the general advance.

Although very recent years have seen some awakening of Britain to its transport needs, a few facts and figures may be mentioned to underline the need for still greater boldness in plans and expenditure.

The projected expenditure of £60 million on new roads and major improvements is no more than the 1939 rate, allowing for the fall in the value of money, though the number of vehicles has grown from 3 to more than 7 million, and is increasing at 8 per cent a year. While attention is now being paid to motor ways, by the end of 1959 only 64 miles will be in use whereas between 1830 and 1850 new railway routes were being built in Britain at an average rate of 320 miles a year. Urban road development lags even more. We have no established centre for training high grade traffic engineers, although the savings to be gained from traffic engineering are immense. An increase of only 5 m.p.h. in average speeds—at present 20 m.p.h. in urban districts and 32 m.p.h. in rural—would give an economic saving of at least £180 million a year and much more as traffic grows.

The railways, too, suffer greatly from past neglect of capital expenditure and technical recruitment. During 1900–55 true capital outlays were very small and as late as 1955 only 0.23 per cent of the employees of the British Transport Commission were qualified scientists or engineers. In comparison in the National Coal Board the proportion was 0.7 per cent and in the Central Electricity Authority 2.9 per cent and in the Atomic Energy Authority 10.0 per cent. The British Transport Commission is making valiant efforts to retrieve the position, and the results are likely to be striking. Nevertheless even bolder thinking is desirable particularly in regard to size of wagons and turn round (wagons now average only 10 miles/day). It must be stressed that in this the users have major responsibilities as well as corresponding opportunities of gain.

In transport abroad and in our newer and progressive industries, scientific engineers play a much larger part than in the road and rail transport organizations of Britain. We need to train more and use them more widely. We must remedy the defects in the transport system of Britain, particularly on the roads, by far greater capital expenditure and by a bolder approach to the technical and organizational problems involved.

ARTIFICIAL ORGANS BIOLOGICAL APPLICATIONS

WE are reminded by Prof. A. Hemmingsway, in his presidential address to Section I (Physiology and Biochemistry), how much the study of isolated organs and tissues maintained under conditions ensuring survival has yielded to the physiologist. These tissues are immersed in, or superfused (a new technique), or perfused with blood, serum or solutions which may be regarded as 'artificial bloods'. A solution in which the ionic concentrations of sodium, potassium and calcium were adjusted to maintain conduction and contraction in cardiac muscle was first introduced by Ringer, but since his day many modifications have been made, including the addition of metabolites such as pyruvate and glutamate. To make a blood substitute for clinical use as an

'expander after haemorrhage or in post operative hypotensive states, dextrans of appropriate molecular size have been prepared and added to these solutions to make them osmotically equivalent to plasma. But so far, it has not been possible, except by employing suspended red blood corpuscles, to make these solutions adequate carriers of respiratory gases.

The introduction of antibiotics and ample supplies of anticoagulants have encouraged and established the use of perfusion and similar techniques for clinical purposes. The 'artificial kidney' which has proved successful in the management of certain types of kidney disorder, is a development of Abell's (1932) vividiffusion apparatus. The principle is that an artery is cannulated and the blood rendered incoagulable, is passed through a 20–30 m length of 'Cellophane' tubing which is formed into a spiral and rotated in a bath of modified Ringer's solution. According to differences in concentration across the membrane, substances will be interchanged between the blood and the surrounding fluid. By this means substances which have accumulated because of renal dysfunction can be removed from the blood, the rate and the extent of the exchanges can be controlled by regulating the composition of the surrounding bath. Ensuing chemical changes in the blood must be followed. Treatment by the 'artificial kidney' is indicated when the pathological changes in the kidney are reversible and the patient's kidneys are likely to resume their functions.

In the field of cardiac surgery more extensive and complicated operations have been made feasible during the past decade by the development of the extracorporeal circulation. This is a method based on techniques well established in physiological laboratories, by which the systemic circulation of the body can be maintained by a mechanical pump and a blood oxygenator for a period during which the heart and the lungs of the patient can be by-passed. The heart and its neighbouring vessels can then be opened and congenital abnormalities or valvular lesions repaired or modified. There are many problems in the design of pumps and oxygenators which while giving, respectively, adequate flow of blood and sufficient exchange of respiratory gases, will not injure the blood. Striking clinical progress has already been made and it seems likely that the improvements in the technique of perfusion will be applied to further studies of organ function and control and, probably, of survival *in vitro*.

PERCEPTION, ATTENTION AND CONSCIOUSNESS

IN her presidential address to Section J (Psychology), Prof. Magdalen D. Vernon points out that we can never be aware at any one moment of the whole of our surroundings. The degree to which we are aware of them varies greatly, from a process of perception of a narrow central field of view upon which attention is focused, to a vague awareness of all other parts. We can vary the amount of attention and the accuracy of perception from moment to moment, and direct it to different parts of our surroundings, but the area of the field, and the number of objects or objects in it, of which we can be aware at any one moment are limited. Focal awareness of one part of the field may preclude the perception of surrounding parts. It appears to be possible, however, to perceive

events without being immediately aware of them and to store the information and attend to it later, but such information cannot be retained for long. However, there is evidence to show that even when such information never reaches consciousness, it may yet have some effect on thoughts and behaviour.

Various factors operate to produce a selection of what is perceived and attended to most closely. We tend to perceive primarily what we expect is most probable to occur in the circumstances, and our previous experience of similar situations does much to determine the estimation of probability. However, expectation is also affected by the reception of special instructions and information, and by training in what to look for. People may also tend to perceive readily what they desire to perceive or are interested in perceiving, but in such circumstances they may imagine they see what is not actually there. Again, they may be unusually slow to perceive what would be disagreeable to them. But they quickly become aware of sudden and unexpected events which are significant and perhaps potentially dangerous, although they may be slower to perceive fully the exact nature of these events.

It is difficult to perceive anything which is exposed only momentarily, or in very dim illumination, or in the margin of the field of vision. Nevertheless, there is some evidence to show that material exhibited below the normal threshold of vision, of which the observer is not directly conscious, may in some circumstances affect his thoughts or behaviour, and in particular produce reactions of the autonomic nervous system. Attention tends to wander after a time from events of no great interest which recur repeatedly and monotonously, and they may cease to be perceived. A long period of exposure to completely homogeneous surroundings produces a decrease in awareness and the power of discrimination, accompanied in some cases by hallucinations and unpleasant emotional reactions.

Recent physiological evidence as to the nature and functions of the reticular formation in the sub-cortical regions of the brain suggests that impulses from this formation may stimulate the cortex in such a way as to produce both a general arousal of consciousness, and also the direction of specific awareness to events of particular significance to the individual. Cortical impulses in turn may facilitate these activities of the reticular formation, or may inhibit them, for example, in situations associated with the withdrawal of attention, such as those of repeated unvarying stimulation of no interest or importance to the individual. Clearly these findings have considerable significance in relation to the psychology of perception and attention, though our understanding of their exact bearing must await further investigation.

PLANTS ON LAND AND IN THE OCEANS

FOR his presidential address* to Section K (Botany), Dr W. R. G. Atkins prepared an account of the many and varied problems on which he had worked and for which his initial training as a botanist had proved invaluable. Starting with a brief account of his work on the suitability and preservation of the

timber and fabrics used for the aeroplanes of the First World War, he passed on to an account of his work after the War for the Imperial Department of Agriculture in India. It was in India that he started his studies on the pH of soils and plant juices, work which he later extended in Britain. After his appointment to the staff of the Plymouth Laboratory of the Marine Biological Association, he was able to use pH measurements for assessing the total quantity of photosynthesis in water masses in the sea and to initiate complementary chemical hydrographical work at the International Hydrographic Station E1—work which has been continued by the staff of the Plymouth Laboratory ever since.

Dr Atkins then gave an account of his extensive investigation into the penetration of light into the sea, a factor of great importance for the growth of the phytoplankton. These studies were later extended to include measurements of light scattering and of the nature of the light fields to which plants in various environments are subject, both in air and under water. In addition to this work, his interest in the plants of the phytoplankton continued. Anomalies were often apparent when the crop of phytoplankton was estimated from measurements of the utilization of different nutrients. That these anomalies were due to the occurrence on occasion of unsuspectedly large amounts of non siliceous species was suggested by Dr Atkins—a hypothesis that his later observations and those of other workers have amply confirmed.

Curious delays in the time of the spring outburst of the phytoplankton when determined by the sudden reduction in phosphate in the water mass were also sometimes observed. These delays did not seem to be due to physical factors, since both the light and temperature were apparently suitable for rapid plant growth. A study of the concentration of silicate and of the various species occurring in the water indicated a sudden influx of a fresh water mass into the area—a phenomenon not apparent from records of the temperature, salinity and phosphate, nor from measurements of the total plant population as measured by chlorophyll estimations. Thus, after thirty years, at least one good reason for the lateness of the phytoplankton crop had become evident. This, however, is not to say that at other times and places changes in the vertical circulation or other factors may not be important. It does, however, indicate the value and necessity of the close integration of studies concerned with the concentration changes of all the known nutrients, the physical factors involved and both the total plant population and the occurrence of individual species.

PATHOGENIC FACTORS IN THE ROOTING SPACE AND THE DEVELOPMENT OF EVEN-AGED PLANTATIONS

IN his presidential address to Section K* (Forestry), W. R. Day says that the distribution of species of tree within the range grown for economic purposes is closely related to productive capacity as determined by available site types—adequate freedom from acutely damaging infestations and freedom from infections are, plainly, related necessities. Production is based on growth as a natural biological process and its economic value depends partly on rate of growth and partly

* Prepared from notes left by Dr Atkins and read posthumously by Dr O. P. Spencer, of the Marine Biology Station, University College of North Wales, Bangor.

on quality of production as determined by market value of produce or services rendered. Ordinarily, the development of the main stem provides the principal interest in production, and this is governed by the interaction of crown and root as functioning correlatives. Given adequate climatic adaptation of species of tree, then, within any suitable limited climatic range, the more important basic environmental variations which determine variations in production rate are to be found in soil conditions as affecting root growth and functioning.

The general tendency in development in forests established as even-aged regenerations is from simplicity towards complexity in canopy structure, the rate of development of this tendency for any given species of tree and assuming relative evenness in climatic conditions is largely a function of the soil conditions which prevail locally. The factors which determine the course of development in canopy structure are partly to be found in silvicultural treatment, but basically in the developing demand by the forest canopy as crowns increase in size, especially during the first decades after regeneration, with reduction in number of stems per unit area and increase in height of tree and according as this demand can be satisfied by supply of root growing space as qualified by available water and nutrients. Potential demand of a canopy of any given specific composition according to size of tree and as influenced by stand density, may be considered as a genetic characteristic. Since the degree to which this potential demand can be satisfied is determined largely by soil supply conditions it follows that, for any given age and type of even-aged regeneration variations in canopy development which are natural to the site will occur according to the distribution of variations in the stage of stand development at which volume of canopy demand becomes marginal with site supply and especially with supply from the root growing space. Examples taken from even-aged Sitka and Norway spruce stands are given which illustrate variations in stand structure determined in this way. Limitations in edaphic supply necessary for root development and action arise from a complex of physical, chemical and biotic factors the action of which is more or less interrelated. Examples based mainly on the physical aspect of clay and sand soils as observed in the field, are given to illustrate edaphically determined limitation in supply which through the prevention of growth naturally attempted, acts as a basic cause of disease and in this way influences stand development and through this, economic production.

Examination of the problem of management of even-aged plantations suggests that if the effects of technical silvicultural treatments are sufficiently to be appreciated, there must be some adequate understanding of the locally occurring interrelationships between canopy development and site supply of the needs for this for this through basically controlling the type of growth possible will largely determine the effectiveness of the technical treatments practised.

WHAT ARE OUR SCHOOLS FOR ?

SIR JAMES R. ROBERTSON, president of Section SL (Education) opens his address by pointing out that it was only within a few weeks of each other that a Scottish judge and the Home Secretary spoke

last winter about increased crime and irresponsibility. They called for greater help from the schools, only to be rebuked by leading educational journals which put the blame on bad influences outside. Such criticisms focus widespread confusion about the schools' functions and society's ability to protect itself.

Our educational philosophy is admirable, but our practice betrays our professions, and, while within the task allotted to them our teachers merit respect and commendation, no part of our national education, except our enlightened infant departments justifies complacency in face of the crisis of our time. Admittedly, the ablest pupils in our grammar schools are equal to the demands made on them. But do we allow time for their knowledge to be fully assimilated? To what extent do we quicken sensibility in them, or nourish imagination, or awaken the sense of dependance on others? Moreover, if we segregate the highly gifted in separate schools at eleven, do we not aggravate the risk of producing 'Lucky Jims' or an arrogant self-appointed élite?

The average grammar school entrants, supposedly most fortunate, are educationally the worst used of all. Despite advantages in staffing and provision they are the victims of an unsuitable curriculum and an external examination too hard for the majority. They suffer from excessive demands on their time, a low level of real attainment, an obsessional concern with examinations, and deplorable neglect of the non-cognitive sides of their natures. The vision of the Norwood Committee and the Scottish Advisory Council quickly died amid post-war careerism and greed.

Equally deplorable is the largely lost opportunity in the secondary modern schools with the discrediting of interest and experiment and the over-increasing participation in the chase after certificates, a participation which can, however be defended if the General Certificate of Education really matters as much as we pretend and we put into secondary moderns children capable of securing even scrappy certificates.

The bright promise of 1943 for the primary schools also faded swiftly in the universal scramble for status. A secondary education like that in Britain presupposes a primary, geared to 11+ with tests and streaming all the way and those pressures that make short work of frills and experiments. Add the excessive size of classes and general inadequacy of provision and you ensure the dominance of class-teaching and the rigid time-table, with disastrous consequences both to secondary schooling and to any further education adequate to our condition.

Further education which is neither vocational training nor purveyed entertainment is at once the most important of all, and in its meagre extent the most disappointing. How can it be otherwise so long as statutory schooling creates distaste and does but scant justice to music, drama and the arts?

Education in Britain accords as ill with recent thinking and discovery as with the sombre realities of our times, taking insufficient account of the rarity of high intelligence, the great range of innate ability and the powerful movements of thought towards an organic and unitary view of man as existent and person. Our great need is to awaken to the *continuum*: both material and spiritual of all true education: reform must begin with a national change of heart.

BALANCE IN BRITISH FARMING

DR H G SANDERS suggests in his presidential address to Section *M* (Agriculture) that the forty-seven years life-time of the Section has seen science applied to British agriculture at an ever-increasing rate, and there have also been violent economic changes. Farming systems which have been built up in more leisurely times have achieved a balance which might be upset by these scientific and economic impacts. There has clearly been an improvement in some aspects of the really basic factor—soil fertility. The lime status of the soils of Britain has been raised markedly and is still improving, and the increasing use of chemical fertilizers has led to better plant nutrient content. In regard to drainage the situation is less satisfactory. There is still uncertainty and much argument over the importance of maintaining the organic matter content of the soil, the danger being that, if it is allowed to fall, soil structure will be lost. New chemicals have proved powerful aids in keeping land clean, but there are obvious dangers in their indiscriminate use. On many farms the ley has replaced the root crop as the pivot of the rotation, and advanced practitioners are showing how great the production from newly established grass can be. Full summer utilization necessitates conserving surplus herbage at peak periods of growth, and silage fits better into advanced grazing control than hay. Much is known about the extra cost involved in making high-quality hay and silage, but little about the increased animal production from first class material and its possibilities in

economizing expensive concentrated foods. There is urgent need for more applied research into such problems.

One aspect of balance in traditional farming systems has been the relation between the feeding-stuffs produced from the land and the head of live stock maintained. A high degree of self-sufficiency is still a sensible economic aim, but its attainment depends on high-quality roughages and more precise knowledge of their potentialities, not only as maintenance ration but also for animal production.

A rough balance in the farming of Britain as a whole has grown up in a somewhat haphazard way. Sales of store sheep in Scotland are well established, and similar ones for store cattle have recently started and are developing rapidly on the Welsh border. The reverse movement of grain and straw from east to west is unorganized and depends on the initiative of individual merchants. British farmers have had outstanding success in the development of pedigree livestock, but the future will probably see more use of crossbreds for commercial exploitation. In poultry this is already widespread and in sheep also, though with them the benefits are often lost by continuing and indiscriminate crossing. The development of a system of pedigree breeders and crossing breeders to provide livestock for the ordinary farmer would help in the simplification of farming which advancing knowledge is making ever more necessary. The ultimate solution of this problem of keeping abreast with science should not be monoculture, but mixed farming with the more scientific processes in the hands of specialists.

THE ST LAWRENCE SEAWAY AND POWER PROJECTS GEOGRAPHICAL BACKGROUND

By Prof T L HILLS
McGill University, Montreal

THE official opening of the St. Lawrence Seaway on June 26 brought to completion five years of design and construction of both the Seaway and Power Projects on the St. Lawrence River. It also brought to fruition more than fifty years of almost incessant agitation in both the United States and Canada for the development of a deep navigable waterway into the heart of the North American continent. Yet most significant of all it will carry one stage further a process that has been under way for nearly four hundred years since Jacques Cartier was halted in his journey up the St. Lawrence by the Lachine Rapids. This process has involved on one hand the gradual exploitation of physical features of the Great Lakes-St. Lawrence drainage system advantageous to navigation, and on the other, the overcoming of natural obstacles to navigation. Successive stages in this process have reflected the economic development of the continent as well as political changes. The St. Lawrence Valley is the natural outlet of the continent to the North Atlantic and western Europe, therefore improvement of this waterway was to be expected. However, nearly four centuries since European man first arrived on the scene the navigation facilities on the St. Lawrence have only just been improved to the point where ocean going vessels of more than 2,500 tons can be accommodated. These navigation facilities are still not comparable with the other great canal systems of the world. At present, the Panama, Amsterdam, Rhine, Kiel, Suez, Texas and Manchester Ship Canals all exceed in size the proportions of the St. Lawrence Seaway facilities. For an explanation of the long delay in the coming to age of the navigation facilities throughout the Great Lakes-St. Lawrence system, geographical, historical, economic and political factors must be considered.

The St. Lawrence River system in combination with the Gulf of St. Lawrence and the Great Lakes provides a continuous waterway extending 2,347 miles into the heart of the North American continent from the Atlantic Ocean. The length of this waterway, its location and orientation, are three of its outstanding geographical characteristics. More length alone is not necessarily an economic attribute. However, in this case the distance of the penetration into the continent, which is comparable with the great circle route distance between west European ports and the estuary of the St. Lawrence is of the very greatest economic significance because the Great Lakes-St. Lawrence system provides an approximate east-west routeway into the heart of one of the richest agricultural and industrial regions on the face of the Earth, a region lying due west of the metropolises of Europe and the British Isles. In relation to resource production and potential this routeway is ideally located. Its hinterland or contributory region, comprising as it does the Canadian Shield, the greater part of the Interior Lowlands and parts of the central and northern Appalachian System is extremely rich in agricultural, forestry, mineral and water power resources. It was natural that one of the world's major trade routes should develop between such a region and a heavily industrialized and densely populated Europe.

The St. Lawrence River provides the only completely natural water gap through the mountain and upland barrier formed by the Appalachians and the south eastern upturned edge of the Canadian Shield but for only brief periods in the past four centuries has it been the chief transportation route between the Atlantic and the interior of the continent. The St. Lawrence has faced competition from Hudson Bay, the Mississippi Valley, the Pacific Coast-Panama Canal route and especially the Lake Erie-Mohawk-Hudson route. The economic and political history of the St. Lawrence can largely be told in terms of its continued competition with the alternative route ways from the interior of the continent. The low level link between Lake Erie and the port of New York provided by the valleys of the Mohawk and the Hudson gained the ascendancy over the St. Lawrence route with the completion of a barge canal between Buffalo and Albany in 1823. The ascendancy resulted partly from a major physical advantage of the more southerly route, and partly from the fact that it was an 'all American' route between the Middle West and Europe.

The major physical advantage of the Lake Erie-New York route is the year round ice-free condition of the port of New York. Inherent in the location of the St. Lawrence, a location which in all other respects has proved advantageous is one of its most serious limitations. The winter climate of a region so located in the north-eastern quadrant of a continent within the northern hemisphere is long and extremely cold. Below freezing temperatures for at least four months result in the St. Lawrence being turned into an ice way rather than a waterway. From the year 1887 until the present day the average date on which the ship channel between Quebec and Montreal has been open for navigation has been April 17, the earliest date throughout that period was March 19 and the latest date May 1. The average date of the last departure from Montreal was December 4, the earliest was November 21 and the latest December 19. Amelioration of conditions during the past decade and more recently assistance from icebreakers have resulted in the lengthening of the navigation season by about two weeks. With the completion of the Seaway it has been suggested that the navigation season might well be even further lengthened by an increase in the number and the efficiency of ice breakers, the use of aerial ice surveys and the improvement of aids to navigation.

An eight-month navigation season on the St. Lawrence and the Great Lakes compared to year round navigation on the Atlantic coast south of the Gulf of St. Lawrence has probably militated against the development of the full potential of the St. Lawrence and the Great Lakes more than any other factor, though if deep navigation had been more readily available this limitation would perhaps not have been considered quite so disadvantageous.

The other major physical limitation of the Great Lakes-St. Lawrence waterway has been of course the series of falls, rapids and shallow connecting channels, which unfortunately abound within the system, especially between Montreal and Lake Huron. The long delay in successfully circumventing these

obstacles has not been due to engineering difficulties but rather to the sheer expense involved. In the upper St. Lawrence, that is between Montreal and Lake Ontario, all the pre-Seaway canalization was undertaken by Canada, at an expense which was very considerable for a relatively small and youthful country. Only in recent years when it became feasible to merge schemes for the provision of navigation facilities and the development of hydroelectric power did the expense appear not too burdensome, for both Canada and the United States. It is fortunate that the most serious liabilities of the whole Great Lakes-St. Lawrence system are, at one and the same time, very great assets. The upper St. Lawrence, which has over the years proved the most serious obstacle to the improvement of navigation, to day provides almost 4,000,000 horse-power of electricity.

The natural deep navigation throughout much of the Great Lakes and on the lower St. Lawrence and the falls and rapids, seen either as obstacles to navigation or as water-power sites, owe their existence to a varied geological and physiographical history. The entire drainage system of the Great Lakes and the St. Lawrence covers an area approximately 678,000 square miles in extent, within three of the major geological and physiographical regions of the continent: the Interior Lowlands, the Canadian Shield and the Appalachians. The Great Lakes and the valley of the St. Lawrence lie chiefly within the north-eastern section of the Interior Lowlands. Here a great series of Palaeozoic sedimentary rocks, primarily limestones, dolomites, shales and sandstones, take a basin-like form, overlapping on to the rocks of the Shield and the Appalachians to the north and the east. Differential erosion on these Palaeozoic rocks has produced a series of cuestas best typified by the famous Niagara Escarpment, and lowlands, which are to-day partly occupied by four of the Great Lakes and sections of the St. Lawrence Valley. In general, dolomites and limestones tend to form the higher parts of the region and are the 'fall-makers', while the shales have been removed extensively to form the lowlands and particularly the four lower lake basins. Lake Superior lies entirely within the Precambrian rocks of the Canadian Shield. The Great Lakes probably owe their origin to a combination of events—structural depression, fluvial erosion, glacial deepening and moraine damming. These events gave rise to the great size and depth of the Great Lakes. The deepest point in Lake Superior is 1,302 ft, that is, 700 ft below sea-level, while Lake Michigan has a maximum depth of 923 ft, Lake Huron 750 ft, Lake Ontario 774 ft, Lake Erie is relatively shallow, with an average depth of only 58 ft. The water surface of the Great Lakes covers an area of 95,000 square miles, an area almost as great as that of the British Isles.

The surface of Lake Superior averages 602 ft above sea-level. The drop to sea-level is concentrated in two sections of the drainage system: between Lakes Erie and Ontario and in the upper St. Lawrence between the outlet of Lake Ontario and Montreal. There is a total drop of 326 ft from Lake Erie to Lake Ontario, with a vertical drop of 168 ft at Niagara Falls, where the outflow of Lake Erie drains across the resistant Lockport dolomite of the Niagara Escarpment. Between the outlet of Lake Ontario and Montreal the St. Lawrence drops a total of 246 ft in a distance of 183 miles, and in doing so flows across alternating resistant igneous and weaker sedimentary rocks, which has given rise in turn to a

series of alternating rapids and lake basins. Immediately on leaving Lake Ontario the St. Lawrence flows across a southerly extension of the Canadian Shield, the Frontenac Axis. This section is known as the Thousand Islands, it is wide, deep and free of rapids. Below it a series of four rapids, collectively known as the International Rapids, because here the Canada-United States border runs along the St. Lawrence, provide a drop of 92 ft in a distance of 44 miles. These rapids, including the famous Long Sault, have to-day disappeared under the power pool of the St. Lawrence Dam. Here the engineers won a brilliant victory over the St. Lawrence by raising the waters of the river 81 ft behind a dam built below these falls. They have developed tremendous water-power and at the same time provided excellent deep navigation which replaces a series of four 14-ft deep canals of the old St. Lawrence canal system.

Downstream from the International Rapids section Lake St. Francis drains via another series of four rapids with a total drop of 82 ft. Again this major obstacle has been circumvented by a combined power pool and deep waterway known as the Beauharnois Canal. Here again there is a potential 2,000,000 horse-power of electricity, three-quarters of which has already been developed. The final major drop of the St. Lawrence occurs where Lake St. Louis drains over the Lachine Rapids. The drop of 50 ft has not yet been harnessed for the development of electric power, and the Lachine Rapids have remained solely as an obstacle to navigation. They have additional geographical significance in that the city of Montreal has developed largely as a result of the Lachine Rapids bringing natural deep navigation to an end at this point.

The value of the many considerable drops in elevation within the Great Lakes-St. Lawrence system as water-power sites is considerably enhanced by two additional physical attributes of the region. The Great Lakes in particular, but also the myriads of large and small glacial lakes within the Canadian Shield, act as vast reservoirs with a tremendous storage capacity which results in the outflow not only being considerable but also in being regulated to a remarkable degree. The maximum average flow is about 310,000 cu ft per sec and the minimum 144,000 cu ft per sec. The variation of about 2 to 1 is in striking contrast to the flow of the Columbia River, with a ratio of 35 to 1, and the Mississippi River, with a ratio of 25 to 1. The average flow in cu ft per sec obviously increases downstream, being 71,000 between Lakes Superior and Huron, 194,000 on the Niagara River, 237,000 in the International Rapids section, and it reaches a maximum volume of 262,000 cu ft per sec where the Ottawa River joins the St. Lawrence. The relatively uniform annual precipitation within the drainage basin also contributes to the uniform flow and the tremendous volume of water in the system. Precipitation varies from 25 to 43 in., with a mean of 33 in.

The completion of the combined St. Lawrence Seaway and Power Projects brings to a satisfactory stage the development of navigation facilities on the Great Lakes and the St. Lawrence and brings closer the complete utilization of the tremendous water power available. Man has long awaited the day when the full economic potential of this vast system would be realized. This stage may not yet have been reached, but economic and technological development will probably no longer hinder absorption of any remaining potential into the navigation and power systems of the Great Lakes and the St. Lawrence.

(Continued from page 34)

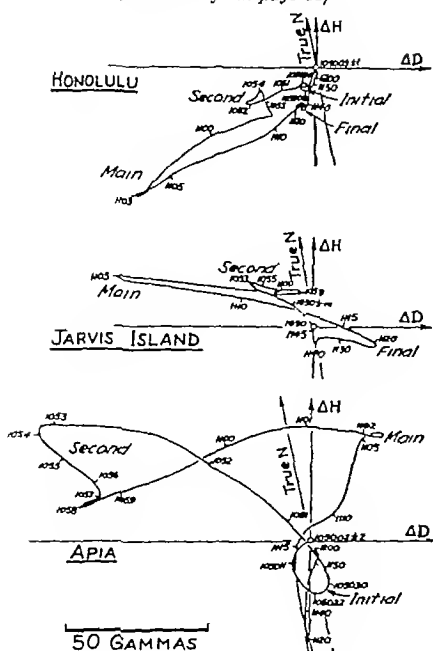


Fig. 2a Vector diagrams showing the horizontal plane magnetic effects of the explosion of August 1. Times are 0 M.T.

local *E* or *F* region winds in the area of increased ionization produced by these particles, particularly near the conjugate point.

Main phase Gas motion due to the explosion which, by the time of maximum of this phase extends to the region of the meridians through Honolulu and Jarvis Islands. G. A. M. King and C. H. Cummeek (personal communication) independently propose a shock front spreading from Johnston Island with radially uniform horizontal speed. They associate the arrival of this at each station with the time of maximum of the main phase there except at Apia, where they associate it with the time of maximum of the final phase.

Adopting the idea of a circular horizontal boundary centred on Johnston Island, applied to an expanding conducting cloud we suggest a broad qualitative interpretation of the magnetic vectors as follows.

Fig. 3A shows the type of distortion produced in the horizontal magnetic field during the main phase. (B) Electric current induced by motion against *X* of northern section of expanding cloud during main phase. (C) Current system in vertical plane across section *X—Y* to approximate distortion in (A) combined with the current system of (B). (D) Electric current induced by motion against *X* of southern section of expanding cloud during final phase.

Fig. 3B shows a current system which might be produced by the o.m.f. induced in the northern section of the cloud moving against the Earth's vertical magnetic field, with return current moving preferentially along the meridian and linking up in the region of high ionization near the conjugate point.

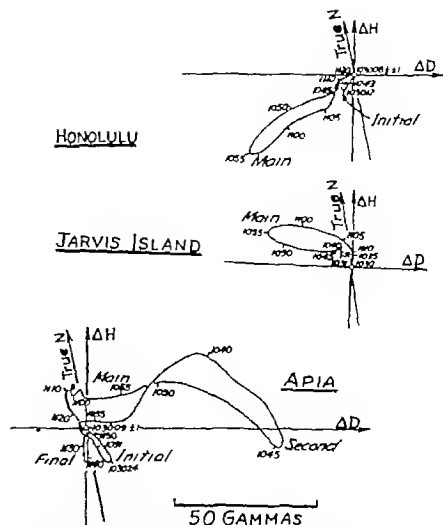


Fig. 2b Vector diagrams showing the horizontal plane magnetic effects of the explosion of August 1. Times are 0 M.T.

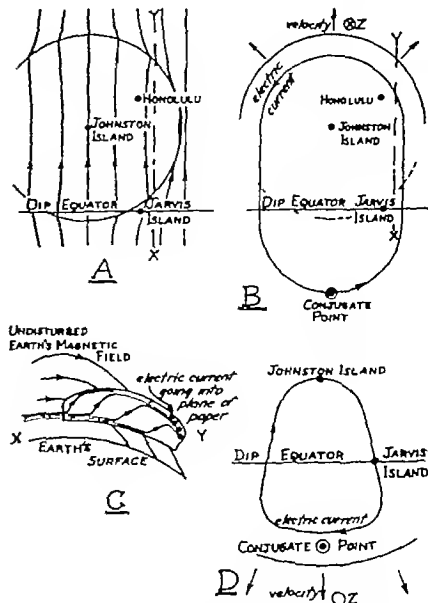


Fig. 3 (A) Distortion of Earth's horizontal magnetic field by expanding conducting cloud during the main phase. (B) Electric current induced by motion against *X* of northern section of expanding cloud during main phase. (C) Current system in vertical plane across section *X—Y* to approximate distortion in (A) combined with the current system of (B). (D) Electric current induced by motion against *X* of southern section of expanding cloud during final phase.

Fig 3C shows a vertical section across X-Y of Figs 3A and B. In this is pictured a current system which is imagined to combine that of 3B with currents to approximate the distortion shown in 3A.

Note that the return current across the equator contributes to the required distortion, and we suggest that this as well as anisotropic conductivity control the direction of flow.

Final phase A later development of the motion producing the main phase, corresponding to the passage of the shock front over Apia as postulated by King and Cummack. In Fig 3D we suggest an interpretation of the magnetic vectors on this idea. This current system would depend on the abnormal ionization still situated in the whole region between Johnston Island and the conjugate point.

The development of all phases after the first explosion is faster, and affects a wider region, consistent with the belief that the first was the highest.

We hope to publish a full account of this work in the *N Z Journal of Geology and Geophysics*.

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May 28

¹ Cullington, A. L., *Nature*, 182, 1305 (1958)

² Kellogg, P. J., Ney, E. P., and Winckler, J. R., *Nature*, 183, 358 (1959)

³ Akasofu, S., *Rep. Ionospheric Res. in Japan*, 10, 4, 231 (1956)

⁴ Fowler, P. H., and Waddington, C. J., *Nature*, 182, 1728 (1958)

Some Geomagnetic Phenomena associated with Nuclear Explosions

THE three International Geophysical Year stations operated in the central Pacific by the Scripps Institution of Oceanography have consistently recorded magnetic disturbances following, and apparently caused by, the various nuclear tests conducted by the British in the vicinity of Christmas Island. This fact is particularly interesting because, unlike the American bomb which was exploded in the ionosphere over Johnston Island on August 1, 1958, producing auroral and magnetic effects over a large area of the Pacific¹, the British tests are believed to have occurred at relatively low altitudes in the lower atmosphere.

Fig 1 shows magnetograms for the explosion of April 28, 1958, and Fig 2 the positions of the observing stations relative to the shot point, which was stated to have been within ten miles of 1° 40' N, 157° 15' W. The altitude has not been disclosed, but official reports indicate that the device was dropped by a *Valiant* jet bomber, and it may be supposed that the height of detonation was substantially less than the ceiling of about 60,000 ft for that class of aircraft.

The pronounced anomalies in Z and D, which reach a maximum at Jarvis and Fanning between 12 and 15 min after the event and at Palmyra about 10 min later, are similar in character to those which followed other tests, and we have no doubt that they are directly related to the nuclear explosion. We have examined magnetograms from the nearest magnetic observatories outside the immediate area,

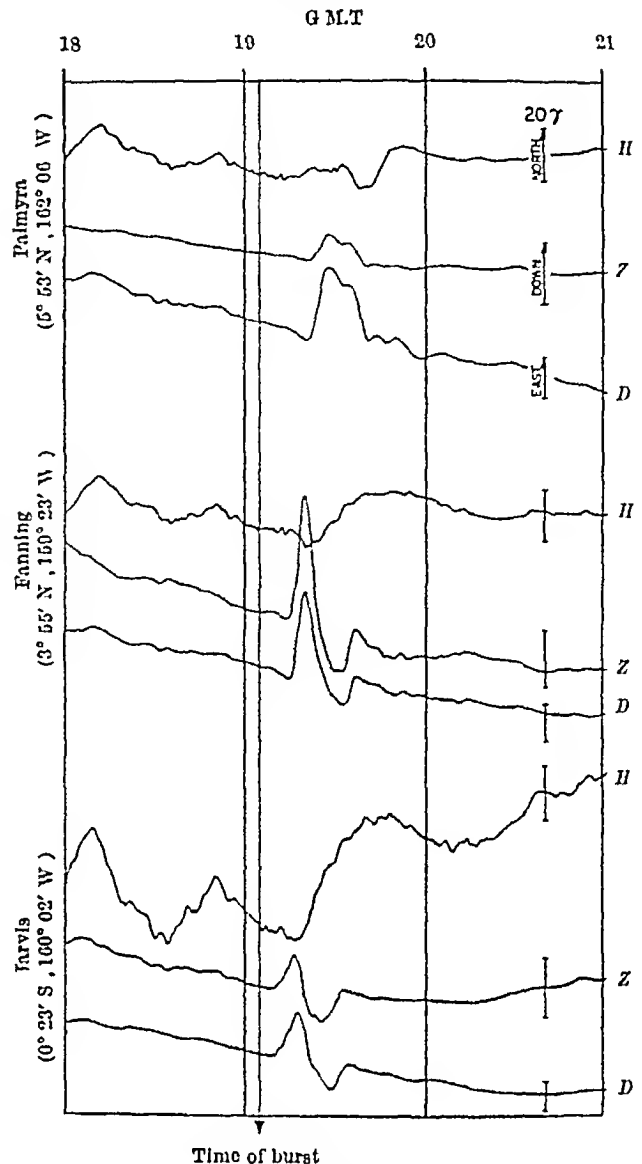


Fig 1 Magnetograms for the Christmas Island nuclear explosion of April 28, 1958

that is, Apia, Guam and Honolulu, but have not found any magnetic effects that we can positively identify with this or with any other of the British tests. This is surprising, because Apia and Honolulu are only about three times as far as Palmyra from Christmas Island.

The disturbances recorded at our three stations have several features in common. They begin quite suddenly after a delay of several minutes (rather longer at Palmyra than at the other two stations), they move in the same relative phase and they persist for about half an hour, but perhaps the most striking feature of the magnetograms is the absence of any observable disturbance in H corresponding to the major disturbance in Z and D (though an unusual, and probably related, type of local disturbance in H at Palmyra commenced about 26 min after the event and lasted for about 20 min). The absence of an H component would be explained if the phenomenon involved horizontal currents parallel to the magnetic meridian, and in this connexion it may be noted that the Earth's magnetic field is very nearly horizontal throughout the area. More generally, possible mechanisms for producing such disturbances include (a) the motion of charged particles, in certain circumstances controlled by the Earth's magnetic field, (b)

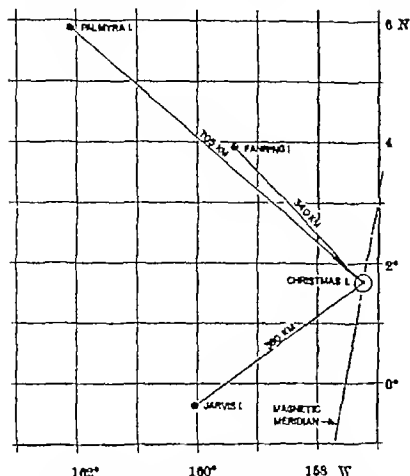


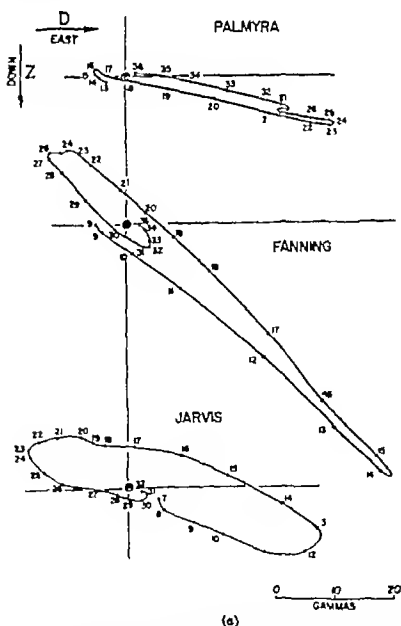
Fig. 2. Positions of the Scripps International Geophysical Year stations relative to the shot point near Christmas Island

the modification of existing ionospheric currents through displacement of the conducting medium or changes in conductivity, (c) the mechanical disturbance of a magnetic field frozen into a mechanically disturbed conducting medium. To these must be added the secondary effect of induction within the Earth.

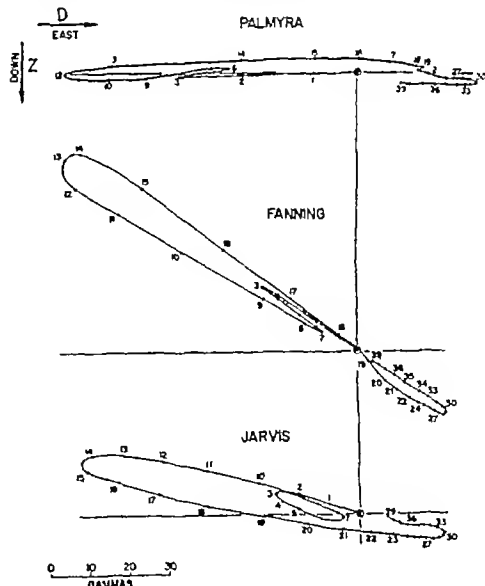
In order to bring out more clearly the vector characteristics of the disturbances, diagrams have been constructed showing the time variation of their projections in various planes, measured as the departure of the observed field from an assumed smooth background (represented by the origin of the vector diagram). Fig. 3a shows diagrams for the vertical plane perpendicular to the magnetic meridian. The explanation of the large time delay at Palmyra is now seen to be that although the vectors at all three stations reach peak values in one direction between 22 and 26 min. and in the opposite direction between 23 and 27 min. the directions and amplitudes of the two peaks at Palmyra are reversed.

Fig. 3b shows the corresponding diagrams for the Johnston Island explosion of August 1 1958. Having regard to the altogether different geographical positions and altitudes of the two events, the similarity of the two sets of diagrams is remarkable. However, unlike the Christmas Island explosion the Johnston Island event produced changes in H comparable in magnitude with those in D and Z . Fig. 4 shows vector diagrams of the disturbance in the horizontal plane, plotted to show the relative directions of the magnetic vector, Johnston Island and the conjugate point (taking Elliot and Quenby's position¹) at each station. This event produced effects not observed in connexion with the Christmas Island tests, for example, an instantaneous change in H of about 10 gammas.

It is clear from the complicated nature of the Johnston Island disturbance, and from the extent to which it resembled the disturbance produced by the dissimilar Christmas Island event, that no simple



(a)



(b)

Fig. 3. Vector diagrams of the disturbance in the vertical plane perpendicular to the magnetic meridian for (a) the Christmas Island explosion of April 29, 1958. (b) the Johnston Island explosion of August 1 1958. The small figures indicate the time in minutes after the event.

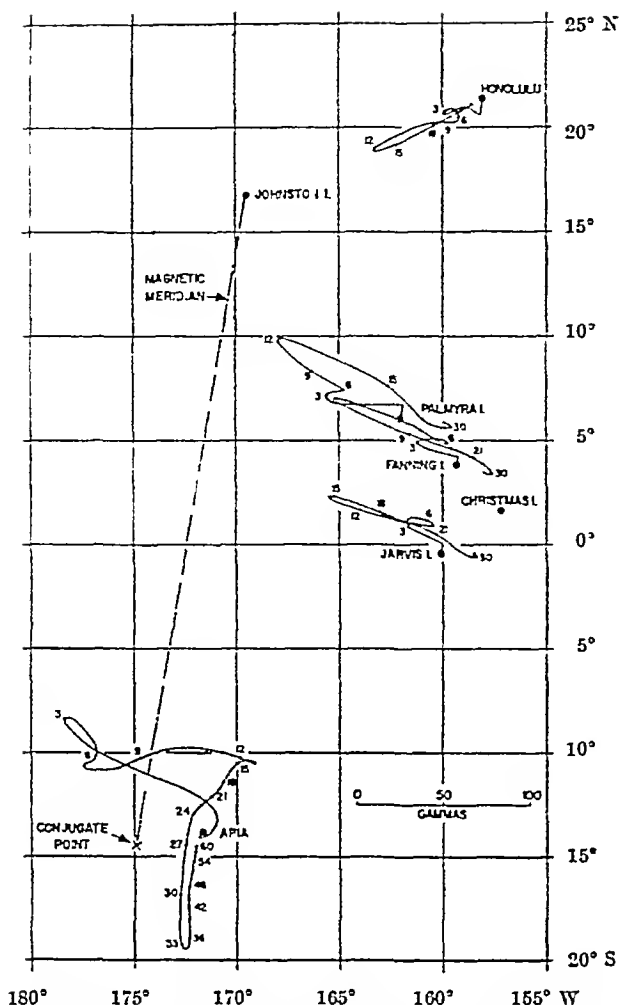


Fig. 4 Vector diagrams of the disturbance in the horizontal plane for the Johnston Island explosion of August 1, 1959. The small figures indicate the time in minutes after the event

explanation of the magnetic phenomena is to be expected, it is probable that several distinctly separate mechanisms are involved

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¹ Cullington, A. L., *Nature*, 182, 1305 (1959)

² Elliot, H., and Quenby, J. J., *Nature*, 183, 810 (1959)

CHEMISTRY

Carrier Gas and Sensitivity in Gas Chromatography

A RECENT article¹ takes issue with the "popular belief that the use of hydrogen or helium as the carrier gas in gas chromatography gives the highest sensitivity with a thermal conductivity detector, because the difference in thermal conductivity between organic vapours and hydrogen or helium is greater than for any other carrier gas". The article goes on to show that, for methane and ethane at least, the sensitivities are considerably higher with carrier gases that have a lower thermal conductivity.

The communication by Dr. Ray, however, treats the special case where the bridge current of the detector is held constant. In practice, not the bridge

current, but the filament temperature is held constant. Under these conditions, helium is nearly ten times as sensitive as argon.

A standard C₄ hydrocarbon mixture was analysed on the same gas chromatographic column under the same condition with both helium and argon as carrier gases, while holding the bridge current constant at 150 m amp. Values of the sensitivity parameter² (*S*-values) were calculated for the entire mixture, the *S*-value for argon was 252, for helium 300. *Ad hoc* experiments show that the filament temperature will be the same with helium as a carrier gas, operating with a bridge current of 350 m amp, as with nitrogen or carbon dioxide as carrier gas with a bridge current of 150 m amp; argon is in the same range as nitrogen or carbon dioxide. The *S*-value for C₄ hydrocarbons in helium, with a bridge current of 350 m amp, is approximately 3,000. In argon, a bridge current of this magnitude would cause the filament to burn out. The *S*-values obtained at the same filament temperature closely check the differences that would be expected for argon and helium based on the differences of their thermal conductivities and the thermal conductivities of hydrocarbon vapours, helium is 3,480, argon 308, and *n*-butane 322.

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¹ Ray, N. H., *Nature*, 182, 1663 (1959)

² Dimbat, M., Porter, P. E., and Stross, F. H., *Anal. Chem.*, 28, 290 (1956)

WHILE it is true that a higher sensitivity can be obtained by using a higher bridge current, it is not usually possible to do this with commercial gas chromatography instruments, because manufacturers wisely limit the supply voltage to a level at which the katharometer filaments do not fuse in air or nitrogen. Even with home-made instruments the bridge supply voltage may be a limiting factor, since to maintain the same filament temperature in helium as in argon the voltage must be increased nearly three times.

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Measurement of Intergranular Diffusion in a Silicate System: Iron in Forsterite

MANY geochemists and petrologists¹ concerned with the role of solid state diffusion in material transfer in silicate systems have noted the possibility that grain boundaries and dislocations might act as avenues for relatively rapid movement of the diffusing ions. Studies on metal systems are usually cited as evidence for this phenomenon. We wish to report some preliminary measurements on a silicate system where grain boundary diffusion seems to predominate in diffusive transfer.

The system used for the study was polycrystalline forsterite (magnesium orthosilicate) with ferrous ion as the diffusing material. Pellets were prepared

from stoichiometric mixtures of the pure oxides by compression at 15,000 lb/sq. in. and sintering at approximately 1,000° C. The samples were broken up and the operations were repeated four times to assure homogeneity. Radioactive iron 55 in a ferrous chloride carrier was used as tracer being applied as a spot in the centre of the forsterite disk. This was baked briefly at 1,000° C to form ferrous oxide and then reduced at 900° C in a controlled atmosphere of carbon dioxide and carbon monoxide adjusted to produce fayalite² (ferrous orthosilicate). After microscopic examination to detect imperfections and non adhesion, the sample was counted with an end window Geiger counter under conditions such that the counting geometry could be reproduced exactly. The surface-decrease technique was used. The application of this method to the diffusion of iron 55 in oxides has been described in detail by Himmel, Mehl and Birchenall³ and by Carter and Richardson⁴ and similar methods were applied here. The diffusion annealing was carried out in the range 1,000–1,200° C in the controlled atmosphere furnace. Exploratory sections were taken in a few samples after diffusion by careful removal of active layers by grinding in a holder, and residual activity and thickness were measured after the removal of each layer. A few samples were ground at an angle, and autoradiographs were taken with Eastman 'No-screen' X ray film.

Results for the diffusion coefficient as a function of temperature are plotted in Fig. 1. The straight line calculated according to the least-squares method corresponds to the equation

$$D = 4.17 \times 10^{-4} \exp(-38.8 \text{ kcal}/RT) \text{ cm}^2 \text{ sec}^{-1}$$

The statistical limits for 95 per cent confidence for the activation energy are ± 3.6 kcal.

The results for sectioning are given in Fig. 2, for one typical example, and are plotted as log activity against both penetration distance and the square of this distance. According to Fisher⁵, theory would predict a straight line in the former case for grain boundary diffusion, and a straight line in the latter case for lattice diffusion. It will be noted that grain boundary movement is indicated. In all cases, autoradiography confirmed this conclusion. Penetration was found to be non uniform and concentrated on lines and spots which were rather poorly defined presumably because of the relative long range of the X radiation from iron 55.

Despite their importance in geological ceramic and metallurgical systems, few determinations of diffusion in solid silicate systems have been made. Most notable have been the measurements of Lindner⁶. His work indicates energies of activation for such systems of 47 kcal or greater. The value of 38 kcal found for the present system may be indicative of the greater ease of material transfer through grain boundaries. The picture of such interfaces as regions of ionic misfit with consequent concentration of lattice vacancies and dislocations makes the easier motion of solute ions through such sites readily understandable.

In most solid systems boundary diffusion is considered to play but a minor part in material transfer in comparison with lattice diffusion at temperatures above the Tammann temperature (approximately $0.5 T_m$ where T_m is the melting point in degrees K.) because of the small area of the boundaries compared with the aggregate crystal area. The temperatures of

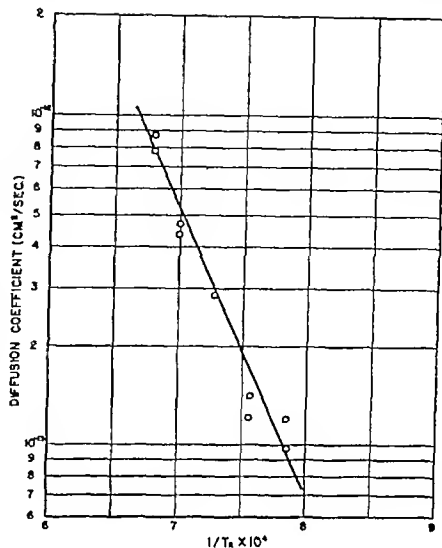


Fig. 1. Diffusion coefficient as a function of temperature

the measurements of this study are in this range. However, in orthosilicates we have a close-packed array of ions which may be considered to offer a singularly unfavourable condition for lattice diffusion and prove an exception to the above rule. In such a system, boundary diffusion might be expected to be greater than lattice diffusion, and measurements do seem to give a relatively unambiguous indication that such boundary diffusion can play a part in transfer in a silicate system.

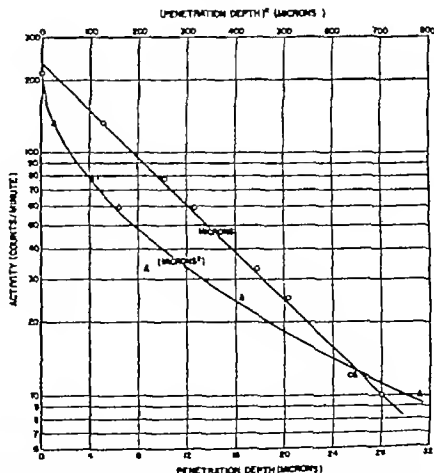


Fig. 2. Variation of activity with the distance and with the square of the distance in a sectioned sample after diffusion anneal.

It is of interest to calculate the distance of appreciable material transfer that would be possible through this intergranular pathway in geological periods of time—say, 10^6 years. By using the mean displacement equation, $X = (Dt)^{1/2}$, giving the relationship between the diffusion coefficient D , the time t , and the distance of transfer of the average concentration of diffusing material X , we can obtain an approximation of this last. In the range of $1,000^\circ$ – $1,200^\circ$ C one finds that a displacement of only 5–17 cm is to be anticipated.

In considerations of petrographic metasomatic processes, particularly those involved in 'the great granite controversy', much argument has centred on the possible mechanisms of transfer of large quantities of matter, sometimes through great distances⁷. One group has sought to account for such transfer by solid state diffusion, and particularly by the intergranular pathway for such diffusion. Within the limitations of the conditions and the system studied, the above results would tend to support those who discount the role of diffusion in long-distance mass transfer, even through the supposedly easy route of the grain boundary.

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³ Himmel, L., Mehl, R. P., and Birchenall, C. E., *Trans. Amer. Inst. Mech. Eng.*, **167**, 827 (1953)
⁴ Carter, R. E., and Richardson, F. D., *Trans. Amer. Inst. Mech. Eng.*, **200**, 1244 (1954)
⁵ Fisher, J. C., *J. App. Phys.*, **22**, 74 (1951)
⁶ Lindner, R., *J. Chem. Phys.*, **23**, 410 (1955)
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Influence of Gold in a Mercury Electrode on Certain Electrode Processes

It is usual to study electrode processes using hanging-mercury microelectrodes. Some authors prepare these electrodes by hanging a small mercury drop on a gold wire or a gold-plated platinum wire^{1,2}, deliberately neglecting the presence of the gold for its electropositive potential. Such an electrode is however an amalgam electrode, and, as we have shown³, gold can influence the electrode processes of those metals which combine with it to form intermediate compounds.

The actual concentration of gold in different parts of the electrode is variable and dependent upon time, partly due to continuous diffusion of the gold. However, adopting certain approximations, it is possible to evaluate it. For a mercury drop with a radius of 0.05 cm on a gold wire with a surface area of 0.1 mm² the concentrations of gold in the mercury 20, 60, 200 sec after the drop was first suspended on the wire are, respectively, 0.001, 0.05 and 0.01 per cent. To ascertain whether those concentrations are sufficient to form intermetallic compounds on the surface of the electrode we have prepared 0.001, 0.01 and 0.1 per cent gold amalgams for use with the

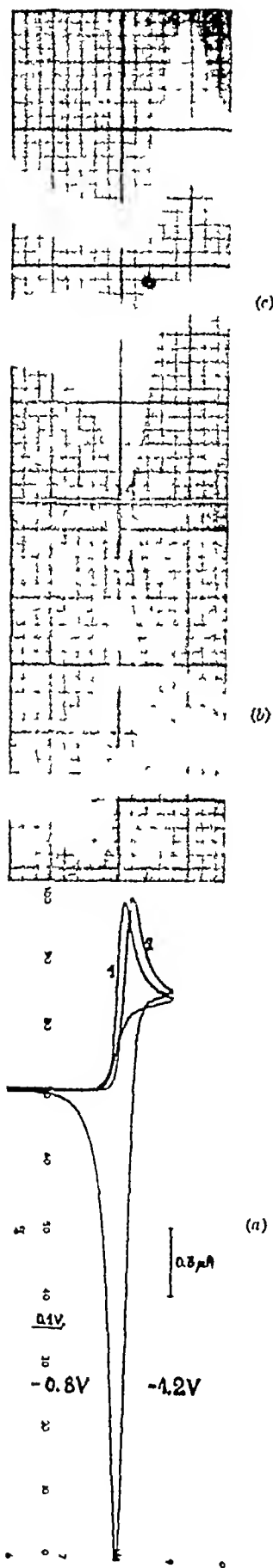


Fig 1

electrodes previously described⁴. With these electrodes, $5 \times 10^{-4} N$ solutions of lead, thallium, cadmium and zinc ions were investigated, by means of cyclic polarization of the electrode using different rates of voltage sweep and recording the corresponding voltammetric and oscillographic curves.

It was confirmed that the presence of gold in the electrode greatly influences the electrode processes of zinc. Fig. 1a shows the cyclic voltammetric curves for zinc on the 0.1 per cent gold amalgam electrode (curve 1) and on a mercury electrode (curve 2). They differ significantly in both cathodizing and in anodizing.

On gold amalgam the cathodic process is shifted about 20 mV towards more positive potentials compared with a pure mercury electrode. The differences in the anodic processes are even more pronounced. Zinc is not oxidized at the reversible potential (about $-1.0 V$) which is caused by the formation in mercury of a compound $AuZn$, that can be oxidized at more positive potentials. A similar effect can be observed even with less concentrated amalgams. Fig. 1b shows the oscillographic curves for zinc at a frequency of 4 c/s when the exposure was 30 sec and the concentration of gold in the amalgam is 0.01 per cent. The more pronounced effect is seen in Fig. 1b where the voltage sweep was 0.3 V/sec. It is evident that both the reduction current for zinc ions and the oxidation current of zinc from the amalgam, decrease with time when the compound $AuZn$ is formed. This does not occur with the pure mercury electrode. The influence of gold can be neglected only when its concentration in the amalgam is less than 0.001 per cent.

Similar effects were observed for cadmium, although the intermetallic compound $AuCd$ is not so stable as $AuZn$. Its formation can be observed when the concentration of gold exceeds 0.01 per cent. No influence of gold on the electrode processes of lead and thallium was found.

These experiments show clearly that the use of gold or gold plated wires for suspending the mercury drop can give erratic results if the formation of intermetallic compounds is neglected.

On the other hand our technique for preparing hanging mercury drop electrodes does not suffer from this difficulty.

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¹ Gerlach H. *Z. phys. Chem.* **B23** 302 (1933)

² Mamontov G. Papoff P. and Delavay J. *J. Amer. Chem. Soc.* **79** 4034 (1957)

³ Kemula W. Galus Z. and Kublik Z. *Nature* **182** 1223 (1953)
Bull. Acad. Polon. Sci. Cl. B **6** 601 (1953)

⁴ Kemula W. and Kublik Z. *Anal. Chim. Acta* **18** 104 (1953)

assumed that it exists in the form of calcite, but in work at this Division^{3,4} and elsewhere⁵ the quantity of calcite detected by X ray diffraction and differential thermal methods is always much less than the amount of carbon dioxide recoverable from the samples. We have investigated this problem in some detail using samples of mortar and carbonated calcium silicate hydrate.

From a study of the X ray diffraction patterns of the materials before and after carbonation, using a Gummery type focusing camera of high dispersion, we have concluded that the carbon dioxide is chemically bound as calcium carbonate largely in the form of poorly crystallized vaterite, aragonite and calcite. These minerals have three-dimensional lattices, this does not support the suggestion of Gaze and Robertson⁶, based on indirect evidence, that the carbon dioxide in carbonated tobermorite could be present as two dimensional calcite. Our results also show that well-crystallized calcite is present in small quantities, but that its amount is not greatly increased by carbonation. In the past, X ray analyses have determined the amount of this well-crystallized calcite rather than the amount of the less easily detected poorly crystalline forms now proved to be present, and so have failed to account for all the carbon dioxide found in carbonated mortars.

Other workers¹⁻³ have shown and we confirm that the calcium carbonate minerals have formed both from the decomposition of hydrated cement minerals and from calcium hydroxide produced during the hydration of $3CaO \cdot SiO_2$ (alite) to $\alpha CaO \cdot SiO_2 \cdot yH_2O$ in the setting of the cement. As a result they are intimately associated with a siliceous residue with which they readily react on heating. In differential thermal analysis the decomposition of the poorly crystallized calcite produces only a slight endothermic effect (at about $700^\circ C$) and its reaction with the siliceous residue to form larnite ($\beta 2CaO \cdot SiO_2$) is not exothermic. Therefore this method, too gives little or no indication of carbon dioxide minerals other than well-crystallized calcite (strong endothermic effect at about $850^\circ C$) in carbonated mortars.

Since carbonation of mortars requires the presence of moisture¹⁻³, we suggest that the process takes place through the action of carbonic acid on cement minerals yielding poorly crystallized vaterite, aragonite and calcite in the following manner: Cement minerals \rightarrow siliceous residue + calcium hydroxide \rightarrow vaterite + aragonite + poorly crystallized calcite \rightarrow well-crystallized calcite.

A more detailed account of the investigation will be published elsewhere.

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¹ Leber I. and Blakely P. A. *J. Amer. Ceram. Inst.* **28** 295 (1956) (Proc. 53)

² Verbeck G. J. A. S. T. M. Spec. Tech. Pub. No. 205 17 (1953)

³ Kroone B. and Blakely P. A. (unpublished results)

⁴ Colt W. F. (unpublished results)

⁵ Gaze R. and Robertson R. H. S. *May Ceram. Rec.* **37** (1956)

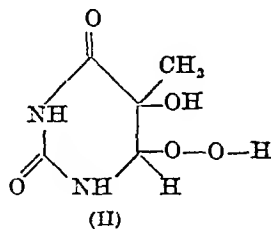
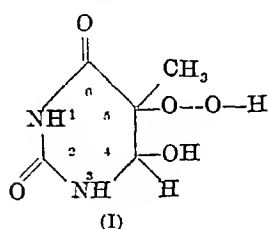
Carbonate Minerals in Hydrated Portland Cement

ALTHOUGH the physical effects of the carbonation of hydrated cements and mortars have been studied¹⁻³, the way in which the carbon dioxide is held has not yet been clearly established. Most workers have

IRRADIATION CHEMISTRY

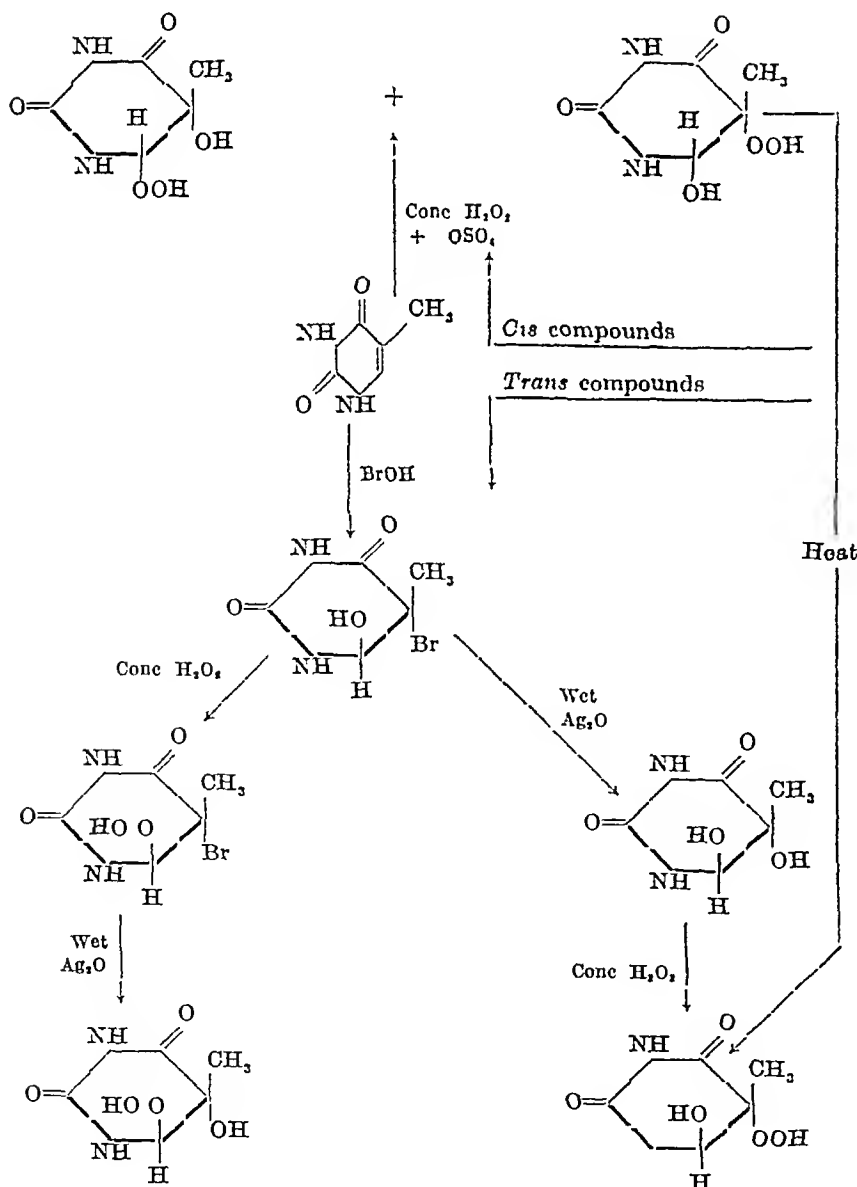
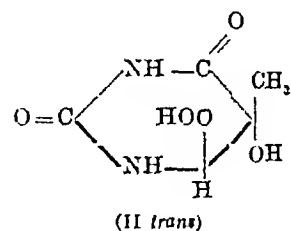
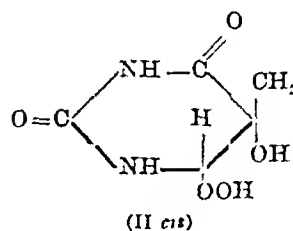
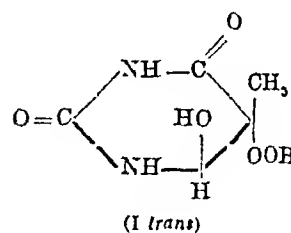
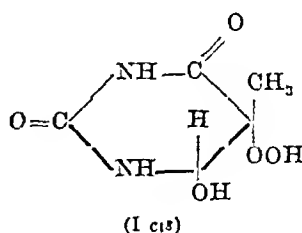
Structure of Thymine Hydroperoxide produced by X-Irradiation

WEISS *et al*¹ have shown that X-irradiation of aerated aqueous solutions of nucleic acids, pyrimidine nucleotides or pyrimidine bases gives rise to hydroperoxides. In the case of thymine, they proposed the following possible structures



which are in agreement with previous preliminary results from this laboratory². As the hydroperoxide produced by X-irradiation of thymine was sufficiently stable to permit isolation, the synthesis of compounds corresponding to formulæ I and II was

attempted in order to compare them with the products isolated from X-irradiated thymine solutions. Each of these two compounds can presumably exist in two forms, *cis* and *trans*.



The *trans* compounds were separately synthesized from a common starting material *trans*-4-hydroxy-5-bromothymine, prepared by Jones's method³. Compound II *trans* was prepared by treatment of the starting material with hydrogen peroxide in dilute hydrochloric acid to give 4-hydroperoxy-5-bromothymine. Bromine was eliminated by shaking with silver oxide and centrifuging. The product was freed of the last traces of silver oxide by extraction with a chloroform solution of dithizone. After lyophilization, the residue could be crystallized, with some difficulty, from acetone-petroleum ether. To give compound I *trans*, the starting material was transformed into 4,5-dihydroxythymine⁴, which was then treated with hydrogen peroxide. After elimination of excess hydrogen peroxide by repeated lyophilizations, the residue could be crystallized from acetone-benzene. Compounds I *trans*, II *trans* and 4-hydroperoxy-5-bromothymine can easily be separated by paper chromatography, using *n*-propanol/1N hydrochloric acid as a solvent (Table 1).

The treatment of thymine itself with hydrogen peroxide in the presence of catalytic amounts of osmium tetroxide gives a mixture of two peroxidic compounds, which can be resolved by paper chromatography, giving spots with R_F 0.51 and 0.62 respectively. Since these two compounds do not behave on paper chromatograms like the *trans* hydroperoxides previously described, they probably are the *cis*

Table 1 PAPER CHROMATOGRAPHY OF HYDROPEROXIDO DERIVATIVES OF THYMINE

Paper Whatman No 1, solvent *n*-propanol/1 N hydrochloric acid (85/15 v/v) temperature during run 2° C

| Compound | | R _F |
|--------------------------------|----------------|----------------|
| 4 Hydroxy 5-hydroperoxythymine | <i>cis</i> * | 0.51 |
| 4 Hydroxy 5-hydroperoxythymine | <i>trans</i> * | 0.33 |
| 4-Hydroperoxy 5-hydroxythymine | <i>cis</i> * | 0.62 |
| 4-Hydroperoxy 5-hydroxythymine | <i>trans</i> * | 0.43 |
| 4-Hydroperoxy-5-bromothymine | <i>trans</i> * | 0.63 |
| 4 Hydrogen peroxide* | | 0.63 |
| Thymine† | | 0.55 |

* Detected by spraying a 4 per cent alcoholic solution of potassium iodide.

† Detected in ultra violet light

compounds. On heating a solution of the mixture the product with R_F 0.51 is transformed into a product giving a spot with R_F 0.33, while the product with R_F 0.62 remains unchanged. Accordingly, it may be suggested that the product with R_F = 0.51 corresponds to formula II *cis*, as indicated in Table 1. These syntheses and the relationships between the compounds are summarized in the scheme on p. 58.

All the compounds can be reduced at the dropping mercury electrode in 0.1 M potassium sulphate at the same potential near 0 volt against the saturated calomel electrode at 25° C. They behave similarly on 'Dowex 50-H⁺' columns.

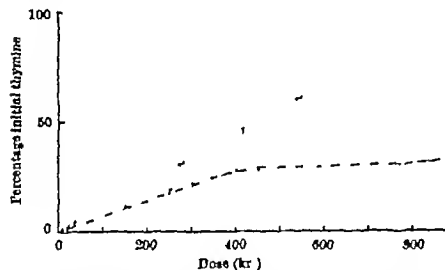


Fig. 1 Destruction of thymine (---x---) and total production of hydroperoxide (—) by X irradiation of a 10^{-4} M thymine solution by X-rays of 40 kV altered through 0.04 mm. aluminium dose 25 kr in air

In Fig. 1 are shown the curves relating dose to thymine destruction and total hydroperoxide production, during X irradiation in air. A 10^{-4} M solution of thymine, after irradiation with 400 kr, contained 2.1×10^{-4} M hydrogen peroxide and 1.9×10^{-4} M hydroperoxide. After repeated lyophilizations, the residue was put on a 'Dowex 50 X 8' column 1 cm. \times 50 cm., in 0.1 N hydrochloric acid. The eluate was collected in 4 ml fractions. Hydroperoxide products detected by the iodide reagent appeared in fractions 6-11 and unchanged thymine in fractions 16-21. After paper chromatography and spraying with iodide reagent, material contained in fractions 5-11 gave a strong spot at the level of the spot given by compound I *cis* and a faint one at the level of the spot given by compound I *trans*. Control chromatographs of various mixtures of synthetic peroxides and peroxides produced by X irradiation demonstrated that the latter cannot be distinguished from the former with corresponding R_F s. Therefore, it may be suggested that X irradiation of thymine in aqueous aerated solutions actually produces hydroperoxides I *trans* and I *cis*.

We wish to thank Dr R. Laterjet for his interest throughout this work.

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* Scholes, G. Weiss J. and Wheeler, C. M. *Nature* 178, 15* (1956)
Daniels, H., Scholes, G. Weiss J. and Wheeler, C. M. *J. Chem. Soc.* 226 (1957) Weiss J. *Les peroxydes organiques en radio-biologie* 42 (Masson Paris 1958)

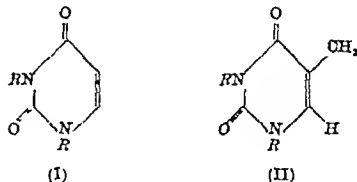
* Ekert B. and Monte R. *Ann. Inst. Pasteur* 93, 556 (1957)

* Jones W. S. *Z. physikal. Chem.* 29, 20 (1890-1900)

* Bandish O. and Davidson D. *Ber. deut. chem. Ges.* 68, 1680 (1935)

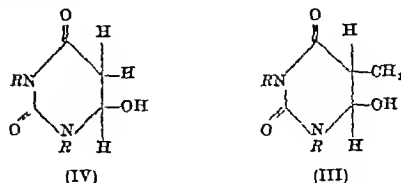
Ultra-violet Irradiation of 1,3-Dimethylthymine

When 5,6-unsubstituted pyrimidines (I) such as uracil, uridine and 1,3-dimethyluracil are irradiated with ultra violet light, the absorption spectra gradually decrease with a simultaneous increase in end absorption. These spectra can be reversed to the original by acid, alkali or heat.



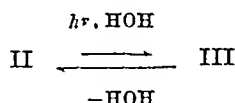
However, compounds substituted in the 5 position (II), such as thymine, thymidine and 1,3-dimethylthymine, do not show reversal under similar conditions. Most investigators have suggested that this difference may be due to totally different photochemical reaction mechanisms in the two cases.

Upon close examination of these two groups of compounds it appears that they probably have the same electronic distribution, because the ketonic form as shown above is probably the common and predominant configuration in both. Since the interaction with ultra violet light is related to the electronic state of a compound, it is not unreasonable to assume that the initial step is similar for both groups of compounds.

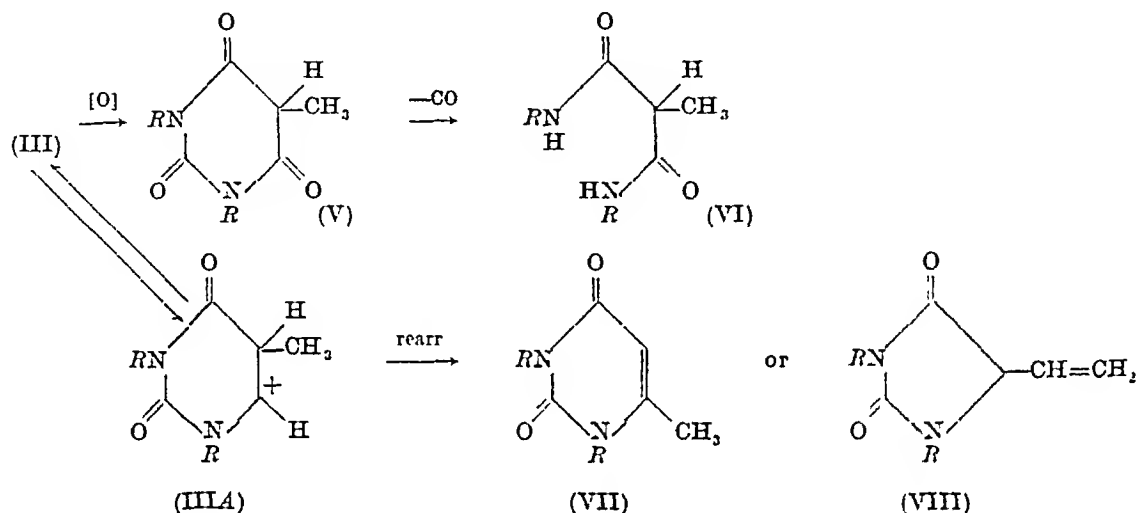


If the above assumption is true then 6-hydroxy hydrothymines (III) would be expected as the first products, because 6-hydroxyhydrouracils (IV) have been shown to be the first products of the irradiation of uracils (I). The reconstitution reactions of uracils were found to be dehydration. For thymines such dehydration would involve the much more reactive III* H rather than the IV* H as in the uracils. There

fore, the dehydration of III is probably much faster than the photo addition of water to II. This reverse



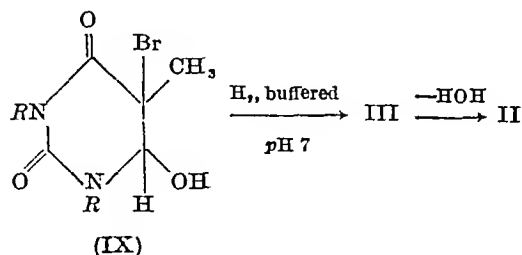
reaction would prevent the detection of III during and after irradiation, and would not be associated with a decrease in the absorption spectrum of II. Actually, however, this spectrum decreased with irradiation, and probably was due to further reactions of III to form irreversible compounds. For such reactions there are two possible routes



If carbonium ions (III4) were formed from III, then through rearrangement either VII or VIII or both could be the products. If 'oxidation' were to occur, according to the route already established for uracils, then V would be the intermediate. Upon decarboxylation N,N'-dimethylmethylmalonamide (VI) would be the product⁴.

In order to support experimentally the above arguments, the following two points would have to be demonstrated: first, the intermediate of hydration (III) must be shown to be much more unstable than that of 6-hydroxyhydrouracils (IV); second, one of the irradiation products via the intermediate (III) would have to be isolated.

We have used 1,3-dimethylthymine as a model compound. First, 5-bromo-6-hydroxy-1,3-dimethylhydrothymine (IX) was prepared and was reduced in a manner identical with that used for the preparation of 6-hydroxy-1,3-dimethylhydrouracil^{1,6}. Examination of the ultra-violet spectrum of the reaction solution suggested that only 1,3-dimethylthymine was obtained as the product with little indication of the existence of 6-hydroxy derivatives.



Upon hydrogenolysis of the 5-bromo-6-hydroxy derivatives of uracils, however, the following yields of 6-hydroxy derivatives were obtained in solution from uridine, 40 per cent, from 1,3-dimethyluracil, 80 per cent, and from uracil, 30 per cent. Therefore, this suggested that III has a much greater tendency for dehydration than uracils have. Second, 1,3-dimethylthymine was irradiated in aqueous solution until a flat ultra-violet spectrum was obtained. The irradiation products were then separated and purified. One of the products has been identified as N,N'-dimethylmethylmalonamide (VI, m.p. 157-158° C). Found: C, 50.08, H, 8.39, N, 19.42. Synthetic VI, m.p. 157-158° C, mixed m.p. with irradiation product 157-158° C. Found: C, 50.02, H, 8.25,

N, 19.65. The infra-red spectra of synthetic VI and the irradiation product were identical. On the basis of this evidence we would like to suggest that 1,4-addition of water to the thymine derivatives is the first step in the ultra-violet irradiation effect.

By examination of the quantum yields of the irradiation of thymine both in light and heavy water, Shugar has drawn the conclusion that the uptake of a water molecule is not involved⁶. From our findings it would appear that the measurements he made were actually of the subsequent slower steps and probably not for the initial fast reversible step.

Therefore, from the above findings, we have demonstrated that uracil and cytosine derivatives react similarly toward ultra-violet irradiation. This emphasized the fact that for the photochemical pathway of ultra-violet irradiation effects, the differences in electronic distributions of compounds are of more importance than the differences in their structures. They further suggest that the hydration product (III) may be of importance in photoreactivation reactions. Although the first irradiation products of uracils exhibit the phenomenon of reversibility, the irradiated uracils are stable under the customary photoreactivation conditions. Under biological conditions, however, the unstable initial thymine products (III) might be stabilized by secondary linkages, for example, H-bonds, in the nucleic acids. The H-bonds so formed could be broken by the usual photoreactivation conditions. Thus, thymines might be reconstituted and again show the biological activity of the original bases.

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¹ Wang S. Y., Apicella M. and Stone B. R. *J. Amer. Chem. Soc.* **78**, 4180 (1956); Wang S. Y. *ibid.* **80**, 6198 (1958) and references therein.

² Sinalheimer R. L. *Radiation Res.* **1**, 505 (1954); Wierchowski K. L. and Shugar D. *Biochim. Biophys. Acta* **23**, 361 (1957); Boroch A., Beckers R., Hlata J. and Berenda W., *Rec. Trav. Chim.* **77**, 423 (1958).

³ Marshall J. R. and Walker, J. *J. Chem. Soc.*, 1004 (1951); Brown D. J., Hoerger E. and Mason S. F. *J. Chem. Soc.* **211** (1955).

⁴ Wang S. Y. *J. Amer. Chem. Soc.* **80**, 6190 (1958).

⁵ Wang S. Y. *Nature* **182**, 91 (1957); *J. Org. Chem.* **24**, 11 (1959).

⁶ Shugar D. and Wierchowski K. L. *Pocheby Biochimii* **4**, 11 (1954) (1958).

Degradation of Thiotaurine by Ionizing Radiations

The degradation of sulphur-containing compounds by ionizing radiation has been extensively studied¹⁻⁶ in view of the protective action of these compounds against radiation damage in animals. Recently, thiotaurine (aminoethylethiosulphonate) has become available for chemical and biological investigation.⁴ Since thiotaurine was discovered as a metabolic product of cystine⁴ and cystamine⁷ in the rat, and since it is chemically related to cystamine, it seemed of interest to study its reactivity towards irradiation with X rays and γ rays.

30 μmoles of pure thiotaurine dissolved in 3 ml. of water were placed in a glass vessel 2.5 cm. diameter. The solution was irradiated for a suitable length of time with a Philips 60 kV X-ray source having a beryllium window. The shorter distance from the window to the centre of the solution was 1 cm. The intensity of irradiation was determined with a ferrous sulphate dosimeter.⁸ 0.15 ml. of the solution was withdrawn for analysis at intervals.

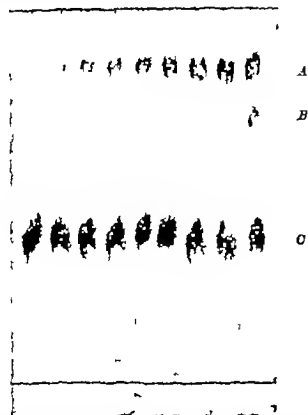


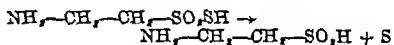
Fig. 1. Progressive chromatogram of the irradiated solution of thiotaurine with X rays. Dose (r), left to right: 0, 13,000, 32,000, 60,000, 84,000, 120,000, 240,000, 360,000, 480,000. Descending chromatogram in collidine-lutidine developed with ninhydrin. 0.5 μmole of initial thiotaurine spotted at the starting line. A, hypotaurine; B, taurine; C, thiotaurine.

As soon as irradiation started it became apparent that some reaction was taking place: the solution became more and more turbid. The degree of turbidity increased with the time of irradiation. The unirradiated control remained clear for a long time.

The material which caused turbidity was identified as colloidal sulphur by sedimentation in a 'Spinco' model L preparative ultracentrifuge at 125,000g followed by conversion of the washed residue to thiocyanate by the procedure of Bartlett and Skoog.⁹

Some of the compounds produced by the radiochemical degradation of thiotaurine have been detected by paper chromatography. At intervals a sample of the irradiated solution was spotted on a Whatman No. 4 filter paper and the chromatogram was run in collidine/lutidine/water (1:1:1 v/v) and developed with ninhydrin. Apart from a residue of unchanged thiotaurine, two main compounds reacting with ninhydrin appeared on the chromatogram. These have been identified, by careful comparison with the synthetic products and by specific reactions⁴ as hypotaurine and taurine. Hypotaurine is the first degradation product to appear; its spot appears after a dose of 12,000 r. Taurine appears later and only in small amounts.

The production of hypotaurine and colloidal sulphur is consistent with the following overall reaction:



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² Shapiro D. and Eldern L. *Radiation Res.* **2**, 393 (1955).

³ Kopolova J., Kolomsek J., Babicky A. and Liebert J. *Nature* **182**, 1074 (1958).

⁴ Cavallini D., De Marco C. and Mondovi B. *Bull. Soc. Chim. Biol.* **40**, 1711 (1958).

⁵ Sorbo B. *Bull. Soc. Chim. Biol.* **40**, 1859 (1958).

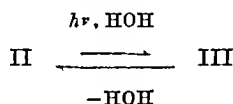
⁶ Cavallini D., De Marco C. and Mondovi B. *J. Biol. Chem.* **234**, 854 (1959).

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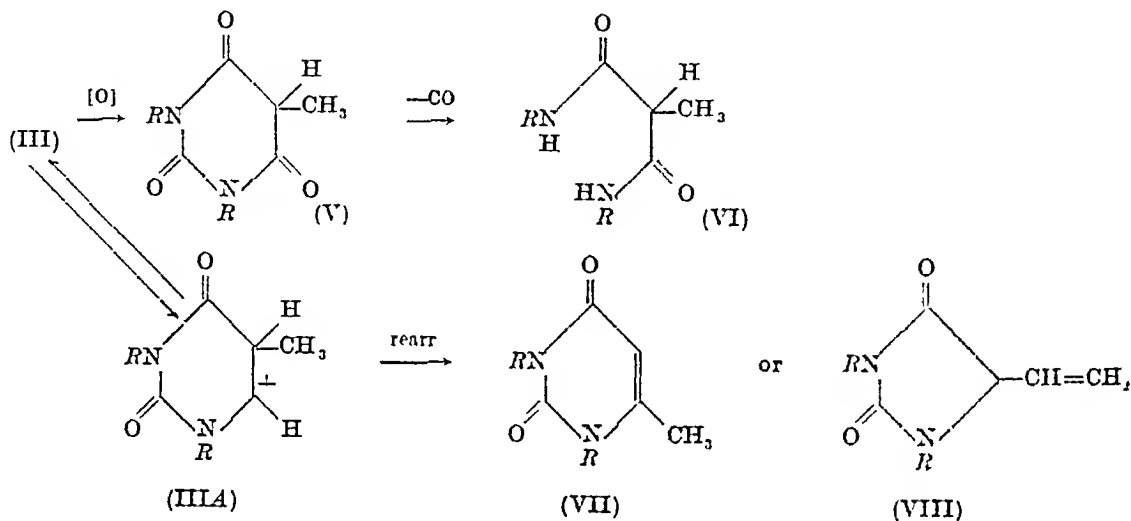
⁸ Weiss J., Allen A. O. and Schwarz H. A. *Conference on the Peaceful Uses of Atomic Energy*, **3**, 170 (1956).

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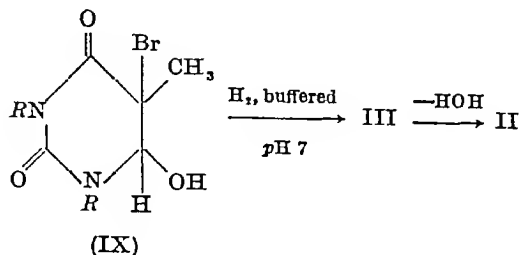
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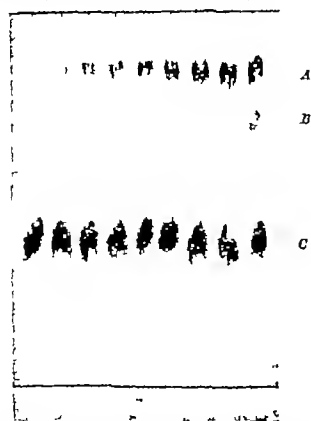


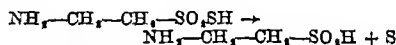
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⁹ Bartlett J. K. and Skoog D. A. *Anal. Chem.* 28, 1008 (1954)

GEOLOGY

The Geological Time-Scale

RECENTLY Dr K I Mayne, Dr R St J Lambert and D York¹ proposed an extended geological time-scale which would place the middle of the Upper Cambrian at about 650 million years ago compared with 450 million years of the Holmes scale². Their scale is based primarily on the ages they obtained by the potassium-argon method on biotite from several British granites, however, they cite many other age measurements for secondary support. It is the purpose of this communication to point out that most of the cases cited are either incorrect or not definitive to the argument. In addition, both they^{1,2} and Prof C F Davidson³ refer at some length to our as yet unpublished isotopic study of the Swedish kolm. These comments contain errors of fact and interpretation which will be clarified by the full report which will appear elsewhere, but in view of the widespread misconception concerning this interesting material some discussion appears needed at this time. The British granites referred to above are being remeasured in this laboratory and results will be reported later.

First, concerning the alleged support of the extended time-scale

(1) Mayne *et al*¹ cite pitchblende measurements in the Upper Triassic Chinle formation of the Colorado Plateau by Miller and Kulp as indicating an age of about 210 million years. The published abstract⁴ of the oral paper to which they refer does not imply this conclusion, and in the full published paper⁵ Miller and Kulp discuss the problems involved and conclude that "The apparent (i.e., isotopic) ages bear no necessary relation to the actual time of deposition".

(2) Mayne *et al*¹ incorrectly list a result of 360 million years from the Georgia Piedmont as being Permo-Carboniferous in age and refer to a paper by Kulp and Long. In the published abstract⁶ the only reference to this area states "In the Southeastern Piedmont of Georgia there is evidence for a younger event occurring around 260 m.y. ago", but there was no attempt to make a stratigraphic assignment. In the oral presentation it was noted that there might be a correlation between this 260 million year metamorphic event and coarse sedimentation in the southernmost part of the Appalachian geosyncline during Carboniferous time, but it was emphasized that no direct stratigraphic correlation with the metamorphic rocks of the Georgia Piedmont is possible. A full report on the age work in the southeastern Piedmont will appear elsewhere⁷ shortly.

(3) The Beryl Mountain pegmatite is actually intruded into the pre-Silurian Ammonoosuc volcanics according to Kruger⁸, and not the lower Devonian Littleton formation. Even if the pegmatite were intruded at the time of metamorphism of the Littleton formation as assumed by Damon and Kulp⁹, there is no stratigraphic reason for suggesting a Carboniferous age as is done by Mayne *et al*.

(4) The samples of feldspar (Dubuque formation and Mynydd Mawr granite) and sylvite give only minimum ages. The retention of argon in these materials has not been sufficiently well defined to use them for quantitative age determination. Mayne *et al*¹ in their latest communication agree that little importance should be attached to these dates.

(5) The Boisdale Hills granite, according to the latest geological information (Hurley, personal communication), is not intimately related to the fossil

sequence, but presumably the same or a similar granite less than one mile away intrudes a sedimentary sequence dated as Middle Cambrian to Lower Ordovician. The age of 490 million years is therefore much more likely to be a minimum for Lower Ordovician rather than being post-Lower Devonian as Mayne *et al*¹ state.

(6) The post-Lower Devonian intrusives in both Nova Scotia and Maine as measured by the Massachusetts Institute of Technology group¹⁰ give ages which group at about 365 million years, not 400 million years as used by Mayne *et al*¹.

(7) The errors on the rubidium-strontium ages on bentonites are too large to allow the ages to be definitive. The Adams *et al*¹¹ report was only preliminary, and further work needs to be done before the apparent ages on bentonites can be properly interpreted.

In their reply to Prof Davidson, Mayne *et al*¹ correctly reject those points cited by Prof Davidson as evidence against their extended scale where "either the stratigraphy of the sample or their measured age is not free from unwarranted assumptions". In the above discussion, these same criteria have been used to evaluate the dates and localities used in the first report by Mayne *et al*¹ as support for their expanded time-scale. The Russian measurements on mica from pebbles in Lower Cambrian rocks, as reported by Davidson³, cannot be dismissed so easily as Mayne *et al*¹ have done. If the measurements have been properly made and the minerals have not been altered since, the results are significant. The two pebbles which give isotopic ages of 566 and 763 million years could represent rocks of different real ages. In this case, the younger age would set an upper limit on that part of the Lower Cambrian. It is concluded that the evidence for the extended time-scale lies almost entirely with the measurements made by Mayne *et al*¹ on the Shap, Cannsmore and Land's End granites.

The extensive consideration which Mayne *et al*¹ and Davidson³ gave the kolm in the Upper Cambrian Swedish black shale is illustrative of the importance of the age of this formation in establishing a time scale. More than twenty kolm samples from this formation collected over a wide geographical area have been analysed in this laboratory. The isotopic uranium-lead ages are grossly discordant and vary from sample to sample¹². The detailed interpretation and discussion of these apparent ages are being prepared for publication in another journal¹³. From these measurements it has been concluded that the discordance among the isotopic ages is caused by a combination of bulk lead loss and additional preferential loss of lead-206 due to migration of an intermediate member in the uranium-238 decay chain during the history of the mineral. On this basis, an analysis of the data indicates a minimum age for this formation of about 500 million years. The complexity of the leaching processes occurring is such that a maximum age cannot be assigned solely on the basis of the isotopic data. Mayne *et al*¹ attribute to us the statement, "They believe the true age to be no greater than 550 m.y." This does not correspond to our opinion, and the reference they cite does not contain this statement. The evidence points to the minimum age as being nearly correct, but there is no unique solution of the data.

Davidson's³ discussion of the meaning of the kolm ages is erroneous. He mentions that the formation contains old radiogenic lead. Our data strongly

Table 1

| Fraction | a | b | c | d | e | f | g | h | i | j | k | l | m |
|---------------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|---------|-----------|-----------|-----------|-----------|
| Average percentage value (M) | 2.1 | 0.1 | 1 | 4 | 4.1 | 5.5 | 10.1 | 19 | 22.5 | 5.2 | 1.0 | 0.0 | 0 |
| Standard deviation (σ) | ± 0.1 | ± 1.8 | ± 2.1 | ± 1.4 | ± 1.1 | ± 1.6 | ± 2.2 | ± 2.2 | ± 6 | ± 1.5 | ± 0.5 | ± 0.3 | ± 0.2 |

The liquid layer, situated beneath the superficial layer of lipids, was used for the electrophoresis itself.

For the agar electrophoresis we used Ilkov and Nikolov's version (personal communication) of Grabar's technique, slightly modified. Instead of Grabar's original cuvettes, we used our ordinary containers for paper electrophoresis with platinum electrodes.

The dimensions of the glass plate were 23.5 cm \times 11.5 cm. The agar is poured on a plate, which was held horizontally in Plexiglass frames pressed against the plate itself. Double strips of filter paper were previously placed along the two shorter sides of the plate. The agar layer was 3 mm thick (45 cm² for each plate). Three grooves (2 cm \times 1 mm) were cut from each plate and their bottoms carefully covered with diluted agar (0.30–0.50 per cent). Dittmer's⁴ veronal-sodium acetate buffer (pH 8.6, $\mu = 0.05$) was used. The ionic strength of the buffer in the agar gel was half that in the chamber. A sheet of filter paper was placed in contact with the underside of the plate, the ends of the sheet being dipped in water in order to cool the plate. During electrophoresis the Plexiglass frame is covered with a glass plate which is turned every 20–30 min. A spread of 10–12 cm was recorded after a 5 hr migration at 180–200 V by staining with amido black 10B. The electrophoretograms were scanned with the Zeiss extinction registrator II.

Livers of 21 experimental animals were investigated. Except in a few cases, two parallel electrophoretograms were run in each case.

Thirteen well-defined fractions were established. These were designated with the letters a to m, beginning with the globulin fractions and ending with the albumin fraction (Figs 1 and 2, Table 1).

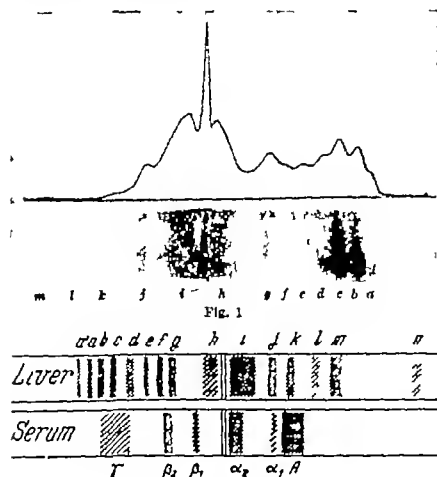


Fig. 1

Fig. 2

We preferred to label these fractions in the direction opposite to that which is customary because the initial globulin fractions were the best defined. Fraction a is situated a little behind the γ globulin, whereas fractions l and m are in front of the albumins of the blood serum.

The interrelations between the remainder of the hepatic fractions observed and the protein fractions of the blood serum can be seen in Fig. 2. Fractions l, i and m occur in negligible quantities and are often scarcely established. Fraction i in Fig. 1 is not sharply delimited from fraction h. In other cases it was clearly delimited so that its existence is out of doubt. A separate fraction migrating beyond fraction a (fraction n) was established in certain cases. In one instance we found a fraction migrating faster than fraction m (fraction n). With these the total number of fractions observed by us was 15. In view of the fact that fraction i is not clearly delimited, however, it is probably composed of a few subfractions. It is possible that this may be the case with fraction h also. Thus the actual number of soluble hepatic protein fractions may be still greater.

The average percentage values for the different fractions and the average standard deviations of their respective variation lines are given in Table 1.

A few of the electrophoretograms were tested for lipoproteins by staining with 'Fettrot'-7-B Ciba. A small amount of lipoprotein could be detected in fraction i only.

Thus our results show that, in the separation of soluble hepatic proteins, agar electrophoresis has certain advantages as compared to free electrophoresis and to electrophoresis on paper.

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Abolition by Chlorpromazine of the Inhibiting Effect of Iproniazid on the Depletion of Adrenal Catechol Amines Induced by Reserpine

It is well known that reserpine induces a decrease of catechol amines in the adrenal medulla.¹⁻³ In the rat pretreatment with iproniazid, a monoamine oxidase inhibitor completely overcomes this catechol amine depletion.⁴⁻⁶

In the present study the modifications of the catechol amine content of the adrenal gland have

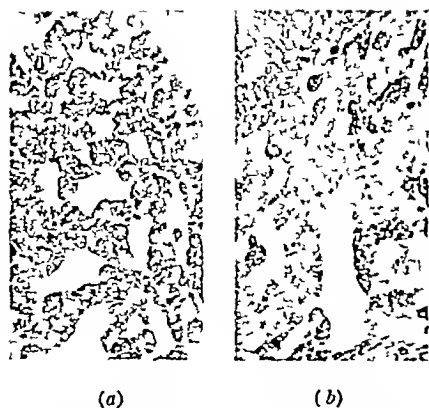


Fig 1 Adrenal medulla of rat Chromaffin reaction (a) A normal degree of chromaffinity is detected in all cells after administration of iproniazid and reserpine (b) After administration of chlorpromazine in association with iproniazid and reserpine numerous islets of cells completely devoid of chromaffin material are observed ($\times 44$)

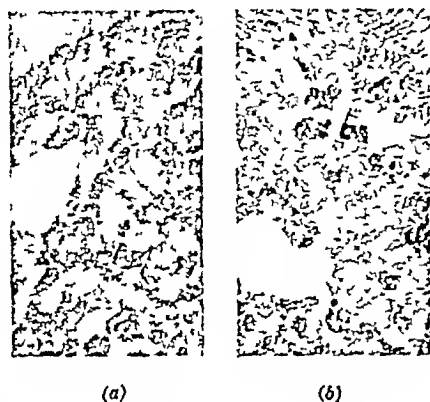


Fig 2 Adrenal medulla of rat Chromaffin reaction After association of chlorpromazine to the reserpine (b), a higher number of chromaffin-negative cells is observed compared to that detected after administration of reserpine alone (a) ($\times 44$)

been investigated when chlorpromazine is added together with reserpine and iproniazid

40 male albino rats, Wistar stock, weighing approximately 250 gm were divided into five groups. Animals of the first three groups were treated respectively with (1) iproniazid (100 mgm/kgm), (2) chlorpromazine (20 mgm/kgm), (3) chlorpromazine (20 mgm/kgm) and iproniazid (100 mgm/kgm). After 5 hr all the animals were given reserpine in a dose of 1 mgm/kgm. The animals of the remaining two groups were treated with chlorpromazine only (20 mgm/kgm) or with reserpine only (1 mgm/kgm). The drugs were injected intraperitoneally. Animals were killed by decapitation 24 hr after the last injection. The adrenal glands were removed immediately after death and then treated with a potassium dichromate-chromate solution.

In the adrenals of rats treated with reserpine the chromaffin reaction shows many groups of cells completely devoid of positive granules irregularly distributed through the normally stained parenchyma (Fig 2a). On the other hand, in the rats treated with iproniazid and reserpine, all the cells of the adrenal medulla show a positive chromaffin reaction similar to that observed in the normal gland (Fig 1a).

The administration of chlorpromazine and iproniazid before reserpine causes consistent changes as compared with the findings observed after the administration of iproniazid and reserpine alone. In these circumstances several groups of cells

completely devoid of chromaffin material can be detected (Fig 1b), moreover, the number of the non-chromaffin cells is considerably larger than in glands of animals treated with reserpine alone. Similar results were obtained for the adrenals of rats treated with reserpine and chlorpromazine (Fig 2b). Chlorpromazine alone does not cause any significant changes in the chromaffinity of the medullar cells.

These results demonstrate that the inhibiting effect of iproniazid on the adrenaline and noradrenaline depletion induced by reserpine can be abolished by chlorpromazine, moreover, this substance alone does not deplete the catechol amines of the adrenal medulla. Since chlorpromazine also increases the depletion of catechol amines following reserpine administration, one could assume that this drug can not only protect the monoamine oxidase from the inhibitory effect of iproniazid but also increases the enzyme activity.

We wish to thank Prof G C Doghotti for his very helpful criticism in this investigation.

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Destruction of Carotenoids in Isolated Chloroplasts

Booth¹ has recently directed attention to the various mechanisms which are responsible for carotenoid destruction in green tissues, two of which, a photochemical reaction and an enzymic reaction, have been examined in alfalfa leaf macerates². Enzymic destruction of β carotene is reported to be greatest in plant tissues containing chlorophyll³, and we have therefore made a preliminary examination of the destruction of endogenous carotenoids in isolated chloroplast suspensions prepared from leaves of spinach beet.

Leaves were ground at -1°C in a medium consisting of 0.5 M sucrose, 0.067 M phosphate buffer (pH 7.3), and 0.01 M potassium chloride. Whole cells and debris were removed by centrifugation at 200g for 1 min, chloroplasts were sedimented by centrifugation at 1,000g for 10 min, washed once, and resedimented before final resuspension in the medium. Carotenoids were extracted from the chloroplasts with acetone, separated chromatographically and estimated spectrophotometrically⁴. The destruction of carotenoids in the chloroplasts was measured by comparing the amounts present before and after reaction.

In order to separate the effect of light from that of heat on the destruction of carotenoids, the experi-

ments on illuminated preparations were carried out at 16°C with illumination from a 100 watt in candescent lamp with a water-cooled condenser. For the dark controls, tubes were covered with aluminium foil.

When non aerated chloroplast suspensions were illuminated, 6 per cent of the β carotene disappeared in 30 min, compared with 4 per cent in the dark. Since none disappeared in boiled suspension the reaction was probably enzymic. Bubbling air through the chloroplast suspensions increased the light-catalysed destruction of β carotene to 27 per cent, while in the dark 14 per cent disappeared. The relative rates of disappearance of the individual carotenoids were β carotene > violaxanthin > lutein, the last only started disappearing after 1 hr. The order of disappearance of these carotenoids is the same as that of the disappearance of carotenoids in autumn leaves⁴.

The addition of Hill reaction oxidants to spinach beet chloroplast suspensions gave varying results. 2,6 Dichlorophenol indophenol¹ reduced the destruction of β -carotene in non aerated chloroplast suspensions to 2 per cent (controls 6 per cent), whereas ferric oxalate-potassium ferrioxalate solution² increased the destruction to 19 per cent. The ferric oxalate-potassium ferrioxalate solution had no effect on the destruction of β carotene in the presence of light and air, but when coupled with the addition of phenazine methosulphate³ there was measurable inhibition of carotene destruction. β Carotene destruction was stimulated by the addition of ortho phenanthroline⁴ to the ferric oxalate-potassium ferrioxalate solution in the presence of light and air. When zinc acetate⁴ was also added, there was a further increase of β -carotene destruction. This result was contrary to expectations since zinc acetate reverses the inhibitory effect of *o* phenanthroline on the Hill reaction⁴.

Further experiments on non illuminated preparations were carried out in which leaf preparations were shaken in a water bath at 30°C in the dark. The activity of chloroplasts from different batches of leaves varied considerably, in some chloroplast preparations 20 per cent of the β -carotene disappeared whereas in others 50 per cent disappeared after 1 hr.

The enzymic destruction of carotene in chloroplasts in the dark at 30°C was inhibited by phenazine methosulphate. *o* Phenanthroline had no effect, but, in the presence of zinc acetate *o* phenanthroline greatly stimulated carotene destruction. These effects are somewhat comparable to those found in the light catalysed destruction and suggest some similarity between the two processes.

In an attempt to locate the enzymic system responsible for destruction of β carotene a comparison was made of the disappearance of β -carotene in leaf homogenates, chloroplasts prepared from them and the supernatant fraction which still contained broken chloroplasts. In spinach beet leaves there was an almost equal destruction in all three fractions, suggesting that the enzyme system responsible for the destruction was closely linked to the pigment-protein complexes. In sugar beet leaves, however, there was more destruction of β -carotene in both the homogenate and the supernatant than in the chloroplast fraction. This could be due to the fact that in sugar beet leaves there are at least two differently located enzyme systems responsible for carotene destruction, which would be in accord with

more recent findings (Faiend, J, and Mayer, A M, unpublished work).

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Use of Porter-Silber and Schiff Reagents as Spot Tests for Steroids applied on Paper and their Application to the Study of Rat Adrenal Lipids

THE formation of phenylhydrazones with an absorption maximum at 410 m μ by the method of Porter and Silber characterizes steroids with a dihydroxyacetone side-chain. These authors recently reported that the reaction also occurred with the aldehydes of corticosterone and of 11 dehydrocorticosterone and that with the latter compounds the phenylhydrazone developed at a more rapid rate¹. The specificity and difference in speed of the reaction are also evident when it is carried out on paper. A bright yellow colour develops when a region containing a minimum of 2 μ g/cm² of the chromogen is passed through the Porter-Silber reagent (25 ml water, 41 ml conc sulphuric acid 34 ml ethyl alcohol and 43 mgm phenylhydrazine hydrochloride). The colour appears instantly with C-21 aldehydes and their acetates, and in 1-2 hr with steroids containing the dihydroxyacetone side-chain and their acetates. It is stable for days provided the paper is not rinsed or warmed, and under these conditions the paper does not char. Corticosterone, 17 hydroxyprogesterone and other steroids tested gave no colour at a concentration of 25 μ g/cm².

C-21 aldehydes freshly prepared by oxidation with cupric acetate after the method of Beyer and Hoffman², may be detected with a Schiff reagent (1 per cent pararosaniline hydrochloride in sulphurous acid), if 10 μ g have been applied over an area of 1 cm². A purple colour appears as the rest of the paper turns pink. The development of the same purple colour in the rest of the paper may be delayed for a few days by encasing the paper in 'Scotch tape'. Steroids with an α ketol and a dihydroxy acetone side chain gave no reaction in amounts of 50 μ g/cm², neither did a sample of aldosterone kindly supplied by Merck and Co. It is to be noted that freshly prepared aldehydes react at a lower concentration than material which has been stored in the refrigerator or chromatographed in the toluene-propylene glycol system.

Both tests have proved helpful in the synthesis and purification by paper chromatography of steroid C-21 aldehydes. When a region on paper gave a positive reaction to the two tests and failed to reduce a tetrazolium derivative, the presence of an aldehyde was assumed.

The sensitivity and simplicity of the Porter-Silber spot-test should make it a useful tool for the detection of Porter-Silber chromogens in lipid extracts of biological fluids. The test has helped in establishing the facts that the incubated rat adrenal secretes little, if any, cortisol or cortisone², that the non-reducing, lipid-soluble Porter-Silber chromogen produced by this tissue has the same mobility in the toluene-propylene glycol system as the aldehyde of 11-deoxy-17-hydroxycorticosterone, and that acetylation of the adrenal lipid yields two ultra-violet-absorbing, non-reducing Porter-Silber chromogens, a component with the same mobility in the benzene-formamide system as a product obtained by acetylation of 11-deoxy-17-hydroxycorticosterone aldehyde and a more polar material⁴.

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Some Observations on Certain Mucoproteins containing Neuraminic Acid

It is now well established¹⁻⁴ that mucoproteins, particularly those containing neuraminic acids, play a major part in the natural defences of the human body. With the object of determining what part is played by such mucoproteins in human cancer we have assessed the amount and distribution of mucoproteins containing neuraminic acid by determination of the neuraminic acid content of tissues obtained in surgical operations for cancer of the stomach, colon and breast, and compared these with those of tissues obtained during removal of ulcers of the stomach and duodenum.

Each portion of tissue was extracted exhaustively at room temperature with acetone and later with methanol-chloroform (3:1 v/v) in order to remove any neuraminic acid-containing gangliosides. Part (50 mgm) of the fat-extracted residue was suspended in water and dialysed against 0.01 N sulphuric acid at 0° for 2 days. The neuraminic acid(s) in the non-dialysable residue was then liberated by heating at 80° for 1 hr with 0.04 N sulphuric acid and recovered from the neutralized solution by dialysis. The neuraminic acid determination⁵ was carried out on this dialysate to avoid interference due to chromogens from other sugars.

When the whole of the surgical tissue from each operation was examined in this way the neuraminic acid contents of two carcinomas (0.33 and 0.43 cent) from the pylorus end and one (0.64 per cent) from the cardia end of the stomach were appreciably higher than those (0.11, 0.13 and 0.14 per cent) of three stomach ulcers or those (0.12, 0.16 and 0.18 per cent) of three duodenal ulcers. In a more meaningful

Table 1 NEURAMINIC ACID CONTENT IN VARIOUS AREAS OF A MALIGNANT GROWTH

| Type of carcinoma | Percentage neuraminic acid content in area | | |
|---------------------------------------|--|------|------|
| | A | B | C |
| Adenocarcinoma of the colon | 0.24 | 0.26 | 0.17 |
| Carcinoma of the pylorus and duodenum | 0.18 | 0.18 | 0.11 |
| Scirrhus carcinoma of the breast | 0.20 | 0.11 | 0.13 |
| Duct carcinoma of the breast | 0.16 | 0.15 | 0.08 |

comparison the tissues obtained from later cancer operations were arbitrarily divided into three portions: (A) the cancerous or centre of the malignant growth; (B) the invasive area in which there is an interlocking growth of the normal and cancer cells; (C) the apparently 'normal' area outside. The results are given in Table 1.

Bearing in mind the difficulty of deciding on the so-called invasive area and the obvious variation in such an arbitrary division, it is nevertheless evident that the amount of mucoprotein containing neuraminic acid is almost doubled in the area of malignancy.

Several types of neuraminic acids (N-acetyl-, N,O-diacetyl-, N-glycolyl-, etc.) have now been recognized. Paper chromatographic and ionophoretic analysis revealed that the neuraminic acid liberated by hydrolysis of the tissue from two stomach ulcers, a duodenal ulcer, a carcinoma of the pylorus, and from all three areas (A, B, and C) of the colon adenocarcinoma and the scirrhus breast carcinoma was N-acetyl neuraminic acid. Both N-acetyl and N,O-diacetyl neuraminic acid were liberated from a malignant tumour situated at the cardia end of the stomach and involving 1 in of the oesophagus.

In another aspect of this assessment of the distribution of carbohydrate-containing substances in human tumours we have determined⁶ the hexosamine contents of some of the tissues studied above. Mucoproteins almost always contain hexosamines, but the hexosamine content of the tissue should not necessarily follow the neuraminic acid values since hexosamines are also components of blood group polysaccharides and many tissue polysaccharides. The carcinoma obtained from the cardia end of the stomach which had the highest neuraminic acid content (0.64 per cent) also had the highest hexosamine content (3.3 per cent) of those studied. The distribution of hexosamine (1.8 per cent in A, 1.6 per cent in B and 1.2 per cent in C) in the colon adenocarcinoma also followed that of the neuraminic acid content. However, the hexosamine content (2.1 and 2.0 per cent) of the whole of the surgical tissue from two stomach ulcers and that (2.3 per cent) of a duodenal ulcer differed little from that (2.2 per cent) of the carcinoma of the pylorus. Analysis⁷ revealed that glucosamine and galactosamine were the only amino-sugars present in the duodenal ulcer (glucosamine, galactosamine, 1.9:1) and in the carcinomas from the pylorus end (glucosamine, galactosamine, 2.1:1) and from the cardia end (glucosamine, galactosamine, 2.3:1) of the stomach. Trypsin digestion⁸ of the fat-extracted tissues from the same duodenal ulcer and the two stomach carcinomas, removal of protein with trichloroacetic acid and addition of alcohol gave crude polysaccharide mixtures in yields of 2.2, 2.1, and 2.3 per cent.

respectively. Acid hydrolysis of these mixtures liberated hexosamines, fucose, and galactose together with small amounts of glucose and mannose. This suggests that most of the polysaccharide in these tissues was of the blood group substance type. The glucose probably originated from the glycogen* which constituted 0.35 per cent of the duodenal ulcer tissue and 0.30 and 0.29 per cent respectively of the stomach carcinomas (all yields calculated on the dried fat-extracted tissue). Ionophoretic analysis of the crude polysaccharide mixtures revealed the presence of small amounts of acidic polysaccharides staining with toluidine blue¹² accompanied by much larger amounts of neutral polysaccharides.

We are indebted to the staff of the West Bromwich and District General Hospital, West Bromwich Staffs, for the provision of tissues. We have also had valuable discussion with Prof. J. W. Orr and Dr. D. L. Woodhouse of the Cancer Research Laboratories. One of us (D. J. T.) thanks the University of Birmingham for the award of a scholarship. The research was supported by a grant from the British Empire Cancer Campaign.

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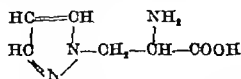
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α Amino- β -(pyrazolyl-N) Propionic Acid a New Amino-Acid from *Citrullus* *vulgaris* (Water Melon)

DURING recent years, several new amino- and imino acids have been characterized as components of the non protein nitrogen fraction of plant materials. Another example has now been found in seeds of *Citrullus vulgaris* (water melon, var. 'Tom Watson'). The structure of this new amino-acid (hereafter termed β PA) is as follows



α Amino β -(pyrazolyl N) propionic acid
or β (pyrazolyl N) alanine

This amino-acid is unique in that it is the first example of a natural product which contains a pyrazole ring. Furthermore in contrast to the other heterocyclic ring-containing amino-acids, histidine

and tryptophan the side-chain of β PA is attached to the pyrazole ring through a carbon to nitrogen bond.

The presence of the amino acid was detected by two-dimensional paper chromatography (water saturated phenol/butanol/acetic acid/water) in a 70 per cent (v/v) ethanol extract of ground seeds. It occupied a position very similar to that of proline on two dimensional chromatograms. The compound reacted with ninhydrin to give a normal bluish purple spot. With Ehrlich's reagent (p-dimethylaminobenzaldehyde) it gave a yellow-coloured spot and it formed a copper complex with copper acetylacetonate, so indicating the presence of an α amino group.

By ion exchange chromatography (Zeokarb 215 and 'Dowex' 50-0 25 N ammonia displacement) 3 gm of β PA was isolated from 10 lb of water melon seeds. The amino-acid was crystallized twice from distilled water (solubility approximately 4 gm/100 ml) and yielded a white solid with an elemental analysis of C, 46.7, H, 5.7, N, 27.1, O (by difference), 20.4. The calculated values for β PA are C, 46.4, H, 5.8, N, 27.0, O, 20.8.

Therefore, the isolated material had an empirical formula of $\text{C}_5\text{H}_7\text{N}_3\text{O}_3$, and was isomeric with histidine. This formula provides too few hydrogen atoms for the more normal saturated open chain amino-acid structure. The compound was found to be stable to strong mineral acid (6 N hydrochloric acid at 100° for 24 hr) and alkali (5 N barium hydroxide at 100° for 24 hr). Treatment of the isolate with 55 per cent (w/w) hydriodic acid at 120° for 24 hr degraded it and alanine was identified as the only ninhydrin reactive product by comparison with an authentic sample of the amino-acid on paper chromatograms developed in water saturated phenol/butanol/acetic acid/water mixture, butanol saturated with 2 N ammonia, and ethyl acetate/pyridine/water (organic phase of 2:1:2 parts by volume mixture). The fission of an alanine moiety in this way not only indicated its presence in the structure of the isolate but also suggested that the alanine residue was attached to the remainder of the molecule through a C—N linkage (the corresponding C—C linkage found in histidine is stable to hydrogen iodide reduction).

The remaining atoms of the formula are most easily accommodated by assuming the presence of an imidazole or pyrazole ring system. It would appear that Shimano and Kaya¹ have isolated a smaller quantity of the same substance from the press juice of water melon. Both isolates had the same elemental analysis and m.p. (decomp.) in the range 230–238° C. The Japanese workers suggested that their isolate was a β -(imidazolyl N) propionic acid, although no definite proof for the presence of the imidazole residue was given. Our evidence provides no support for the idea of an imidazole ring. The isolate failed to give the Pauli test, and did not possess a pK in the pH range 6–7, normally a feature of imidazole derivatives. Pyrazole derivatives have an analogous pK in the pH range 2–3, the titration curve of the isolate showed a weak point of inflexion in this range. Nuclear magnetic resonance spectra² performed on the isolate and various N-substituted imidazole and pyrazole derivatives proved almost certainly that the isolate contained the pyrazole ring system. The fine structure of the spectrum of the isolate also indicated an unsubstituted α amino group in the alanine residue and the presence of a $-\text{CH}_2-$ group and an N—O linkage. These requirements are all met by the above structure for β PA.

Crude, small-scale preparations of β PA and β -(imidazolyl-N) alanine (β IA) have been made. The silver salts of pyrazole and imidazole respectively were refluxed in methanol with the methyl ester of β -chloroalanine hydrochloride (prepared by the method of Fischer and Raske³). After removal of the methanol and hydrolysis with 6 N hydrochloric acid, the reaction mixtures contained three amino-acids: Serine and a trace of a compound, probably alanine, accompanied either β PA or β IA. The synthetic β PA was inseparable from the isolated material on paper chromatograms, whereas β IA was easily resolved from the isolate. β IA had an R_F very similar to that of histidine in water-saturated phenol, in butanol/acetic acid/water mixture it moved slightly more slowly than histidine. The yields obtained in these preparations were low, but it is hoped that a future large-scale preparation of β PA may provide sufficient crystalline material for comparisons to be made with the natural substance using other accepted physico-chemical techniques.

We wish to thank the Ferry-Morse Seed Co. (California) for supplying the seed, Dr I. L. Finar for advice on the syntheses, and Drs J. H. Ridd and R. F. M. White for their help with the nuclear magnetic resonance spectra.

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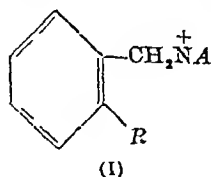
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ANIMAL PHYSIOLOGY

New Antiadrenergic Compounds

WE have found that the benzyl quaternary ammonium compounds (I, patents pending) have a novel and highly specific blocking action on the peripheral sympathetic nervous system, which resembles that following section of adrenergic nerves and differs from that produced by adrenolytics, ganglion-blocking agents and reserpine.



Compounds of the above type were screened by examining their efficacy in relaxing the nictitating membrane when injected subcutaneously in the cat. Activity was highest in the quaternary compounds (I, $R = H$) and the *ortho*-substituted analogues (I, $R = Me, F, Cl, Br, I$, and NO_2). Activity was also very sharply influenced by the cationic head, high activity being encountered in the compounds I with $NA = NMe_2Et$, $NMe_2(CH_2)_2OH$, $EtN(CH_2)_4$, $HO(CH_2)_2N(CH_2)_4$. Lower homologues such as I with $NA = NMe_3$, $R = Br$ were inactive and higher homologues showed much reduced activities. There was no mydriasis or other overt effect in cats injected

with any of these compounds, except one (I, $NA = NMe_2Et$, $R = H$) which caused marked parasympathomimetic effects.

One of the most active compounds, 373C57 (I, $NA = NMe_2Et$, $R = Br$), was examined in detail, as its bromide, and the findings indicating its mode of action are summarized as follows.

After subcutaneous injection of 5–10 mgm/kgm of 373C57 in the unanaesthetized cat, the nictitating membrane gradually relaxed, becoming fully exposed in 4–6 hr, and retracted only after approximately 24 hr. Similarly, in cats under chloralose anaesthesia, 373C57 gradually inhibited the effect of indirect stimulation of the nictitating membrane irrespective of whether the stimuli were applied to the pre- or post-ganglionic nerve, the block was most marked when the stimulation was continuous. This inhibitory effect was accompanied by a gradual and prolonged fall in blood pressure often preceded, when the drug was given intravenously, by a small temporary rise. The response of the heart to stimulation of the cardio-accelerans nerve was blocked, and the pressor effects of intravenous injections of adrenaline and noradrenaline were increased.

373C57 blocked the response to stimulation of the adrenergic nerve in various isolated preparations. Thus it prevented the vasoconstriction caused by stimulating the greater auricular nerve in the perfused rabbit ear, the relaxation of the rabbit ileum during stimulation of the visceral efferents, and the contraction of the rabbit uterus elicited through the hypogastric nerve. The effects of adrenaline and noradrenaline on these preparations were enhanced after giving 373C57.

In the cat, the pressor effects of intravenous dimethylphenylpiperazinium iodide and splanchnic nerve stimulation which are mediated by the adrenal medulla were greater after giving 373C57, whereas the hypertension caused by the ganglion-stimulating action of dimethylphenylpiperazinium iodide in the adrenalectomized animal was blocked. This shows that the antiadrenergic action of 373C57 is not accompanied by an interference with the adrenal mechanism, such as occurs with the ganglion-blocking drugs or reserpine.

Some of the properties of 373C57 resemble those of the 2,6-xylylother of choline bromide, TM10², but unlike this compound, 373C57 does not cause parasympathomimetic effects or deplete the pressor amine content of the rat adrenal. The latter finding, if it applied also to the adrenergic nerve, would indicate that it is unlikely that 373C57 acts either by depleting the local stores of catechol amines or by inhibiting the biogenesis of noradrenaline in adrenergic nerves, as was postulated² might be the mode of action of TM10. 373C57 caused no overt behavioural changes in animals, and thus together with the absence of depletion of the catechol amine content of the adrenal medulla of rats is in contrast with the actions of reserpine.

Together with our colleagues, Drs A. McCoubrey and W. G. Duncombe, we have studied the distribution in tissues of 373C57 labelled with carbon-14 in one of its methyl groups. Following subcutaneous injection in cats, much higher concentrations of radioactivity were found in adrenergic nerves, sympathetic ganglia and tissues with a rich adrenergic innervation, than in other tissues. The concentration of 373C57 indicated to be present in adrenergic nerves, when applied topically, blocked the physiological responses to stimulation of the pre- and post-ganglionic cervical

sympathetic nerves in the cat, the visceral adrenergic nerves of rabbit intestine, and the greater auricular nerve in the rabbit ear

We conclude that the blocking effect of 373057 on the peripheral sympathetic nervous system is due to an action on adrenergic nerves and that its specificity is related to the selective accumulation of the compound in adrenergic nerves following systemic administration

The properties of 373057 and related antiadrenergic compounds may render them useful for the reduction of sympathetic tone, for example in the treatment of hypertension, they do not impair parasympathetic functions as do ganglion blocking agents nor depress the central nervous system as does reserpine

Note added in proof We have just learned that the open name, approved by the British Pharmacopoeia Commission, for 373057 *p*-tolueno sulphonate is bretilum tosylate

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Action of Ganglion Blocking Drugs on Choline Acetylase

THE first practical hypotensive drugs which acted by causing autonomic ganglionic block were *bis* quaternary ammonium salts recently substances containing only a single secondary or tertiary amine group have been introduced as hypotensive agents of a similar type. There are however, differences in the details of the pharmacological actions of the two types of drugs, for example the mono-amine compounds, mecamylamine and pempidine, are slower in onset of action but more prolonged when compared with the older group (for example, hexamethonium or pentolinum). The *bis* quaternary ammonium drugs paralyse ganglia by extracellular competition with acetylcholine for synaptic receptor sites, the differences in action might be explicable if the newer compounds acted in some other way for example, by inhibition of acetylcholine formation. Their ability to penetrate cell lipid membranes or barriers makes such an intracellular action plausible.

Choline acetylase preparations from guinea pig brain have therefore been used to compare the effects of three of these mono-amine compounds with those of a hemicholinium (*HC* 3) a compound which is known to owe its high toxicity to interference with acetylcholine synthesis.¹⁻³ The enzyme preparations used were modifications of those previously employed and were more dependent on the addition of choline for their activity. *HC* 3 inhibits only the weaker 'P' preparation, this action results from its competition with choline for some limited path of entry into the less damaged particles of that preparation.⁴

The three mono-amine compounds tested (mecamylamine, pempidine, and its ethyl analogue, Imperial Chemical Industries Cpd 26530), showed no significant inhibition of either enzyme preparation when tested in the concentration (10^{-4} M) at which *HC* 3 reduces the activity of the 'P' preparation by one

PARTICULATE CHOLINE ACETYLASE PREPARATIONS FROM GUINEA PIG BRAIN

Chilled fresh brains homogenized (0-4) in 9 vol 9 per cent w/v sucrose (10^{-4} M with respect to ethylenediamine tetraacetic acid pH 7.4)

10 min at 550g (0°)

supernatant 45 ml taken 10 min at 15 000g (0°) sediment (discarded)

sediment resuspended in sucrose solution to make final vol. 12 ml. Supernatant (discarded)

7 ml suspension

5 ml suspension + 5 ml buffer/saline + 2 ml diethyl ether (peroxide free)

Stand at 0-4° for 20-30 min

+ 7 ml buffer/saline

2 vol 0.0 per cent w/v sodium chloride
1 vol 0.15 M sodium dihydrogen phosphate
1 vol 0.15 M sodium pyrophosphate

P' suspension

E' suspension

half Pempidine was also ineffective at 10^{-4} M a concentration which would be expected to reveal any ability to interfere specifically with the enzyme system

The response of the frog rectus abdominis muscle used to assay acetylcholine was affected by the presence of the drugs, especially by mecamylamine and it was necessary, to prevent a progressive reduction in sensitivity, to adopt a routine of regular repeated washing and resting of the tissue after each estimation

Contrary to the results reported here a brief note⁵ appeared earlier indicating that mecamylamine can inhibit acetylcholine formation but recent discussion with the authors has clarified the position. The suggestion arose from preliminary experiments in which a soluble choline acetylase was used prepared from an acetone powder of rabbit brain, the acetylcholine formed being estimated colorimetrically. Mecamylamine was used in amounts equimolar with choline and since the assay method adopted necessitates a high choline concentration (10^{-2} M or more) there was a serious possibility that the inhibition was non specific. Subsequent studies with other secondary amines confirmed this and the work was discontinued.

In their investigation of pempidine Corne and Edgo⁶ showed that a large dose (10 mgm) could reduce by 40 per cent the acetylcholine output from the cat's perfused superior cervical ganglion in response to pre ganglionic stimulation. Their experi-

Table 1

| | P' preparation | E' preparation |
|---|------------------|---------------------|
| Average acetylcholine content 0.1 mole/ml suspension | 1.7 (1.8-2.5) | 0.16 (0.0-0.5) |
| Average net synthesis of acetylcholine 0.1 mole/ml suspension | 5.0 (4.0-5.7) | 21.4 (10.7-24.7) |

Reaction system contained in 2 ml. 0.1 μ mole acetyl-coenzyme A 0.05 μ mole choline chloride 3 μ mole tetraethyl pyrophosphate 0.2 μ mole inhibitor (if any) 50 μ mole sodium dihydrogen phosphate 50 μ mole sodium pyrophosphate, 2 ml. P' or E' enzyme suspension incubation for 15 hr at 37° with gentle shaking. After incubation reaction stopped by acidification and heating alkali treated control prepared and the acetylcholine content assayed on frog rectus abdominis muscle preparation sensitized with tetraethyl pyrophosphate

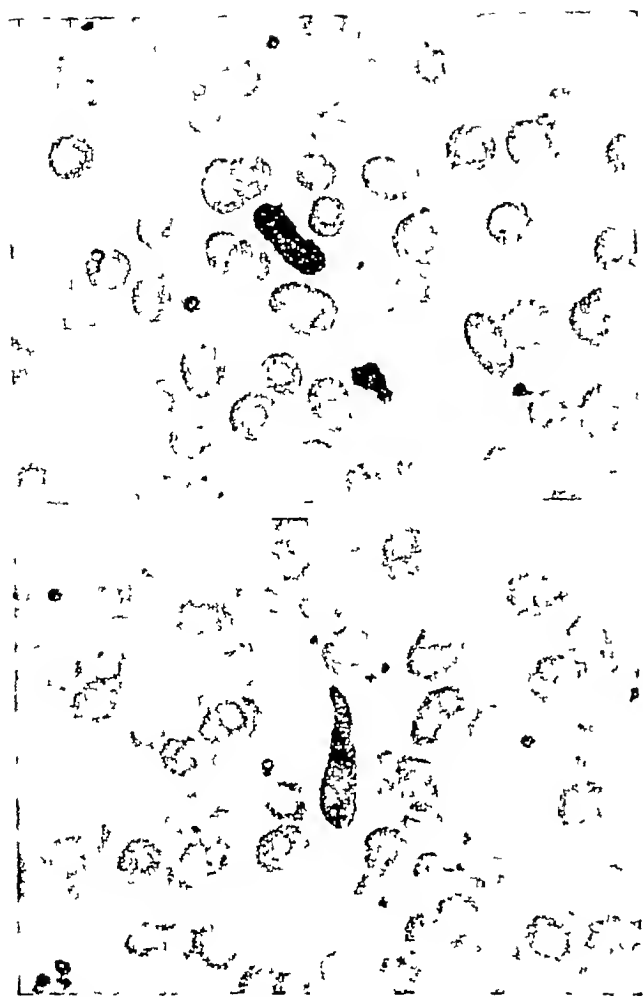


Fig 3 (above) Sausage-shaped long human blood platelet ($\times 830$, oil immersion) Fig 4 (below) Long human blood platelet ($\times 830$, oil immersion)
(Photograph Robert T. Duckworth)

indicate that the presence of these cells in mammalian lung vessels is a normal phenomenon, where they appear to break up into platelets. Their studies demonstrated that the cells seen in the lung vessels were identical histochemically and morphologically with the bone marrow megakaryocytes and that they were transported from the bone marrow to the lungs by the venous circulation. Their histological observations indicated that the megakaryocytes are too large to pass the lung capillaries intact (Fig 1) and that the cells appeared to break up in the capillary anastomoses by the pumping action of the right heart ventricle (Fig 2). The megakaryocytes appeared to be moulded into the shape of the capillaries and divided by their anastomoses. It was postulated that in assuming the capillary outline by being pressed into the vessels the cells can emerge as casts of the vessels, thus occasionally being encountered in blood smears as long platelets (Figs 3 and 4). It can be further postulated that further break up of these elongated platelets may occur in the eventual passage through the peripheral capillary vascular system. It also would appear that the elongated forms are more commonly seen in individuals with high platelet counts where the platelets appeared freshly formed.

In summing up, it would appear that long platelets may be formed from pulmonary megakaryocytes by being pressed into the lung capillary blood vessels and emerge as casts of the same.

This work was supported in part by a grant from the Westchester Heart Association

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A Seasonal Rhythm in the Presentation of Bone Sarcoma in Man

FROM a study of the aetiology of osteogenic sarcoma in man carried out during the past four years, it has been possible to demonstrate certain trends in the age and sex incidence of these relatively rare neoplasms^{1,2}. Probably the most interesting features are the observations that the tumours tend to arise at an earlier age in females among adolescents, and also the higher incidence of tumours of the arm and pectoral girdle at an earlier age compared with those of the leg and pelvis in juveniles of both sexes. On comparison of the mean ages of groups of osteogenic sarcomata in adolescent males and females, whether for the whole skeleton or for individual bones, the differences of mean ages (male minus female) are seldom statistically significant, nevertheless they are almost invariably in the same direction.

The most likely explanation of these differences in age, sex and site would seem to lie in the relatively advanced skeletal growth of girls, and in the general cephalad-caudad sequence of growth progression. It is well known of course that the majority of osteogenic sarcomata of adolescents arise in the metaphyses of the major long bones, although this feature of consistent anatomical location is not so clearly defined in tumours of persons over the age of fifty-five years, among whom Paget's osteitis deformans forms the background of the majority of cases—at least in Great Britain¹. In this older age-group the trends mentioned above cannot be shown to occur.

Among the characteristic patterns of juvenile bone growth is a seasonal rhythm with the maximum velocity peak in the spring months of April, May and June. The literature on this subject has been discussed by Brody³ and by Tanner⁴, the former author comparing the human growth-cycle with other photoperiodic phenomena of mammals and birds. In discussing this topic Tanner⁴ states that the monthly height-gain average for the period April-June may be as much as 2-2½ times that of the months October-December.

In the light of these considerations an analysis was made of the case-histories of 102 osteogenic sarcomata included in the records of the Bristol Bone Tumour Register, and from among these were eventually separated a group of 40 tumours of long bones all in persons less than 30 years old. This small series was supplemented by the addition of a further 34 cases from four other hospitals, details being furnished by the consultant surgical staffs and medical records officers of these institutions. These 74 cases have been plotted in Fig 1 according to the month when they

first complained of any definite symptom directly related to their subsequent clinically apparent tumour. This initial symptom was most often bone pain—less frequently pain and local swelling. The data are cumulative over a period of 18 years (1941–58). It will be noted that the incidence of tumours is greater during the months June–November inclusive, when the monthly average was 9.2 tumours per month, than for the months December–May when the average of 3.2 tumours per month was encountered. (This difference is statistically significant $\chi^2=16.33$, $P < 0.01$.)

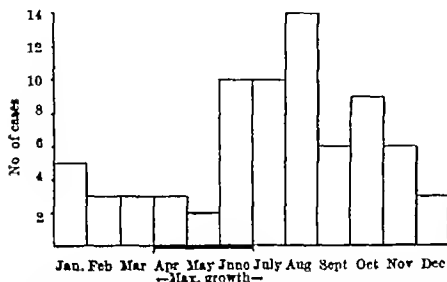


Fig. 1. Osteogenic sarcoma—long bone cases only, all less than 30 yr old. Plotted according to month of presenting symptom. 'summer' period (June–November inclusive) 55 cases; 'winter' period (May–December inclusive) 19 cases; total 74 cases.

The same data were re-examined by annual groups (1943–58), but excluding 4 tumours which were recorded for the years 1941–42. Although the numbers each year are small, the trend of numerical preponderance in 'summer' still appears. The annual distributions are shown in Fig. 2. In 13 of 16 recorded years the number of tumours presenting during the 'summer' period is greater than that encountered for the corresponding 'winter' period. (These differences are again significant, $t=3.04$, $P < 0.01$.)

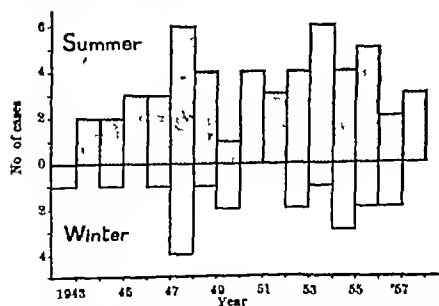


Fig. 2. Osteogenic sarcoma—same series as Fig. 1 plotted by years according to timing of presenting symptom. Comparing numbers in summer and winter periods the difference is statistically significant ($P < 0.01$).

For brevity's sake it may simply be stated here that these differences in monthly incidence do not appear in a similar analysis of a series of 55 osteogenic sarcomata in older persons more than thirty years of age. This negative result might be expected in view of the modified aetiology of bone tumours of this age group.

It may be added that this increase in 'summer' incidence in the presentation of sarcomata holds for either sex when the whole series is so sub-divided. Moreover it exists in each of the four major component groups of cases which were derived from Bristol, London, Manchester and Glasgow. (It has also appeared in a further group of 15 patients, details of whom were received too late for inclusion in the present study.)

With the material available it is not yet possible to define the shape of the 'summer peak' or its precise timing, but in all probability it appears some time during July and August, that is, about 3 months after the spring peak in the bone growth velocity curve.

In adolescents the growth of bone in length with subsequent remodelling continues throughout the year, and is responsible in some obscure way for the basic monthly level of incidence of bone sarcoma. The probable size of the lag period between the two peaks of spring growth and presentation of bone sarcoma would seem however to suggest a biological linkage especially in the light of collateral evidence which relates these two phenomena. Inquiry has not indicated any extraneous factors which might otherwise account for this abnormal distribution of tumour presentation during the yearly cycle.

Dr Grace M. Jeffree has assisted in this work by examining the case records of the Bristol group, and Mr G. M. Clarke has given invaluable advice with the statistical treatment of the material.

Details of patients have been freely given by the contributing members of the Bristol Bone Tumour Registry: by Mr H. Jackson Burrows, and the Medical Records Officer and Committee of the Royal National Orthopaedic Hospital, London; by Dr Ralston Patterson of the Clarendon Hospital and Holt Radium Institute, Manchester; by Mr Rowland Barnes, and Dr Mary Catto, of the Glasgow Western Infirmary; and by Dr Constance A. P. Wood of the Hammeramith Hospital, London.

This investigation was supported by grants from the British Empire Cancer Campaign.

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PLANT PATHOLOGY

Needle Transmission of a New Maize Virus

THE rough dwarf disease of maize ("Nanismo Ruvido del Maiz") has been known from Italy since 1949¹ and has lately been reported from Israel too.² The symptoms of the disease and its epidemiology were described in both countries^{3,4} with the assumption that the causal agent is a plant virus. Since no experimental transmission of the disease had been accomplished it was not certain that the agent was a virus. All attempts to transmit the disease by rubbing sap into maize leaf blades, using various abrasives, have failed. Transmission trials with a local dodder species *Cuscuta eigna* Smolov also proved negative.

Recently, however, transmission has been achieved for the first time by the following method. Hybrid maize plants showing severe dwarf symptoms were ground in a meat mincer, the sap squeezed through a cheese cloth and then centrifuged for 5 min at 3,000 r.p.m. The supernatant fluid was injected by means of a 1 c.c. tuberculin syringe into the stalks of 3-week-old hybrid maize seedlings (Neve Yaar hybrid 22, single cross) grown under insect-proof conditions. The dosage was about 0.2 c.c. per seedling divided into 5 punctures at different sites. A control series was injected with healthy sap in the same manner. Three out of twelve plants injected with diseased sap, in two different series, developed both stem and leaf symptoms (including the rare symptom of split blade) within two months. As this was done in winter, without artificial illumination, it is believed that during summer the development of symptoms should be faster. Infectivity of the sap, when frozen, was retained for at least 24 hr. Since the virus is not transmitted by seed, the reliability of the test seedlings is unquestionable.

Similar cases where mechanical transmission of plant viruses could be obtained by needle inoculation only are those of sugar beet curly top⁵ and clover wound tumour⁶. Both these viruses are leaf hopper-borne and, at least in the case of curly top, the virus is believed to exist in the phloem which might be considered inaccessible to ordinary surface rubbing⁷. In the case of the maize rough dwarf virus it may be inferred from Biraghi's studies⁸ on the pathological anatomy of the disease that the virus tends to inhabit the phloem, though its natural vector is still unknown.

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BIOLOGY

Black Marlin in British East African Waters

RECENTLY I stated that only the striped marlin (*M. audax*) had been caught by the East African Marine Fisheries Research Organization, and records of the black marlin in these waters were of doubtful value¹.

Since that communication I have taken two black marlin while using a longline 10 miles off the Tanganyika coast at latitude 8° S, the fish were of standard length 2,130 and 2,325 mm and weight 125 and 135 lb respectively. On capture and comparison the differences from the striped marlin were most obvious—a very low dorsal fin, deep body, steeper head profile and 'rigid' pectoral fins. Proportional measurements confirmed the field observations and an examination of the morphology of the

pectoral girdle showed it to be similar to that described by Morrow² as diagnostic for the black marlin. Colour was as follows: in life, upper two-thirds of body and fins blue-grey and lower third of body white, the join between the two colours being distinct; on death, the colour fades rapidly and the body and fins become grey, a little darker above. There are at no time any signs of the vertical stripes or brilliant cobalt blue coloration of the striped marlin.

Morrow (personal communication) reveals that his Pemba specimen of marlin weighed 159 lb at 2,151 mm and not 259 lb, as reported in his paper on East African fishes³, and thus the record is validated as that of a black marlin.

In a recent paper on marlin taxonomy, Morrow⁴ examined the pectoral girdle of the remains of Playfair's type specimen of *H. brevirostris* from Zanzibar and found it to correspond exactly to that of the black marlin⁵. Thus the position of this fish is clarified, the original proportional measurements and later examinations of the type specimen being insufficient for exact identification as stated earlier¹.

The black marlin is rare in this area, only two having been caught hitherto by this Organization, as compared with eighty-four striped marlin.

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A Chimæric Duck with the Head of a Chick

It is well known that the chick embryo fails to produce detectable antibodies against various foreign antigens, so providing a favourable environment for culturing viruses and transplanting various tissues of



Fig 1 A duck embryo with the grafted head of a chick, after 28 days of incubation

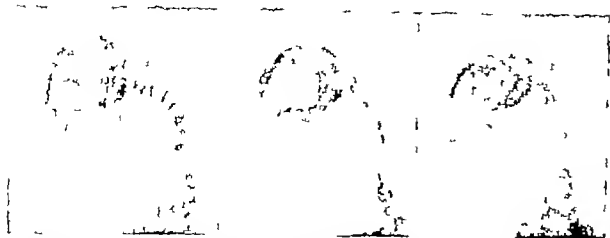


Fig. 2. X-ray photographs of the skulls at hatching. Left a duck, centre the chimera (Fig. 1), right a chick. Note the striking similarity between the duck and the chimera except the upper beaks.

birds and mammals.⁴ It is also known from the work of Bingham *et al.*⁵ that "actively acquired tolerance", the power to react immunologically against foreign homologous tissue cells with which they have been inoculated in fetal life, is never developed by birds and mammals, or developed only to a limited degree. A renewed interest in heterotransplantation stimulated us to graft various types of tissue primordia between embryos of two different genera of birds, the chick (*Galliformes*) and the duck (*Anseres*). Using the same combination Hašek and his co-workers were not successful in inducing a tolerance for skin heterografts between young obtained by embryonic parabiosis⁶ or between young injected with each other's spleen or bone marrow cells shortly after hatching.⁴ On the other hand, some cases of limb bud grafting during early days of incubation by Eastlick⁴ seem to indicate a certain degree of tolerance, although his experiment was carried out from a point of view of tissue incompatibility in heterologous combination.⁴

As one of an experimental series of reciprocal chick-duck heterotransplantation, the grafting of the forebrain region following the technique originally developed by Martinovitch on the chick embryos⁷ was performed. The heads were covered just behind the optic vesicle, and were exchanged between the embryos of white duck and a coloured breed of chick, Barred Plymouth Rock, at stages corresponding to Hamburger and Hamilton's stage 10-11. These stages were reached by the chick after about 42 hr., and by the duck after about 55 hr. of incubation at 37.5°C. While the chick embryos grafted with duck heads did not survive for long one of the duck embryos with the head of a chick survived through the whole length of its embryonic life 28 days of incubation (26 days after grafting). Fig. 1 illustrates this chimera embryo.

In size and in growth of feathers, the chimera resembles the average duck embryo at hatching. However, the umbilical ring was still large and the withdrawal of the yolk into the body cavity had not begun. The host duck was found by examining the gonad to be a male. The contribution made by the graft was represented by the upper beak and eyes, the under-developed crest and the melanophores. The latter spread over both lateral surfaces of the head far caudad beyond the auditory opening, leaving unpigmented only the feathers on a mesial portion in the occipital region. It was clear that an extensive migration of the chick melanoblasts had taken place because the ear region is obviously of duck origin. At the top of the head, there was a round area where no feathers and melanophores were present. The cause of this is not clear. When an X-ray photograph of the skull of the chimera embryo was compared with those

of normal duck and chick embryos at hatching (Fig. 2), it proved to resemble the former much more than the latter. This indicates that skull of the chimera was derived mainly from duck head mesenchyme.

While this grafting was being undertaken, Martinovitch published the results of grafting by the same method and combination⁷ in which considerable abnormalities were reported. Our efforts to hatch these chimeras have been unsuccessful, and the prospect is rather dubious (Martinovitch P. N., personal communication). However a greater possibility of survival could be expected in the combinations of genetically more closely related species.

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The Benthos of Soft Sea-bottom in Arctic North America

QUANTITATIVE surveys of the benthos of soft sea bottom were made in Baffin Island, N.W.T., during 1954 and 1955 in Greenland during 1958, and in Foxe Basin, N.W.T., during 1957, as part of expeditions organized by the Arctic Institute of North America and the Fisheries Research Board of Canada. These surveys, and others made previously in Greenland show that *Macoma calcaria* communities¹ with standing crops generally greater than 200 gm./m² (fresh weight) occur in shallow water to about 60 m. depth in many localities in Arctic North America. Other communities, some with very small crops, also occur in shallow water under localized special conditions. They are the *Venus fuciosa*, *Portlandia arctica* and *Chiridothea sabini* communities. The soft-bottom benthos in water deeper than about 50 m. forms at least two communities, the Foraminifera and *Arca Astarte crenata* communities¹ with standing crops generally less than 100 gm./m².

The distribution of these communities can be related to the environmental conditions. In these arctic regions the water at depths greater than 50 m. has permanently low temperatures which may either be just above 0°C or below Ekman's² eurythermal zone with such temperatures "low-arctic" and "high-arctic" respectively. However overlying the deep water is an annually insulated layer the temperature of which may occasionally rise to 5°C or more in summer. Low-arctic conditions can and often do

occur temporarily at the surface over high-arctic deeper water. The two terms can apply to temperature zones arranged vertically in the sea, as well as zoogeographical regions. As such they are convenient for an ecologist to use, but their significance is mainly as a guide to the temperatures, they imply nothing about the dynamics of the oceanographic conditions, unlike other systems of naming the arctic marine regions³.

The *Macoma calcaria* communities have only been found where sea temperatures are permanently or seasonally low-arctic. Thus they occur in surface insolated water in the regions farthest north, but may extend deeper elsewhere, for example, Spitsbergen, Iceland¹. They have a wide geographical range, apparently because some of the component species can adapt their breeding season to the time of year when appropriate temperatures occur, namely, in summer in the Arctic, in winter in warmer areas. The *Venus fluctuosa* and the *Portlandia arctica* communities appear to be restricted to certain bottom sediments within the low-arctic environment: types of coarse sand and fine mud, respectively. The *Chiridothea sabini* communities have only been found in two localities, in which the most obvious common environmental factor is very low summer temperature, that is to say, permanently high-arctic. The two deeper water communities occur below the depths affected by insolation where temperatures may be either low- or high-arctic.

Scattered dredge collections from Greenland to Alaska suggest that communities of *Macoma calcaria* are very widely spread in shallow water throughout arctic North America, but are replaced by other communities in deeper water. This pattern of vertical zonation appears to be very common.

An account of the collections and a more detailed discussion of the ecological and zoogeographical concepts mentioned here is being prepared for publication. Tables listing the species collected, and their numbers and weights per grab haul, are included in a doctoral thesis⁴ deposited in the Redpath Library, McGill University, Montreal.

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CYTOLOGY

Nuclear Deoxyribonucleic Acid Content and Endopolyploidy in the Meristem of Onion Roots

PHOTOMETRIC analysis of the deoxyribonucleic acid content of nuclei would afford an interesting approach to the problems connected with polyploidy, polyteny and endomitosis, our knowledge of which is still fragmentary. It would also help us to understand the evolutionary processes and trace the relationships of species. If, in accordance with the hypothesis of deoxyribonucleic acid constancy, there is a strict correlation between the deoxyribonucleic acid content

and the number of chromosomes, or more exactly the number of chromonemata, measurement of deoxyribonucleic acid would be the easiest way of studying polyploidy, polyteny and endomitosis, particularly in the interphase or prophase nuclei where the chromosome numbers cannot be counted. Evolutionary processes involving polyploidization from one species to another close one can be traced by means of photometric analysis, as the deoxyribonucleic acid content of the sperm or of the normal diploid nucleus appears to be characteristic of a species. The utilization of deoxyribonucleic acid content in problems of evolution is well illustrated by Hughes-Schrader's¹ work on a number of closely related species of mantids the karyotypes of which are not analysable by the usual methods of comparative cytology. The deoxyribonucleic acid content of the spermatids of two species, one having twice the number of chromosomes as the other, was the same, agreeing well with cytological studies which led to the conclusion that redistribution of chromosomal material rather than polyploidy was involved in the evolution of these species. On the other hand, in two other close species the deoxyribonucleic acid ratio of the spermatids was very near 1.2, indicating that polyploidy had played a part in their evolution.

During the course of studies on the deoxyribonucleic acid content of nuclei in the meristem of onion roots² in one of the central rows of cells which later become central vessels an unusual prophase was found in one of the roots. Each of its chromosomes showed very distinctly two relationally coiled strands. In these sections of roots fixed in acetic acid/alcohol (1:3) pairs of sister chromatids at prophase usually appear as single strands. Each strand in this exceptional prophase, furthermore, corresponded in thickness to a whole chromosome of a normal mid-prophase, and the former can be identified as a mid-prophase by the length and relic coiling of the chromosomes. No doubt this nucleus has a diploid complement of chromosomes with four, instead of two, chromatids each. Judged by the number of genomes, such a nucleus is essentially tetraploid. This prophase nucleus happened to be completely, or practically completely, within the section (15 μ thick) in spite of its large volume of 3,638 μ^3 (as compared with 903–1,004 μ^3 found in diploid mid-prophases). (The volume in μ^3 was computed as $V = 2hA/3$ where A is area in μ^2 of the largest cross section of the nucleus measured by a planimeter from a camera lucida drawing, and h is height in μ found as the average difference of four pairs of readings from the microscope fine-adjustment screw.) The deoxyribonucleic acid content measured in arbitrary units, according to the two wave-length method of Patau³ with modifications⁴ was $\gamma = 46.34$, almost exactly twice the mean obtained from seven diploid prophase nuclei ($\bar{\gamma} = 22.88 \pm 0.44$) which is here taken as the best estimate of 40.

Similar tetraploid prophases have, of course, been observed before in differentiated root tissue (for example, in great numbers in *Rhoeo* roots treated with indoleacetic acid⁵). What makes the present nucleus highly unusual is its location well within the meristematic part of the root. It is, however, a region in which the cells of the central rows do not ordinarily divide any more, instead, many or most of the nuclei in these rows step up their deoxyribonucleic acid content to what must be about 80 or more as judged by their striking combination of large size and intense staining. One of these was measured

The value obtained, $\gamma = 41.36$, is somewhat less than 80. It probably had not finished synthesizing deoxyribonucleic acid. In sections of 16μ most of these nuclei are cut so that when choosing the nucleus to be measured selection for small volume was inevitable. This nucleus was $1,634\mu^3$, much less than the volume of the tetraploid prophase nucleus and almost the same as the volume, $1,603\mu^3$, of a 40 interphase nucleus ($\gamma = 22.87$) which was also found in a central cell row. A volume of $1,634\mu^3$ falls well outside the range of interphase nuclei of the diploid mitotic cycle. Lying in a central cell row this nucleus may have been approaching another deoxyribonucleic acid synthesis. In that event it would be more proper to call this nucleus a tetraploid interphase I rather than a diploid interphase III. (During deoxyribonucleic acid synthesis an interphase I with the deoxyribonucleic acid content 20 is followed by an interphase II with intermediate deoxyribonucleic acid content, and this by an interphase III with deoxyribonucleic acid content 40.) The ambiguity of interpreting deoxyribonucleic acid classes in terms of polyploidy has already been stressed by Patau and Swift.⁴ What can presumably safely be said in the case, say, of an 80 interphase is that such a nucleus must be at least a tetraploid and no more than octoploid. In central cell rows within the meristem, though in its proximal part, the nuclear deoxyribonucleic acid content is occasionally stepped up still further. These nuclei are usually too large to be included in one section. The two cut parts (identified by their position relative to eight surrounding nuclei which were also cut) of one such nucleus in neighbouring sections were measured separately. The total deoxyribonucleic acid content $\gamma = 81.50$ is 11 per cent less than 160. The difference could again be plausibly ascribed to uncompleted deoxyribonucleic acid synthesis, as the volume $4,575\mu^3$, of this interphase nucleus was not much more than that of the 80 prophase.

It is noteworthy that the appearance of deoxyribonucleic acid values higher than 40 in the central cell row is accompanied by an almost complete disappearance of mitotic nuclei. The tetraploid prophase was the only exception observed. All other nuclei were clearly at interphase. In these cells, contrary to those of the surrounding tissue the initiation of mitosis has been blocked, but deoxyribonucleic acid synthesis has not. Precisely the opposite situation was found by Patau¹ in the corresponding cell rows of *Rhoeo*. In these, mitotic activity also stops long before it ends in the surrounding tissue but deoxyribonucleic acid synthesis is blocked even earlier, for, in these rows (not only in the proximal meristem but also in the elongation zone) all but a very few nuclei have the deoxyribonucleic acid content 20. This means that the great majority of nuclei after their last deoxyribonucleic acid synthesis still underwent a mitosis, as this is presumably the only process capable of halving the deoxyribonucleic acid content. The fact that either of the two processes—deoxyribonucleic acid synthesis and mitosis—may be blocked first characterizes them as essentially independent of each other, even though a normal mitosis presupposes a previous deoxyribonucleic acid synthesis.

It is concluded that in central cell rows of onion roots mitotic activity ceases deep in the meristem. Instead, endopolyploidy develops, with the deoxyribonucleic acid content going up to 80 or even 160. One quite exceptional prophase was found in a central

cell row in the meristem that presumably had the diploid number of chromosomes with four instead of two chromatids. Its deoxyribonucleic acid content was 80.

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A Partial Chemical Characterization of Maize Coleoptile Cell Walls prepared with the Aid of a Continually Renewable Filter

The present work was undertaken with the objective (a) of preparing plant cell wall fragments free of contamination by intact cells, cytoplasm, plastids and other cell inclusions, but containing most of the constituents of the cell wall including proteins, and (b) of characterizing such a cell wall fraction chemically. The procedure differed from those previously reported in that a filtration technique was employed for purification of the cell wall fragments and in that isolation was accomplished in an essentially non-aqueous media. It is believed that the filtration technique may prove generally useful in the preparation of cellular components where purification by differential or gradient centrifugation proves impossible. Previous reports of the chemical composition of plant cell wall tissue have been based on the residue remaining after extraction of tissue macerates with water.¹ Such residues undoubtedly contain particulate cellular inclusions.

Maize (*Zea mays*) coleoptiles were chosen for the present study because of the information already available regarding coleoptile tissue. The coleoptiles were excised from 5 day old seedlings of Michigan 350 hybrid maize which had been germinated at 25° C and 90 per cent relative humidity. 25 gm of the coleoptile tissue were homogenized (Sorvall Omnimixer) for 10 min at 16,000 r.p.m. together with 180 ml of glycerol and 37 gm of glass beads 200 μ in diameter (Minnesota Mining and Manufacturing Company Saint Paul, Minnesota). The homogenate so obtained was permitted to stand for $\frac{1}{2}$ hr during which time the bulk of the beads settled out. The supernatant fluid (Fig. 1A) was decanted into a 150 ml coarse porosity sintered glass funnel containing a filter bed consisting of 1 cm of the 200 μ glass beads. Filtration was accomplished at the suction pump with continual stirring at gradually increasing depth in the glass bead filter so as to prevent mat formation. Plastids, nuclei, mitochondria and soluble protein appeared in the filtrate while the cell walls remained in the glass bead filter.



Fig 1 Photomicrographs of cell-wall preparations at two stages of purification. A, crude homogenate showing cell wall fragments and plastids, B, purified cell wall fragments after fourth filtration

mat The beads together with cell-wall material were resuspended in 50 ml of glycerol and the mixture again allowed to settle for $\frac{1}{2}$ hr. The supernatant fluid containing the suspended cell walls was again decanted into a fresh glass-bead funnel and the filtration and settling procedure repeated three times. After the last resuspension, the beads were again allowed to settle and the traces of beads remaining removed by centrifugation for 5 min at 500*g*. The cell-wall material was then collected as a pellet by centrifugation at 25,000*g* for $\frac{1}{2}$ hr. Purified cell-wall preparations so obtained constitute about 5 per cent of the initial dry weight of the corn coleoptile tissue and are practically free of microscopically visible and histochemically detectable cell inclusions as shown in Fig 1B. If the filtration fluids are reworked until all visible cell-wall fragments have been removed, a yield of 20 per cent of the coleoptile dry weight is obtained. For chemical analysis, the cell-wall material was washed free of glycerol by suspension and resedimentation five times in a ten-fold volume of absolute alcohol and dried to constant weight.

The results of analysis of cell-wall preparations and of whole dried coleoptile tissue are presented and compared with those of other authors in Table 1. To our knowledge, no previous reports of the sulphur, calcium or magnesium contents of primary cell-wall tissue have been published. In general our results are in accord with previously published values with the notable exception of the protein content of the cell walls. Thumann and Bonner reported 12 per cent protein for *Avena* coleoptile (corresponding to 1.9 per cent nitrogen) while Nakamura and Hess reported 30.4 per cent protein for a water-insoluble fraction of maize coleoptile. In the present work, protein, calculated from the nitrogen determinations, would be 2.5–5.1 per cent. Probably the higher values previously reported are due to a greater degree of

Table 1 COMPOSITION OF COLEOPTILE AND CELL-WALL PREPARATION OF COLEOPTILE OF *Zea* AND *Avena**

| | Whole coleoptile (per cent dry weight) | Coleoptile cell wall (per cent dry weight) |
|------------------|---|---|
| Ash | 4.1, 4.4† | 0.6, 1.3‡ |
| C | — | 45 |
| H | — | 7 |
| N | 4.1 | 0.4–0.8, 4.0‡ |
| P | 0.8 | 0.03, 0.00‡ |
| S | 0.25 | 0.07 |
| Ca | 0.05 | 0.00 |
| Mg | 0.15 | 0.07 |
| Protein | 25.5, 15.2†, 3.1‡ | 2.5–5.1, 30.4‡, 12‡, 9.5‡ |
| Cellulose | 14.2, 13.2†, 10.1‡, 11.0‡ | 27.4, 32.7†, 42‡, 24.8‡ |
| Pectin | 4.0†, 2.3‡ | 8.4, 10.2†, 8‡, 0.3‡ |
| Lignin | 0.0 | 5.4 |
| Ribonucleic acid | Less than 0.0 | Less than 0.15 |

* We are indebted to Dr. Peter Albersheim for the anhydrouronic acid and to Mrs. Mary A. Vacasey for the calcium and magnesium determinations.

† Maize coleoptile (ref. 1c).

‡ Maize coleoptile (ref. 1b).

§ *Avena* coleoptile (ref. 1a).

¶ *Avena* coleoptile (ref. 5).

contamination of the cell-wall preparation by cytoplasmic substances.

A limited characterization of the polysaccharide components of the cell wall was made by the general procedure of Norman.² Cellulose was extracted from the 0.5 per cent ammonium oxalate insoluble cell-wall fraction with 72 per cent sulphuric acid after hydrolysis with 2*N* hydrochloric acid. The extract was diluted to 5 per cent sulphuric acid, hydrolysed, and glucose was determined with the aid of glucose oxidase. By this procedure the cellulose content was calculated to be 27 per cent. The 'pectin fraction' as isolated by the usual precipitation method from ammonium oxalate extracts constituted 28 per cent of the dry weight of the cell-wall preparation. Paper chromatographic examination of the 'pectin fraction' following exhaustive methylation and acid hydrolysis³ indicated that only 2–5 per cent of the cell-wall weight was polyuronic acid. Since losses of uronic acid by this method might be expected, the value of 8 per cent obtained by Dr. Albersheim seems correct. The ribonucleic acid content of the cell wall was found to be less than 0.15 per cent as determined by the method of Ogur and Rosen.⁴ This would account for approximately half the total cell-wall phosphorus.

In summary, our present analysis accounts for only approximately 45 per cent of the cell-wall dry weight. Qualitatively, it may be stated that starch and dextrins are absent but there are large amounts of pentose and hexose polysaccharides. Further studies of these as yet uncharacterized carbohydrate fractions and the enzymatic activities of cell-wall fragments are in progress.

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EDUCATIONAL PROBLEMS OF THE COMMONWEALTH

SEVERAL recent events of great public importance have received little or no public discussion, due presumably to the stoppage in the printing industry in Great Britain. Among these events the Commonwealth Education Conference, which met in Oxford during July 15-29, is outstanding. As the Secretary of State for Commonwealth Relations Lord Home, stated in the House of Lords on July 2, this Conference was called primarily to work out detailed arrangements for the new scheme for a thousand Commonwealth scholarships and fellowships which was agreed upon by Commonwealth Ministers at the Trade and Economic Conference held in Montreal in September 1958. The Conference, however, was also to review existing arrangements for co-operation between the Commonwealth countries on education generally, and although it was to settle its own agenda Lord Home indicated that the supply and training of teachers and scientific and technical education would be subjects of particular importance.

In making this statement, Lord Home expressed the hope that from the Conference there would emerge practical schemes for furthering co-operation in this vitally important matter of education where the needs are so great and where Commonwealth countries have so much to offer one another. Lord Home emphasized, too, the high standing of the Commonwealth representatives at the Conference of which Lord Halifax was president and Sir Philip Morris was chairman and he referred also to the seven study tours of the United Kingdom designed to give the delegates a balanced insight into our present system and its working, one of which each overseas delegate would make before the Conference opened. The contribution of the United Kingdom in Commonwealth education is also described in a book, let prepared specially for the Conference by the Central Office of Information (Hercules House Westminster Bridge Road, London, S E 1).

The simple fact to which also Lord Home directed attention on July 3, that any schemes which the Conference might propose would almost inevitably involve money sufficiently indicates the importance of wide and informed public discussion of the whole subject. The magnitude of the contribution which Britain is already making in this field must be fully understood, both in Britain and in the Commonwealth, and the implications elsewhere in terms of man power even more than in terms of material or financial resources, if the proposals of the Conference are to be correctly appraised, still more if the resources required are to be forthcoming. There can be few subjects which better illustrate the bearing of informed discussion on the functioning of democratic institutions, as there are also few in which party politics could be more damaging or dangerous. Indeed over wide areas, and especially in Africa, the success of self government and the survival of

democratic institutions may largely depend on our success in solving the problems involved in the expansion of education, especially secondary education and in reconciling the clash between the comparatively slow, healthy growth in educational institutions and the mounting demand for rapid political change.

In opening the Conference on July 15, the Earl of Halifax stressed the practical objectives of the Conference, and pointed out that to-day it is a question of the right sort of education at the right time. Freedom itself will depend upon the education we are now providing for our young people, both because of the technical skills that education can provide and because of the qualities of character and mind that go with it. Lord Home, in a speech on the opening night of the Conference, referred to the importance of the common pattern of education in the Commonwealth and the practical co-operation on which it is based both in relation to the particular objectives of the Conference itself and in the wider context of the promotion of international understanding, to which the interchange of teachers and students could make a most effective contribution.

Speaking in the House of Lords on July 29 Lord Home claimed that the Conference had been an outstanding success. In the ten working days at Oxford, plans had been made not only to bring into operation the Commonwealth scholarship scheme approved in principle at Montreal but also to provide for both short and long term assistance to those Commonwealth countries where a shortage of teachers at all levels is holding up the development of education and the progress of the economy. The scholarship scheme itself will cost about £5 million during the first five year period of which the 500 scholarships provided by the United Kingdom will take about half. With the 250 offered by Canada, 100 each by India and Australia, 30 by Pakistan, 25 by New Zealand, 12 each by Malaya and Nigeria, 10 each by Ghana and Rhodesia and Nyasaland, 6 by Ceylon and 4 by East Africa, the target of 1,000 scholarships is already exceeded. For the most part the scholarships will be given to graduates for research or work for higher degrees in universities and comparable institutions in other Commonwealth countries than their own and the scholarships will be tenable for an average period of two years and be comparable in standing with the best offered by any other country or in any other way.

A small number of visiting fellowships to enable distinguished Commonwealth professors to visit other Commonwealth countries and to work at institutions of their own choice will supplement the scholarships and a few scholarships will also be tenable at the undergraduate level where the courses required by the candidates are not available in their own countries. It may be recalled that the United Kingdom has

already contributed in grants and loans under the Colonial Development and Welfare Acts some £13 million to higher education, and that there were in 1958-59 more than 7,000 full-time students from other parts of the Commonwealth enrolled in universities of the United Kingdom with some 6,600 students in technical colleges, and of these some 250 were trainees under the Colombo Plan, so that the new scheme is only an extension in scale, and Lord Home pointed out in the House of Lords that the Conference itself recognized that it was only making a start on the most urgent and specific needs. It therefore recommended that another Commonwealth Education Conference should meet in 1961 to review progress and to make further plans.

Lord Home's statement in the House of Lords showed that the Conference also frankly recognized that the most serious problem is that of teachers, and especially of those qualified to teach in the secondary schools, and that this special need of the emergent countries can only be met by special efforts on the part of the senior members of the Commonwealth. The United Kingdom is already sending some 2,500 teachers a year to Commonwealth countries, but the Conference estimated that about a thousand more teachers are wanted each year for secondary schools, and two hundred for technical schools, in addition, 500 are wanted at once for teacher-training colleges.

Lord Home said, quite correctly, that in the short run the quickest way is to send out teachers already trained to occupy key posts overseas, and thus the older Commonwealth countries are proposing to do. University lecturers and professors would be encouraged to take up overseas posts, and in the United Kingdom a special effort will be made to help with teachers in those scientific and engineering subjects in which Commonwealth countries have reported their needs are greatest. These subjects are, of course, those where the shortage of teachers is felt acutely in the United Kingdom, and Lord Home commented that, if the objective is to be achieved, administrative measures will be necessary including the topping-up of salaries calculated on the local scale, the provision of passages for the teacher and his family, preservation of his pension rights and promotion prospects and assistance in resettlement on return. In promising the Conference that the British Government would help with such measures, Lord Home appealed also to teachers to respond to the challenge presented to men and women of talent, imagination and sympathy.

The United Kingdom proposals provide for some four hundred additional United Kingdom teachers to serve in Commonwealth countries, but the long-term solution must be to build up the educational resources of the smaller Commonwealth countries by providing the staffs for new teacher-training institutions which they may decide to establish, either in their own territory or jointly to serve the needs of a particular region. Accordingly, said Lord Home, we would provide in the United Kingdom five hundred more places for teacher trainees from those countries as from the academic year 1960-61, and £250,000

a year for grants to the students occupying them. There were already, in 1958-59, 728 Commonwealth students training as teachers in the United Kingdom and if, as Lord Home stated, Canada, Australia, New Zealand, India and other countries make considerable contributions, the position should be significantly improved when the next Conference meets.

The expansion of technical education will take time, but here also the Conference has initiated new efforts to speed the process. The need for trained teachers in technical subjects, the continuing need for industrial training and the great shortage of suitable books and equipment were all emphasized. In the United Kingdom, it is planned that during the next ten years some 4,000 additional places will be available to the Commonwealth students in technical colleges. The Federation of British Industries and the industrial research associations have already indicated their intention to continue the facilities now offered to overseas students and to expand them in certain directions.

These further projects discussed at the Conference are estimated to cost at least a further £5 million during the next five years, of which the United Kingdom contribution will be about £3.5 million, making a contribution of some £6 million out of the total of at least £10 million. This, as Lord Home observed, is a substantial contribution, and it does not stand alone. Indeed, it is not easy to estimate the full financial magnitude of the United Kingdom contribution to Commonwealth education even at the university-level. Account has to be taken of what is being done through the British Council, the Nuffield Foundation and like institutions, and through the Commonwealth University Interchange scheme.

Even if the financial magnitude of the British contribution could be accurately assessed, this is possibly the least important aspect. Compared with the magnitude of expenditure on education in Britain alone—estimated as likely to exceed £1,000 million within the next decade—it is relatively trivial, and it is small also in comparison with expenditure in Britain on scientific and industrial research, with which it is so closely connected. Essential as it is that adequate financial resources should be available for Commonwealth education, man-power is the decisive factor, and it is imperative that financial resources should be wisely applied so as to remove so far as possible all obstacles to the free interchange of students and teachers. The benefits of such movement are reciprocal, and the Conference should at least have emphasized that in such wandering scholars the Commonwealth has one of its most valuable assets.

On that there are perhaps two points of special interest at the present time. Prof Kenneth Robinson has directed attention to the value of extending interchange to research and to the need for research fellowships and studentships which would enable young United Kingdom graduates to spend a year or two in one of the other countries of the Commonwealth, studying some aspect of the history, culture

or contemporary social, political or economic problems of that country. There are, he claims, many urgent and important pieces of research in this field which young United Kingdom graduates cannot at present be encouraged to undertake because of the lack of opportunity to spend the necessary time in the Commonwealth country concerned. Such work is at present often done by Americans, although the Nuffield Foundation has supported some such studies and the Commonwealth universities are fully alive to the value of such Rhodes scholarships in reverse. Nevertheless, there is an undoubted need for a rapid extension and increase of funds and facilities enabling United Kingdom graduates to spend substantial periods on research work overseas, and it should not be forgotten that a further beneficial result would be to build up in Britain a growing corps of graduates who would have first hand knowledge of the problems and culture of other parts of the Commonwealth.

The second and even more urgent point is that of the supply of teachers, and especially secondary school teachers. Prof Arthur Lewis, when economic adviser to the Ghana Government, estimated that countries emerging from Colonial status are not self-sufficient in secondary school teachers until about 4 per cent of each generation is entering the secondary schools. Only in Western Nigeria is this proportion reached, though in Ghana great efforts are being made in the current development plan to exceed the present 2 per cent. Many other territories, such as Kenya, Nyasaland and Northern Nigeria, are far behind and although in some territories the primary school numbers are creditable, until comparatively recently there has been practically no secondary education in many areas.

What the Commonwealth Education Conference has emphasised above all is that advance in education depends not only on sufficient financial resources but still more on foresight, patience and sacrifice. Teachers of the calibre demanded for secondary schools, especially for work in the sixth forms, are not to be found overnight. Their training calls for tutors of high calibre, and time to complete that training not simply in secondary courses but also in teachers' training courses and sometimes to graduate level in university institutions.

This is the real—and the key—problem in education for the emergent territories, and it is only in directly and in the long term that the scholarship scheme at the university level will contribute to its solution. Meanwhile, the emergent territories depend on the older members of the Commonwealth for the help essential to build up as rapidly as possible systems of secondary education capable of meeting the demands for emergent nationhood. Financially, this is bound to involve expenditure far in excess of the £10 million immediately contemplated at the Commonwealth Education Conference, including capital expenditure as well as grants for recurrent expenditure on secondary education, while an even greater strain may be put on the human resources of the Commonwealth.

Of this Lord Home was manifestly conscious in his appeal, at the closing of the Conference, so far as higher education is concerned and it is no less true of secondary education. Most of the senior members of the Commonwealth are themselves short of secondary school teachers—in some the shortage is a result of the racial policies pursued by them—and special measures are already being concerted in the United Kingdom to meet the situation arising as 'the hulk approaches our sixth forms'. The measures promised by Lord Home may help to increase the numbers of teachers which we already send to Commonwealth countries though it may still be necessary to explore other possible emergency measures which changes in our economy may offer. These alone will not suffice, however, without the imaginative response and enthusiasm for which Lord Home appealed. To create the public and professional understanding on which such a response can be soundly based is an urgent and primary task for which the Government has a primary responsibility. For this reason it is imperative to expedite as much as possible the publication of the full report of the Conference, and ensure that it is widely discussed both in Parliament and outside.

BERTRAND RUSSELL, PHILOSOPHER

My Philosophical Development

By Bertrand Russell Pp 278 (London George Allen and Unwin, Ltd, 1959) 18s net

ALL those whose study of philosophy is grounded in the empirical tradition regard Lord Russell as the greatest living philosopher. His philosophizing started in the 'nineties when philosophy in Britain, in Europe and most of the United States was dominated by idealisms deriving either from Hegel or from Kant. After a few years as a full fledged Hegelian (p 42) Russell tells us that in 1898 both G E Moore and he 'rebelled against both Kant and Hegel' (p 54). From this rebellion sprang the current of empiricist or scientific or 'analytic' philosophy which to-day, in one form or another, dominates philosophical thinking and teaching throughout the English speaking world and plays an important part in the pattern of our contemporary culture. Although one should not neglect other influences—in particular, that of Moore, of Frege, of the Polish philosophers, of C S Peirce and the American pragmatists, and of the greatest of Russell's pupils Wittgenstein (about whom there is a good deal in this book)—there is no doubt that the main responsibility for the present state of philosophy lies squarely on Russell's shoulders. Without his work in the first quarter of this century it is difficult to see how the logical positivist movement could have arisen and, if philosophers' interest in the use of language had developed independently of analytic philosophy, it would have taken a much less realist form. Russell's influence has been largely due to his immense fertility of ideas and to his willingness to publish them even though he might later have to retract or modify his conclusions. There are few philosophers in history who have written important philosophical works almost con-

tinuously for fifty years. Russell has added to the immense debt we owe him by now giving us a full-scale account of his philosophical development, written with all the clarity, verve and wit we are accustomed to expect from anything he writes.

"My philosophical development," Russell starts the book by saying, "may be divided into various stages according to the problems with which I have been concerned and the men whose work has influenced me. There is only one constant preoccupation. I have throughout been anxious to discover how much we can be said to know and with what degree of certainty or doubtfulness" (p. 11). Considering rational bases for geometry and for mechanics led Russell back to arithmetic, and four chapters of this book are devoted to general questions involved in his attempt to derive mathematics from logic, which culminated in Whitehead and Russell's "Principia Mathematica." Russell gives a lucid informal account of the logical paradoxes which caused him so much trouble, and of the theory of types which he invented in 1908 to solve them. Though systems of mathematical logic have been constructed recently which do not explicitly make use of distinctions of type in Russell's manner, they almost all presuppose restrictions upon the use of symbols which are virtually equivalent to a type theory. The philosophical insight in Russell's theory is that a sentence may be perfectly well constructed according to grammatical rules and yet lack meaning: there are logical restrictions upon the significant combination of symbols as well as purely grammatical ones. The emphasis later laid by logical positivists upon the nonsensicality of many apparently sensible expressions was foreshadowed in Russell's theory of types (see pp. 14, 160).

After 1910 Russell turned his attention to theory of knowledge, and in 1914 put forward his well-known programme of substituting, so far as possible, logical constructions for inferred entities. This programme, and the similar 'operationalist' programme advanced by P. W. Bridgman in 1927, has made great appeal to philosophers of science, many of whom have attempted to apply it to the construction of various scientific concepts. In this book Russell says that he "soon became persuaded that this is an impossible programme and that physical objects cannot be interpreted as structures composed of elements actually experienced" (p. 105). I do not think that Russell ever published his reasons for his change of view. Cogent reasons for the impossibility of the logical construction programme were first given by F. P. Ramsey in 1931. In Russell's later writings, and in this book, similarity of structure is taken as being the connecting link between the electromagnetic waves used in broadcasting and auditory sensations (p. 204). Though Russell speaks (not very happily, I think) of scientific knowledge using "artificially manufactured entities", "real or supposed entities", "scientific abstractions" (pp. 205-6), "constructions composed of events and taken as units for the convenience of the mathematician" (p. 27), he would not now regard these as having to be given, directly or indirectly, in terms of experience. "I cannot see that there is any ground whatever for this opinion [that there can be nothing which is not experienced or experience], nor even for the view that we cannot know that there are things we do not know" (p. 144).

Other problems with which Russell has been concerned and which he treats in this book are those of consciousness and perception, of non-demonstrative

inference, of truth, of names and of language in general. With regard to language, Russell recounts how he moved from regarding it as "transparent" to realizing its philosophical importance. Nevertheless "the essential thing about language is that it has meaning—that it is related to something other than itself, which is, in general, non-linguistic" (p. 14). "In regard to truth and falsehood, a sentence is only important as a vehicle of belief" (p. 154). Russell wholly rejects the view that the study of language is an end in itself for a philosopher. Nor does he accept any hard and fast separation of philosophy from science. "Philosophy cannot be fruitful if divorced from empirical science" (p. 254). Of the outcome of his recent work on inference he says that "the reasons for accepting it are the ordinary reasons applied in scientific work, not remote reasons derived from some metaphysical theory." There is no claim to certainty" (p. 207). In this book Russell does not (as he did in 1914) speak of "scientific method in philosophy", a phrase which may mean anything or nothing. But if by the scientific spirit is meant the persistent and single-minded attempt to "understand the world" (p. 230) by envisaging bold but tentative hypotheses without ever losing sight of the facts which these hypotheses are intended to explain, Russell's work exemplifies this spirit better than does that of any other contemporary philosopher.

R. B. BRAITHWAITE

CATALYSIS

Catalysis

Edited by Paul H. Emmett. Vol. 5. Hydrogenation, Oxo-Synthesis, Hydrocracking, Hydrodesulphurization, Hydrogen Isotope Exchange and Related Catalytic Reactions. Pp. vi+542. (New York: Reinhold Publishing Corporation, London: Chapman and Hall, Ltd., 1957.) 120s.

Advances in Catalysis and Related Subjects

Edited by Adalbert Farkas. Vol. 9. Pp. xviii+847. (New York: Academic Press Inc., London: Academic Books, Ltd., 1957.) 16 dollars.

VOLUME 5 of "Catalysis" continues the description of various hydrogenation processes which has already extended through the previous two volumes, and the allotment of so much space, even in a major treatise on catalysis, is in itself a sign of the importance which this type of reaction has attained in modern academic and industrial chemistry. Following an introductory section on the general reactivity of carbon monoxide, I. Wender, H. W. Sternberg and M. Orchin contribute a well-written chapter on the high-pressure hydrogenation of mixtures of carbon monoxide and olefins to long-chain ketones by the oxo reaction. In this, considerable interest is attached to the use of soluble catalysts derived from cobalt or nickel carbonyls since, in this way, homogeneous liquid hydrogenation systems can be obtained. A good survey is also given of the general theory of the reaction mechanism involved and of the part played by carbonium ions in this. The next chapter, by G. Natta, U. Colombo and I. Pasquon, deals with the use of promoted mixed-oxide catalysts for the hydrogenation of carbon monoxide to higher aliphatic alcohols and supplements a section in an earlier volume on the synthesis of methyl alcohol. There is, in this field, abundant scope for the further study of the basic mechanism of promoter action,

about which relatively little is known in spite of the very large amount of work which has been done on the subject

The long monograph on the hydrogenation of aromatic compounds by H. A. Smith, who has himself contributed considerably to our knowledge of this subject, stands out as a comprehensive survey and reviews systematically a very large number of papers covering the catalytic reduction of carboxylic and heterocyclic substances. This detailed treatment also occurs in the chapter by T. I. Taylor on the use of hydrogen isotopes for the detection of subsidiary processes involving hydrogen exchange, bond migration or other reactions which are superimposed on the hydrogenation itself and, in many cases cannot easily be recognized in other ways. In addition, the method throws considerable light on the internal complexity of hydrogenation generally. Finally, the article by J. B. McKinley on the hydrodesulphurization of liquid petroleum fractions gives an authoritative survey of a type of process which has done much to improve the general quality of commercial motor spirit and which has only become practicable economically by the recent availability of very large quantities of by-product hydrogen derived from hydroforming reactions.

In a major work of this type, published with rather long intervals of time between the issues of the individual volumes, it is difficult to avoid some lack of logical sequence. For example, the wide separation of the article on the synthesis of higher alcohols in the present volume from that of methyl alcohol in Volume 3 and the chapter on the hydrogenation of aromatic compounds from those on the reduction of olefins and acetylenic derivatives. This, however, is a minor criticism, and the work as a whole is to be recommended as an up-to-date treatise on catalysis, which should be of great value to the many chemists who are interested in this subject.

The publication, as a volume of 'Advances in Catalysis', of the 84 papers which were read at the international congress on catalysis held in Philadelphia in 1958 constitutes an alternative policy to the spreading of these contributions in a single and rapidly growing field of knowledge among a relatively large number of individual journals some of which may be accessible only with difficulty to chemists working in smaller institutions. In addition, it forms one way of relieving the increasing pressure which is being felt by some of the various publishing societies in providing adequate space for the accommodation of all the otherwise suitable papers now sent in to them.

Following introductory addresses by Sir Hugh Taylor and by Sir Eric Rideal on general aspects of catalysis and on the course of its development from a historical point of view, the large mass of new material has been arranged in four main groups covering respectively the chemistry and physics of solid catalysts, homogeneous catalysis, surface chemistry generally, and miscellaneous catalytic reactions, many of these groups being subdivided into subsections. While it is difficult in a short review to select individual papers for special comment, considerable interest is attached to the first of these groups to the contribution by R. E. Cunningham and A. T. Gwathmey on the relative rates of hydrogenation of ethylene on the various crystal planes which are exposed as outcrops on the surface of a spherical single nickel crystal. The relative rates observed could not be explained in terms of the ease of geo-

metrical accommodation, without undue strain, of the ethylene molecule and it is probable that bulk dislocations, which begin within the catalyst, lead to unusual interatomic distances in the surface lattice. Prof. J. H. de Boer amplifies this point by discussing the part played by pore structure in providing sites for reaction within the gross external surface of supported and other catalysts.

In a further introductory address, Prof. W. E. Garner gives a good account of the present state of work on reactions involving electron transfer on and in mixed oxide catalysts, including semiconductors, and this is supplemented by a number of further papers in this field, including one by Prof. G. M. Schwab in which the effect of illumination on electron transfer processes between the surface of semiconductor and catalysable substrates is discussed. Reaction paths and energy barriers in homogeneous catalytic systems have been dealt with by Prof. D. D. Eloy, who also includes processes catalysed by organozymes. Later subsections contain a large number of papers on the relation of surface chemistry to catalysis, the catalytic reactions of hydrocarbons (which is introduced by Dr. E. J. Houdry) tracer techniques with an introduction by Prof. P. H. Emmett and miscellaneous catalytic reactions. The subsequent discussions to all the papers are printed in full. E. B. MANTON

INTRODUCTORY ELECTRONICS

Principles of Electronics

By Prof. M. R. Gavin and Dr. J. E. Houldin (Physical Science Texts) Pp. xii+348 (London: English Universities Press, Ltd. 1959) 30s. net

THE trouble with this book is that it is not really clear for whom it is written. The general editor's foreword states that each volume in the series 'is designed to give the reader an integrated account of a subject up to the level of an Honours Degree of any British or Commonwealth University'. But the authors claim that it is only a general introduction to the subject of electronics or, as shown on the dust cover, 'an introductory course for a first degree or diploma in physics or electrical engineering', then they go on to claim that, for most of the book the standard of mathematics required is no more than that of the Advanced Level of the General Certificate of Education. Whatever the intentions there is little doubt that the book is very suitable for the early years of an electrical engineering course but will scarcely cover the requirements of the final stages of an honours course in electrical engineering.

Within the restrictions mentioned above, the book is a good one. Its descriptions are extraordinarily lucid and straightforward—almost anyone could understand them, and the book might be useful even to technicians. It is a book one can enjoy reading, the subject-matter is well selected and strikes a pleasant balance between thermionic valves on one hand and transistors on the other, between physics on one hand and circuits on the other. The coverage of the subject-matter is wide including the basic electron physics (nearly 100 pages), amplifiers (about 90 pages), oscillators (sinusoidal and relaxation), very high frequency valves, rectification, modulation and detection, wave-shaping and noise. It is not surprising that the authors do not find room for communication and control systems or for any

study of passive circuits. The book is not at any stage abstruse, and unimportant and irrelevant matter seems absent. A very valuable feature is the inclusion of about 250 examination-type problems. The production is very attractive and the price is reasonable.

Not only can the book be recommended as an introductory text for electrical engineering students, but it may also prove useful to many fully fledged engineers and physicists who wish to get up to date on the proper relationship of thermionic and transistor circuits. It compares favourably with other recent books on this subject.

One or two faults in the book should be mentioned. The reviewer did not take kindly to the split infinitives on p. 28—"to just ionise" and "to just excite"—nor to the spelling "alinement" on p. 37. There is an error in the analysis of a circuit on p. 242 (and another similar one on pp. 251-2) where the authors neglect the existence of the voltage across the load of a diode.

D. G. TUCKER

HISTOLOGY

Textbook of Comparative Histology

By Dr Warren Andrew. Pp. xix+652 (London and New York: Oxford University Press, 1959) 120s net.

Histochemical Technique

By Dr W. G. Bruce Casselman (Methuen's Monographs on Biological Subjects). Pp. 205 (London: Methuen and Co., Ltd., New York: John Wiley and Sons, Inc., 1959) 18s net.

A SURVEY of the histology of both invertebrates and vertebrates in a single volume is indeed a formidable task, and even partial success must rank as a considerable achievement. Certainly a cursory examination of Andrew's book does throw its deficiencies into some relief, and more continuous reading is required to reveal its virtues. The temptation of saying too little about too much is not entirely avoided and rather many topics are treated too briefly to be easily intelligible, nor is the difficulty overcome of being reasonably up to date, for references from the last decade are somewhat infrequent. The chapter bibliographies are unduly short, for the excretory organs of all invertebrates there are thirteen titles ending at 1940, and in general they refer mainly to American and older German work; there is little attempt either to include all the great classical papers or to present a scheme for further reading. The coverage of the subject is often correspondingly restricted and there are some disappointing omissions. Nevertheless the advanced undergraduate audience for whom the book is primarily intended will find in it much pleasant ancillary reading, arranged in a manner which should stimulate their further interest. The broad comparative and essentially functional approach emphasizes the general similarities of the problems facing all animals, and brings out underlying analogies in their solutions. The illustrations are numerous and well chosen and the writer's style agreeable, so that such a volume might well lead a student towards one of the most attractive entries into the practice of zoology.

The scope and precision of classical histology have been rapidly extended in recent years by the increasing use of physical and chemical methods, and any further assistance in their technical application is welcome. Casselman opens with some interesting chapters on the general methods, potentialities and limitations of microscopical histochemistry, followed

by succinct accounts of the main groups of substances studied by these techniques. The chapter on lipids and their separation, at least to the degree of separation so far feasible, is particularly helpful, but that on proteins does seem to under-estimate some of the technical difficulties involved. The point of view throughout is chemical and the book can be recommended to biologists primarily as a very useful addition to the other texts now available.

T. KERR

GENETIC ANALYSIS

Trends in Genetic Analysis

By Prof. G. Pontecorvo (Columbia Biological Series, No. 18). Pp. x+145 (New York: Columbia University Press, London: Oxford University Press, 1959) 25s net.

THE past fifteen years have seen a revolution in genetics comparable to the introduction into physics of quantum theory. Several lines of research have contributed to this revolution. The study of biochemical genetics established the concept of 'one gene, one enzyme'. The analysis of transformation and transduction in bacteria showed that hereditary information is carried by nucleic acid. These two conclusions made clear the need to analyse the structure of nucleic acids, to relate this structure to the processes of replication and of protein synthesis, and to seek for the kinds of changes in proteins which result from genetic mutation. But most important of all has been the increase in what Prof. Pontecorvo has called the "resolving power" of genetic analysis. This has caused the abandonment of the old picture of chromosomes consisting of a series of hereditary units or genes connected by regions at which, and only at which, recombination can take place, and the recognition that genes themselves have a linear structure resolvable by crossing over.

Prof. Pontecorvo's book is mainly concerned with this last field of research, although conclusions from other fields are mentioned where they are relevant. The six chapters deal with genetic analysis and its resolving power, allelism, the structure and function of the genetic material, recombination, mapping chromosomes via mitotic recombination and novel genetic systems.

This is an exciting book, partly for the logic and clarity with which new ideas are presented, and partly because the problems which it raises are as fascinating as the ones which it answers. Prof. Pontecorvo has himself made a decisive contribution to the study of the fine structure of genes by his recognition and subsequent demonstration that the phenomenon of "position pseudo-allelism" described by E. B. Lewis is not a genetic anomaly, comparable, for example, to the Notch deficiency in *Drosophila*, but is a typical effect, to be expected if the genetic material is linear in its fine structure as well as in its gross morphology, and if its proper functioning depends on the integrity of functional units, which Benzer has since persuaded us to call cistrons. For the general biologist who wants to know how this idea has been developed, and how it has been combined with discoveries in other fields to give a coherent picture of what genes are and what they do, this book is an admirable although sometimes a difficult guide.

But the book is mainly intended for geneticists, and it seems unlikely that many will be so unwise as to leave it unread. For them, Prof. Pontecorvo's greatest virtue is his gift for throwing into relief what

we do not know. The search is already on for the geneticist's Rosetta Stone, that is, for a protein which can be analysed in the same detail as haemoglobin, determined by a gene the fine structure of which can be resolved in the same detail as Benzer has resolved the *rII* locus in phage T4. But there are other problems to which no answer is at present in sight. One is the relationship between the structure of deoxyribonucleic acid, and the processes of chromosome replication and recombination, it is not clear at present whether replication and recombination are separate processes or different aspects of the same event. A still more fundamental difficulty is the relationship between gene action and morphogenesis. If the revolution in genetics achieves its present objectives, we shall know how a fertilized egg resolves the instructions which tell it how to make a large number of specific proteins, but there is a big difference between a bag of proteins and an animal or plant.

J. MAYNARD SMITH

A NEW APPROACH TO IMMUNITY

The Clonal Selection Theory of Acquired Immunity
By Sir Macfarlane Burnet (The Abraham Flexner Lectures of Vanderbilt University, 1958) Pp. ix + 209 (Cambridge At the University Press, Nashville, Tennessee Vanderbilt University Press, 1959) 22s. 6d. net

THE basic problem of immunology is to understand how the body responds by making antibodies against foreign macromolecules while refraining from making antibodies against the great variety of macromolecules which are present in its own tissues. No satisfactory instructive theory has been yet put forward to explain how the presence of the antigen causes cells to synthesize antibody molecules with a complementary surface structure. In the Abraham Flexner Lectures given at Vanderbilt University for 1958, and published in this book, Sir Macfarlane Burnet has approached the problem at quite a different angle. He postulates that individual mesenchymal cells are genetically endowed with the potentiality for making globulin capable of combining with a particular antigenic configuration. In the adult organism, contact of the mesenchymal cell with the right antigen causes that cell to proliferate and to differentiate so as to produce a clone of cells making or capable of making antibody which combines with the antigen. The mesenchymal cells are regarded as being subject to a high rate of somatic mutation, so that, when a clone proliferates, some members will produce globulin better adapted to the antigen, and these cells in turn will be stimulated selectively to proliferate, and so on. In this way, more and more cells will produce antibody capable of combining with more of or more firmly with, the antigen surface. The problem of antibody production in response to an antigenic stimulus becomes therefore a problem in cell population dynamics, and the often amazing specificity of antibody for the antigen is achieved by a selective rather than by an instructive process. To account for the phenomenon of immunological tolerance, and the failure of antibodies to be formed against molecules present in the organism at birth Burnet suggests that, during the stage of immunological immaturity contact of antigen with cells potentially capable of making antibody against it results not in stimulation but in deletion of those clones. Hence the adult animal possesses cells

capable only of being stimulated by molecules with surface configurations not shared by its own components. All other clones become forbidden.

If this ingenious theory is correct—in essence even if not in detail—a fairly ready explanation is available not only for many of the cardinal features of immune responses, such as the difference between primary and secondary, or immunological memory and anamnestic reactions, but also for the development of auto-antibodies. According to the clonal selection hypothesis auto-antibodies could be evoked by body constituents which were screened from mesenchymal cells during the stage of immunological immaturity (for example lens protein, or thyroglobulin) or which only developed later (for example spermatozoa). They might also arise by somatic mutation in adult life of clones of cells capable of responding to forbidden patterns, such as to nucleic acid. Burnet makes the good point that antibodies are normally never formed against even heterologous deoxyribonucleic acid, but that when for some unknown reason they do appear, in persons with disseminated lupus erythematosus, they react with deoxyribonucleic acid from all sources including the nuclei of the sufferer's own cells. On the basis of his theory clones capable of making antibody against any deoxyribonucleic acid are forbidden, and eliminated, for the very reason that when antibody is formed, as a rare result of a somatic mutation it will be an auto-antibody.

This example illustrates the self-consistency and the attractiveness of the theory. It is important to remember, however, that there is very little direct evidence to support its main assumption that clones of mesenchymal cells have a built-in response to a particular antigenic pattern, or to explain their deletion during embryonic life and stimulation later. The embryonic hypothesis that lymphocytes, macrophages, plasma cells and primitive reticular cells are all interconvertible is one of the truths of which is convenient rather than proved and so is the assumption that mesenchymal cells are hypermutable as regards somatic mutations. Biochemically minded readers may be disappointed by the frank rejection of a biochemical approach and by the relegation to chance variations in a basic globulin structure of the problem of how antibody is synthesized with a pattern complementary to the antigen. Some may even be stimulated to try to show that a single cell can produce two or more unrelated antibodies at the same time—a finding which would be difficult to accommodate into the theory and on which the evidence is at present conflicting.

The later chapters set out to show how the theory would apply to a wide range of phenomena from collagen disease to cancer, and to some of the latest experimental findings in immunology. Burnet manages with elegance in some cases ingenuity in others and occasionally a good deal of stretching to accommodate them all—including at least two experimental findings which have since become highly suspect or been withdrawn. This last is mentioned no more than as a warning that Sir Macfarlane has such enthusiasm and confidence in his latest ideas that he can sweep up everything, including the readers in his path. The ideas are in any event, original and stimulating and have been carried farther than any one has tried to carry any of the alternative hypotheses. It is likely that a good deal of future work will be influenced by them for their author has a reputation of having hit the right nail on the head on notable occasions in the past.

J. H. HARRIS

Statistics of Extremes

By Prof E J Gumbel Pp xx+375 (New York Columbia University Press, London Oxford University Press, 1958) 120s net

THE theory of extreme values is concerned with the probability distribution of the largest values encountered in samples of finite size. It has many applications including the occurrence of floods and droughts and the breakdown of materials, such as aircraft components, subject to varying stresses and strains.

Prof Gumbel has for many years been a leading authority on the subject and his book is likely to become a standard work. Although the book appears to contain little essentially new theory, it collects and elaborates previous work hitherto widely scattered in the statistical literature and contains many tables and graphs of functions occurring in the theory. There is an excellent bibliography containing references to both theoretical and applied work. The text includes numerous exercises for the reader. The eight chapter headings are "Aims and Tools", "Order Statistics and Their Exceedances", "Exact Distribution of Extremes", "Analytical Study of Extremes", "The First Asymptotic Distribution", "Uses of the First Asymptote", "The Second and Third Asymptotes" and "The Range".

Although several examples of applications are discussed, this book is not a 'cook-book' of practical methods, but it should prove extremely useful to the statistician required to analyse extreme-value data. The scientist interested in practical applications will need considerable mathematical and statistical experience to follow the rather concentrated and sophisticated mathematics. In particular he may find difficulty in assessing the practical importance of some of the concepts defined and some of the results derived.

The high cost probably makes this book one for the library rather than for the individual and is presumably due to the large number of graphs it contains.

R N CURNOW

The Chemistry of Natural Products

Vol 1 The Alkaloids By K W Bentley Pp vii+237 4 dollars Vol 2 Mono- and Sesquiterpenoids By P de Mayo Pp vii+320 52s Vol 3 The Higher Terpenoids By P de Mayo Pp vii+239 42s (New York Interscience Publishers, Inc, London Interscience Publishers, Ltd, 1959)

BOOKS on natural products have in the past usually suffered from several disadvantages: they have tended to consist of catalogues, and quite frequently have been written by specialists who had rather lost contact with the general body of advancing science and did not emphasize relations to chemistry in general. A very welcome tendency is for young and enthusiastic men, themselves deeply involved in the subject from the research side, to summarize fields of research in what might be described as super Ph.D. theses. The advantage of their approach is that it is fresh, but nevertheless authoritative, and that their acquaintance with modern theories of reaction mechanisms and biosynthetic theories enables them to produce monographs which are of general interest and general importance. The three books in the title are in this class. They should interest and inform advanced undergraduates, research students and university or college teachers who have not had the time to keep up with the literature. They are not

perhaps exhaustive enough for research specialists but should provide useful starting-points for research. The general resemblance to theses, particularly in the formulae, will not please lovers of beautiful books, but presumably they would otherwise have been more expensive. They can be heartily recommended to all who are interested in rapidly advancing fields whether as teachers, students or research workers.

A J BIRCH

The Psychology of Social Class

By Maurice Halbwachs Translated by Claire De Javenay (Heinemann Books on Sociology) Pp xvii+142 (London William Heinemann, Ltd, 1958) 16s net

MAURICE HALBWACHS was a French sociologist who learnt in his early manhood to share the liberalism and democratic principles which deeply influenced the generation destroyed by the First World War. It was his inheritance of these principles which led to his own death in Buchenwald in 1945, and it is for this that he must be remembered and honoured. His work as a sociologist is typical of a transitional age, and his writings on the sociology of class distinctions and behaviour are of interest in so far as they illustrate the swing-over from the over-systematic thinking of the sociologists of the nineteenth century to the empiricism which appears to be gaining ground in the second half of the twentieth.

It is evident, however, that Halbwachs had not shaken off his attachment to abstract theories even as late as 1938, when he wrote this book, moreover, it is also evident that he had not mastered the difficulties of basing generalizations on evidence in such a way that a framework of truly scientific theory might be constructed. On one hand, Halbwachs was unable to resist the temptation to quote from the works of the great classical philosophers, as well as the theorists of his own age, such as Durkheim and Weber. On the other, he was only too ready to present a mass of often undigested information derived from such sources as the German Government's survey of working-class budgets, carried out in 1927-28. What was lacking in his work was a serious attempt to relate the evidence to the generalizations founded on it.

T S SIMEX

Toward a Systematic Pragmatics

By R M Martin (Studies in Logic and the Foundations of Mathematics) Pp xv+107 (Amsterdam North-Holland Publishing Company, 1959) 24s

THIS recent addition to "Studies and Foundations" is a valuable monograph in a highly specialist field, and adds lustre to that distinguished series. The main discussion concerns type-theoretical systems, pragmatological meta-language, analytic truth and absolute intensions. These subjects are introduced by a preliminary chapter on the nature of pragmatics. In brief, language-systems can be either syntactical, semantical or pragmatological, and this corresponds to the order of abstraction.

Thus, in syntax, it is only the signs or expressions (and their inter-relations) which are interesting. In semantics, the objects which the signs denote come into the picture. Finally, in pragmatics, the speakers or users of the language are involved. The author's point of view is wholly extensional, whereas that of Carnap is intensional. The power of extensional meta-languages to cover a large part of mathematics, physics, and even biology, is clearly advantageous.

F I G RAWLINS

STRONTIUM-90 IN THE AUSTRALIAN ENVIRONMENT, 1957-58

By DR. F J BRYANT

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AND

L J DWYER DR. J H MARTIN and Prof E W TITTERTON, CMG

Australian Atomic Weapons Tests Safety Committee

Introduction

DURING the past four or five years a considerable effort has been made notably in the United States and the United Kingdom, to gain precise information on the world wide distribution of radioactive fallout from nuclear weapon tests. Results of such measurements to about mid 1957 were included in the extensive review of the subject prepared by the U.N. Scientific Committee in August 1958¹. Further results for 1957 and also for 1958 for the United States, the United Kingdom and other areas have since been published, notably by Bryant *et al.*²⁻⁴, Stewart *et al.*⁵ and the U.S. Atomic Energy Commission Health and Safety Laboratory⁶⁻⁹.

In April 1957 the programme of fallout measurements, initiated by the Australian Atomic Weapons Tests Safety Committee¹⁰⁻¹² to cover local weapon tests and to monitor global fallout, was extended to include the determination of strontium 90 in representative Australian materials. Arrangements were made for the sampling of soil, powdered milk, cabbages and human and sheep bone tissue. All samples were sent to the United Kingdom for radiochemical analysis by the Atomic Energy Research Establishment Group at Woolwich Arsenal, under the direction of one of the authors (F J B). In this report results are presented for the early part of the programme extending from May 1957 to September 1958, during which period 243 samples were processed. In order to minimize the radiochemical effort, a number of the bone samples were bulked and the actual chemical analyses were reduced in this way to 148.

Sampling Programme

It is well known that strontium 90 in global fallout enters the human body mainly as a contaminant of dietary materials, the uptake through inhalation is very small by comparison¹³. Therefore, the sampling programme was designed to monitor levels of strontium 90 in materials which are representative of the phases between deposition of strontium 90 on the ground and its absorption into human bone. The primary material of the programme was human bone tissue. Because milk products, generally, are a major contributor of calcium and strontium 90 to the Australian diet milk was chosen as the important representative dietary material and for convenience, samples of powdered milk were taken for analysis, however cabbages were included to monitor the contribution to the diet made by leaf crops. Soil and yearling sheep bone tissue were assayed to provide information on the accumulation and rate of

deposition of strontium 90 at ground level, measurements were also made on total precipitation collected in stainless steel pots during the latter half of 1958.

The materials selected, and the sampling procedures adopted were not expected to allow a complete examination of the uptake processes. This can most satisfactorily be done by controlled experimentation within a laboratory, of the type carried out by Russell and his Agricultural Research Council group¹⁷⁻¹⁸.

Samples of human bone tissue, powdered milk cabbages and soil were taken from the Perth, Adelaide, Melbourne, Sydney and Brisbane areas during 1957 and 1958, while sheep bones were

Table 1a STRONTIUM 90 IN AUSTRALIAN HUMAN BONE SAMPLES*
DECEMBER 1957-SEPTEMBER 1958
UNDER 5 YEARS

| Locality | Bone | Age* | Strontium 90 (µm/gm calcium) | |
|-----------|-----------|--------------------|--|------------|
| | | | Analytical result | Mean |
| Perth | Femora | Stillborn and 3 m | 0.3 0.3 0.3 1.0 1.2 0.6 | 0.5 |
| | Femur | 4 m | 0.3 | |
| | | 9 m | 1.0 | |
| | | 18 m | 1.2 | |
| | Vertebrae | 31 y | 0.6 | |
| Adelaide | Femur | 1 d | 0.5 | 0.53 |
| | Femora | 1 d and 3 d | 0.2 | |
| | | 10 d and 24 d | 0.4 | |
| | | 1 m and 3 m | 0.3 | |
| | Femur | 3 m | 0.35 | |
| | | 4 m and 6 m | 0.7 | |
| | | 7 m | 1.5 | |
| Melbourne | | 13 m | 0.0 | 0.59 |
| | Vertebrae | 2 d and 21 d | 0.35 | |
| | | and 2 m | 0.6 | |
| | Craula | 6 m and 10 m | 0.85 | |
| | | 24 m and 30 m | 1.4 | |
| Sydney | | 31 y | 0.3 | 0.61 |
| | Femora | 0 d and 16 d | 0.2 | |
| | Femur | 3 m | 0.5 | |
| | Femora | 6 m and 7 m | 0.6 | |
| | | 11 m and 23 m | 0.5 | |
| | Femur | 2 m and 23 m | 0.65 | |
| | Femur | and 24 m | 1.0 | |
| Brisbane | Vertebrae | 30 m | 0.7 | 0.70 |
| | | Stillborn and 11 m | 0.7 | |
| | | 1 m and 7 m | 0.45 | |
| | | 18 m | 0.7 | |
| | | 24 m and 28 m | 0.4 | |
| Total | | 55 samples | 0.75 0.0 | (0.50-1.0) |

* The age distribution of the specimens is shown in the 1

Table 1b STRONTIUM 90 IN AUSTRALIAN HUMAN BONE SAMPLES* DFCMBFR 1957-SEPTEMBER 1958
ALL AGES

| Locality | Under 5 years | | | | 5 years-20 years | | | | Over 20 years | | | | |
|-----------|------------------|---------------|----------------|---|------------------|---------------|----------------|---|---------------|---------------|----------------|--|-----------------|
| | Bone | No of samples | No of analyses | Mean strontium-90 $\mu\mu\text{c/gm}$ calcium | Bone | No of samples | No of analyses | Mean strontium-90 $\mu\mu\text{c/gm}$ calcium | Bone | No of samples | No of analyses | Strontium 90 $\mu\mu\text{c/gm}$ calcium | |
| | | | | | | | | | | | | Mean | Normalized† |
| Perth | Vertebrae Femora | 10 | 15 | 0.57 | Vertebrae Femur | 31 | 11 | 0.30 | Vertebrae | 11 | 1 | 0.2 | 0.11 |
| Adelaide | Femora | 13 | 0 | 0.53 | Femur | 1 | 1 | 0.3 | Femora | 16 | 1 | 0.04 | 0.06 |
| Melbourne | Vertebrae Crania | 04 | 23 | 0.50 | Vertebrae Crania | 28 | 11 | 0.30 | Vertebrae | 12 | 1 | 0.3 | 0.17 |
| Sydney | Vertebrae Femora | 212 | 16 | 0.64 | Vertebrae Femora | 16 | 11 | 0.33 | Vertebrae | 18 | 1 | 0.2 | 0.11 |
| Brisbane | Vertebrae | 8 | 0 | 0.70 | Vertebrae Ribs | 21 | 11 | 0.30 | Vertebrae | 8 | 1 | 0.25 | 0.14 |
| Total | | 52 | 33 | 0.00 ± 0.10 | | 25 | 0 | 0.33 ± 0.05 | | 65 | 5 | | 0.12 ± 0.02 |

* The age distribution of the specimens is shown in Fig. 1

† Normalization of the analytical results of the adult tissue has been performed using the factors of Schulert *et al.* (ref. 22)Table 1c STRONTIUM-90 IN AUSTRALIAN HUMAN BONE SAMPLES*
DECEMBER 1957-SEPTEMBER 1958
ALL AGES AND LOCALITIES

| Age group | Femora | | Vertebrae | | Crania | | Ribs | |
|-----------------|-----------------------------|----------|-----------------------------|----------|-----------------------------|----------|-----------------------------|----------|
| | $\mu\mu\text{c/gm}$ calcium | Mean age | $\mu\mu\text{c/gm}$ calcium | Mean age | $\mu\mu\text{c/gm}$ calcium | Mean age | $\mu\mu\text{c/gm}$ calcium | Mean age |
| Under 24 months | 0.54 (30, 10)† | 0 m | 0.57 (11, 5)† | 0 m | 0.85 (2, 1)† | 23 m | — | — |
| 24-59 months | 1.0 (1, 1) | 30 m | 0.61 (6, 5) | 30 m | 0.0 (2, 2) | 33 m | — | — |
| 5-20 years | 0.34 (8, 3) | 8 y | 0.31 (8, 4) | 12 y | 0.35 (8, 1) | 7 y | 0.3 (1, 1)† | 14 y |
| Over 20 years | 0.04 (10, 1) | 60 y | 0.23 (49, 4) | 57 y | — | — | — | — |

* The age distribution of the specimens is shown in Fig. 1

† Number of samples, number of analyses

supplied from 23 localities throughout Australia during the same period, these materials were taken from sites across the continent within a range of latitudes of 20°-38° S. The analytical methods used for the determination of strontium-90 were those described by Bryant *et al.* 2, 3, 16, 20

Sampling Methods and Results

The results are given in Tables 1-5 and wherever possible mean values and the corresponding errors have been derived to facilitate comparisons with the results of similar surveys conducted elsewhere.

(a) *Human Bone Tissue* Between December 1957 and September 1958 pathologists in the five capital cities supplied a total of 142 specimens of human bone tissue. For each area the specimens were divided into three age-groups, namely, under 5 years, 5-20 years and over 20 years. In the latter two groups some bulking of material was employed to reduce the number of analyses, while the majority of the infant specimens were analysed individually. In all, 47 analyses were performed.

It was impracticable to restrict the survey to a single type of bone, and samples of vertebrae, femora and crania were accepted, when adult femora were supplied only the shafts were analysed, but whole bones were included for the younger specimens. Each specimen comprised at least 20 gm of wet bone.

For each age-group and area the various bone types were not mixed in the bulking of material prior to analysis. Information could, therefore, be obtained on any variations of strontium-90 concen-

tration among the bone types employed. Because the proportion of calcium in bone ash is approximately constant²¹, the bulking of specimens was performed on the basis of equal masses of ash.

The final stage of the radiochemical analysis took one of two courses depending on the activity of the

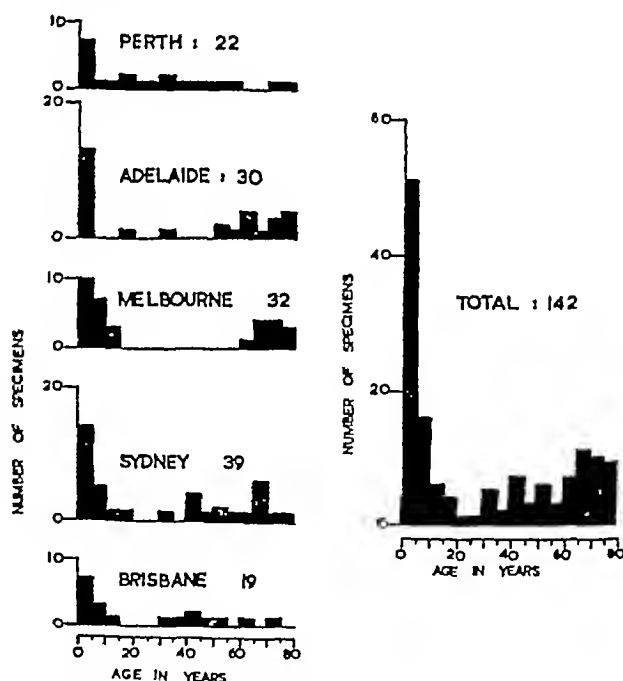


Fig. 1 Age distribution of the human bone specimens

extracted strontium isotopes, strontium 89 and 90. Where possible yttrium 90 was separated for counting after equilibration with mother strontium 90. On the other hand, for low activities the unwanted strontium 89 was allowed to decay for about two half lives and the strontium 90 content estimated. Both methods gave consistent results.

Fig 1 shows the age distribution of the specimens collected, from which it will be seen that the unequal availability of material, particularly in the middle years, has led to emphasis on very young and old tissue. The complete data are recorded in Tables 1a, b and c and the distribution of strontium 90 concentration with age is exhibited in Fig 2.

The mean values derived in the tables, and also those plotted in Fig 2, are considered to refer to strontium 90 levels in human bone at May 1958.

Table 1c shows that there is no evidence for a bone variation in age groups up to 20 years, however, for older tissue, vertebrae have a considerably higher contamination than femora, as reported by the Lamont Group^{21,22}, from more extensive measurements. The results for adults, therefore, have been normalized to the skeletal mean using the factors derived by Schulert *et al*.²³

No significant variations of strontium 90 in human bone were observed between the five capital cities, and so the five groups of data were combined to give the mean strontium 90 concentrations in age groups, plotted in Fig 2. The estimated standard deviations and the number of specimens on which the mean values were based are also shown. A distribution of strontium 90 concentration with age, computed by

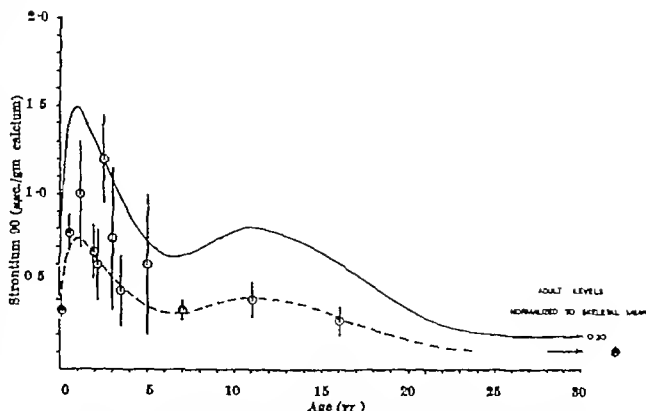


Fig 2. Variation with age of strontium 90 concentration in human bone tissue. O Australia May 1958 — North America and Europe January 1958 (ref 23) --- 0.5 (North America and Europe January 1958)

Kulp *et al*²⁴ gives a good description of their North American and European bone tissue data of January 1958. This distribution is shown as the full curve in Fig 2, while as the broken curve, it has been scaled down by 2 to facilitate comparison with Australian data of May 1958.

(b) *Milk* The powdered milk samples were taken from factories supplying the five capital cities in August 1957 and March and August 1958. In each case the milk was of known age and origin and the later samples were taken from cattle grazing in the same locality, although not necessarily the same pasture. All but a few samples were full-cream powdered milk.

The analytical results are given in Table 2 and show the March 1958 levels to be lower than those for August 1957 and 1958 suggesting a seasonal variation of the type noted by other authors, for example, Stewart *et al*.²⁵

(c) *Cabbages* During August 1957 and 1958 two or three cabbages grown within the vicinity of each of the five capital cities were asked for analysis without prior washing or other preparation. Before the determination of both calcium and strontium 90 contents the ash from each sample was decomposed with a mixture of HF and HClO₄ in the presence of strontium and barium carriers. The analytical results are presented in Table 3.

(d) *Sheep Bone Tissue* This material was included in the programme because the strontium 90 accumulation in the bones of yearling sheep can be used as a monitor of fallout deposition. Moreover, through their habit of grazing extensively, sheep

Table 2 STRONTIUM-90 IN AUSTRALIAN POWDERED MILK SAMPLES*

| Grazing locality of cattle | August 1957 | March 1958 | Rainfall August 1957-March 1958 (in.) | August 1958 | Rainfall March 1958-August 1958 (in.) |
|--|--|--|---------------------------------------|--|---------------------------------------|
| | Strontium-90 $\mu\text{mc./gm. calcium}$ | Strontium-90 $\mu\text{mc./gm. calcium}$ | | Strontium-90 $\mu\text{mc./gm. calcium}$ | |
| Brunswick Junction 90 miles south of Perth | 2.0 | 1.6 | 5.9 | 4.0 | 20.0 |
| Mt Compass 30 miles south of Adelaide | 4.2 | 3.8† | 6.6† | 7.7 | 23.3† |
| Mafra 110 miles east of Melbourne | 4.0 | 2.7 | 15.1 | 4.4 | 7.0 |
| Lower Hunter River Valley 90 miles north of Sydney | 2.4 | 1.6 | 14.0 | 1.8 | 8.0 |
| Mary River Valley 100 miles north of Brisbane | 5.3 | 2.2 | 23.7 | 5.1 | 24.2 |
| Mean | 3.8 ± 1.0 | (2.4 ± 0.8) | | (5.0 ± 1.6) | |

* Each sample was at least 1.5 km. † Taken in January 1958
‡ Rainfall periods taken to and from January 1953

Table 3 STRONTIUM 90 IN AUSTRALIAN CABBAGES

| Locality | August 1957 | | August 1958 | |
|-----------|---------------------------|--|---------------------------|--|
| | Calcium in ash (per cent) | Strontium 90 $\mu\text{mc./gm. calcium}$ | Calcium in ash (per cent) | Strontium 90 $\mu\text{mc./gm. calcium}$ |
| Perth | 8.0 | 4.0 | 12.2 | 4.0 |
| Adelaide | 6.9 | 2.3 | 11.1 | 4.3 |
| Melbourne | 7.7 | 1.1 | 6.0 | 0.4 |
| Sydney | 7.0 | 1.1 | 13.0 | 4.1 |
| Brisbane | 6.6 | 2.0 | 11.8 | — |
| Mean | | (2.6 ± 0.7) | | (5.0 ± 1.6) |

tend to integrate out local variations in fallout deposition, and sheep bone tissue is available in areas of Australia where other representative samples are difficult to obtain.

The first collection of sheep bones was made from 13 widely separated areas during May-June 1957, and further collections were made from 16 areas in

August 1957 and 1958. The grazing localities are shown in Fig. 3. In each case representative long bones were selected from the legs of up to three sheep each of which had grazed over natural grasses throughout most of its life.

In all, 59 analyses were performed on material collected from 89 sheep during the three surveys and

Table 4 STRONTIUM 90 IN AUSTRALIAN SHEEP BONE SAMPLES

| Locality | May-June 1957 | | | August-September 1957 | | | August 1958 | | |
|--|---------------|--------------------------|--|-----------------------|--------------------------|--|--------------|--------------------------|--|
| | No. of sheep | Approximate age (months) | Strontium 90 $\mu\mu\text{c/gm}$ calcium | No. of sheep | Approximate age (months) | Strontium 90 $\mu\mu\text{c/gm}$ calcium | No. of sheep | Approximate age (months) | Strontium 90 $\mu\mu\text{c/gm}$ calcium |
| Beverley 70 miles E Perth | 3 | 8 | 5.3 | 1 | 12 | 7.0 | 3 | 13 | 6.4 |
| Salisbury 20 miles N Adelaide | 2 | 8 | 21* | 1 1 1 | 15 15 15 | 7.5 9.1 9.5 | 3 | 14 | 8.8 |
| Quorn 180 miles N Adelaide | | | | 1 1 1 | 15 15 13 | 10.2 7.0 11 | 3 | 15 | 10 |
| Marree 360 miles N Adelaide | 1 | 8 | 3.0 | 1 1 | 14 14 | 2.1 1.9 | 1 | 12 | 3.7 |
| Ingomar 430 miles N N W Adelaide | 3 — | 12 12 | 5.7 5.4 | | | | | | |
| Coober Pedy 470 miles N N W Adelaide | | | | 1 1 1 | 15 15 15 | 5.5 7.7 9.0 | 3 | 15 | 4.7 |
| Mabel Creek 480 miles N N W Adelaide | 2 — | 12 12 | 6.5 7.3 | | | | | | |
| Evelyn Downs 530 miles N N W Adelaide | | | | 1 1 | 14 14 | 7.0 6.3 | | | 3.8 |
| Mt Willoughby 550 miles N N W Adelaide | 2 — | 10 12 | 10 11 | | | | | | |
| Victory Downs 700 miles N N W Adelaide | | | | 2 | 16 | 4.6 | 3 | 12 | 4.2 |
| Yarra Valley 30 miles E Melbourne | 2 1 | 8 8 | 13 14 | | | | | | |
| Yarrawonga 140 miles N N E Melbourne | | | | 1 | 13 | 12 | 3 | 13 | 7.9 |
| Sydney | 1 | 9 | 12 | 1 | 13 | 8.2 | 2 | 11 | 6.9 |
| Canberra | 1 | 8 | 7.3 | | | | | | |
| Dubbo 180 miles N W Sydney | | | | 1 | 11 | 4.6 | 2 | 13 | 3.8 |
| Bourke 400 miles N W Sydney | 1 1 | 9 8 | 3.8 2.7 | | | | | | |
| Lismore 370 miles N N E Sydney | 1 | 8 | 5.8 | | | | | | |
| Brisbane | 3 | 8 | 1.5 | 1 | 12 | 1.6 | 1 | 14 | 1.2 |
| Southport 50 miles S S E Brisbane | | | | 1 1 | 11 11 | 8.1 9.2 | 2 | 12 | 6.3 |
| Rockhampton 320 miles N N W Brisbane | | | | 1 | 11 | 5.3 | 1 | 13 | 4.6 |
| Charleville 430 miles W Brisbane | 1 | 0 | 8.0 | 1 | 12 | 7.2 | 2 | 12 | 5.3 |
| Townsville 680 miles N W Brisbane | | | | 1 | 11 | 6.1 | 2 | 12 | 3.9 |
| Cloncurry 930 miles W N W Brisbane | | | | 1 | 12 | 1.0 | 3 | 16 | 1.5 |
| Mean Total No. of analyses | 25 | 18 | (7.9 \pm 2.2) | 26 | 25 | (6.6 \pm 1.5) | 34 | 16 | (6.3 \pm 1.5) |

* The sheep from which this bone tissue was taken grazed in the Mt. Compass area.

Table 5 STRONTIUM-90 IN AUSTRALIAN SOIL SAMPLES*

| Locality | August 1957 | | | | August 1958 | | | | Rainfall August 1957- August 1958 (in) |
|-----------|-------------------------------------|---------------------|---|--|-------------------------------------|---------------------|---|--|--|
| | Sample area (m ²) | Calcium gm./kgm. | Soil surface density kgm./m. ² | Strontium 90 mc./km ² | Sample area (m ²) | Calcium gm./kgm. | Soil surface density kgm./m. ² | Strontium 90 mc./km ² | |
| Perth | 0-041 | 0.6 | 124 | 2.7 | 0-041 | 0.8 | 60 | 3.5 | 30 |
| Adelaide | 0-041 | 3.0 | 20 | 1.8 | 0-041 | 1.5 | 61 | 2.0 | 17 |
| Melbourne | 0-041 | 2.7 | 10. | 3.4 | 0-039 | 1.0 | 70 | 2.2 | 24 |
| Sydney | 0-030 | 2.3 | 80 | 2.5 | 0-040 | 2.3 | 88 | 3.7 | 54 |
| Brisbane | 0-04 | 1.0 | 06 | 2.6 | 0-041 | 0.6 | 41 | 1.0 | 30 |
| Mean | | | | (2.4 ± 0.4) | | | | (2.5 ± 0.7) | |

* Top 10-cm soil plus surface matt

the results are shown in Table 4. Results which are systematically low for all three surveys are apparent for some areas. These low values may be associated with variations in rainfall, soil and grazing conditions.

However, Table 4 also shows that the mean strontium 90 level in yearling sheep bone is virtually constant for the three successive surveys. This implies that the strontium 90 levels in sheep bone tissue of this age depend mainly on the rate of deposition of fallout lending support to Russell's¹² recent suggestions concerning the relative roles of total fallout and the fallout rate in the take up of strontium 90 into plants.

Apart from the systematic variations at particular locations referred to above, the skeletons of yearling sheep throughout Australia appear to be contaminated with strontium 90 to approximately the same extent. Fallout is therefore uniform across the continent, the slight latitudinal variation suggested by other measurements¹³ is not reflected in these results.

(c) *Soil*. During August 1957 and 1958, samples of soil to a depth of 10 cm were taken from uncultivated land within each of the five capital cities. At each site succeeding samples came from the same immediate vicinity but the sites themselves were associated with neither milk production nor market gardening. The surface dimensions of the samples lay between 0.04 and 0.05 m², the surface matt was analysed with the soil.

The 10 samples were treated using the hydrochloric acid leaching method which is considered to give complete extraction of both calcium and strontium 90. The analytical results shown in Table 5 would imply that within the errors there has been no overall accumulation of strontium 90 in Australian soils during the period of the investigation. This conclusion is unacceptable because measurements of

total precipitation collected in open pots at eight sites in Australia during part of this period and discussed below, suggest an annual deposition rate of nearly 1 mc./km². This figure is similar to that reported for Australia by Alexander¹⁴, in the course of a world wide survey of strontium 90 in soil, his results for 1956 and 1958, for samples taken at six Australian sites, are shown in Table 6.

Table 6 STRONTIUM 90 IN AUSTRALIAN SOIL SAMPLES* (Taken from "Strontium-90 Distribution as determined by the Analysis of Soils" by L. T. Alexander (ref. 27))

| Locality | May 1956 (mc./km ²) | March 1958 (mc./km ²) |
|---------------|------------------------------------|--------------------------------------|
| Perth | 1.0 | 1.8 |
| Adelaide | 2.0 | 4.5 |
| Hobart | 0.6 | 4.3 |
| Brisbane | 1.3 | 4.5 |
| Allee Springs | 0.7 | 2.2 |
| Katherine | — | 1.5 |
| Mean | (1.1 ± 0.4) | (3.0 ± 1.0) |

* (1) Top 15-cm soil plus surface matt (2) two samples of 0.125 m² were taken on each occasion at each site. Results quoted are averages.

This conflict between the two sets of results is most probably related to certain characteristics of the soil samples. Although the same sites were revisited annually, as Table 5 shows the samples showed considerable fluctuations of density and calcium content and such factors might account for the low values recorded for the accumulated deposit of strontium 90.

Taken at face value the present data lead to a mean level at August 1958 of about 2.5 mc./km², somewhat lower than the mean value 3.0 mc./km², of Alexander's data for Australia.

(f) *Total Precipitation*. Commencing in June 1958 stainless steel pots, 12 m in diameter and 12 in high were exposed continuously at the eight stations shown in Fig. 3. This aspect of the fallout monitoring programme was carried out in co-operation with the U.S. Atomic Energy Commission, as part of its open pot sampling effort¹⁵.

Both precipitation and solid deposition were collected over monthly periods and in each case the

Table 7 AUSTRALIAN HIGH WALLED POT SAMPLES JUNE-DECEMBER 1958

| Locality | Period | Accumulated strontium 90 (mc./km ²) | Estimated annual rate (mc./km ²) |
|------------|--------------------|---|--|
| Perth | June-November 1958 | 0.38 | 0.8 |
| Adelaide | | 0.74 | 1.7 |
| Melbourne | October | 0.74 | 0.9 |
| Hobart | | 0.68 | 1.6 |
| Sydney | November | 0.60 | 1.3 |
| Brisbane | July | 0.44 | 1.0 |
| Townsville | June | 0.5 | 0.7 |
| Darwin | July | 0.86 | 2.1 |
| Mean | | | (1.2 ± 0.4) |

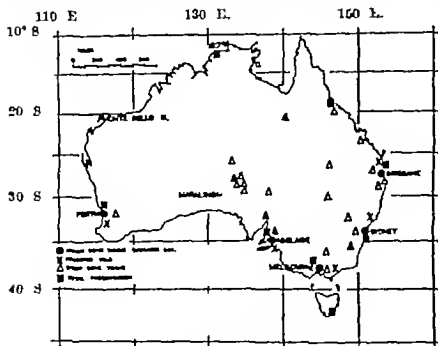


Fig. 3 Sampling localities

catch was analysed for strontium-90 by the Health and Safety Laboratory of the U.S. Atomic Energy Commission, the results are shown in Table 7.

Taking into account the seasonal variation in fallout rate the mean annual rate of deposition of strontium-90 for Australia approximates to 1 mc/km². Further work, now in progress, will establish this rate more definitely.

Comparisons of Australian Strontium-90 Levels with those in the Northern Hemisphere

The nearly uniform fallout of strontium-90 in Australia contrasts with considerable fluctuations observed in the United Kingdom and the United States, where the bulk of northern hemisphere measurements have been made. Nevertheless, rough average levels can be compared in those cases where data are available for the appropriate time (the United States does not measure sheep bones or cabbages).

The human bone results given in Fig. 2 show that the Australian levels are somewhat less than one-half those for the northern hemisphere. In the cases of milk and cabbages, comparisons with American⁴⁻⁶ and British⁴ data again indicate levels which are about one-half the northern hemisphere values while Australian sheep bone results for 1957 indicate levels less than one-half those in the United Kingdom⁴ at that time.

Australian soil-levels lie between one-fourth and one-third of those of the more densely populated regions of the northern hemisphere²⁷, while the open-pot measurements indicate a strontium-90 fallout rate of less than one quarter that operative in the northern hemisphere.

Conclusions

(1) Within the sampling errors, and apart from some local variations noted, the levels of strontium-90 in the material examined are uniform throughout Australia. This indicates that the strontium-90 fallout over the continent arises from high-yield fission weapon tests overseas, as expected the contribution from local weapon tests is too small to be detected.

(2) The rate of deposition of strontium-90 and its accumulation in Australian soils are one-fourth to one-third those in the more densely populated areas of the northern hemisphere. The levels of strontium-90 in Australian human bone tissue and milk lie between one-third and one-half those in the northern hemisphere. This level is a little higher than would be expected from the fallout rate and the soil data, but the difference is not established statistically. If further experiments prove this difference to be real it would be hard to explain satisfactorily.

A similar difference between bone and soil-levels was reported by Kulp *et al.*²³ for other southern hemisphere samples and they considered that it might be due to the movement into the southern hemisphere of foodstuffs containing strontium-90 produced in the northern hemisphere. This explanation is unsatisfactory in the Australian case for the continent is self-sufficient in most primary production, especially of milk and cereals. Further results from the Australian survey should elucidate the position.

(3) The possible biological consequences to the population of Australia, of the fallout-levels reported in this paper, have been assessed by the Australian National Radiation Advisory Committee²⁸. The Committee concluded that the possible hazards are very small in comparison with those already accepted in technically advanced communities.

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EVOLUTION OF HOST-PARASITE RELATIONSHIPS

PROF JEAN BAER (Neuchâtel) opened a symposium held by Section D (Zoology) at the recent British Association meeting in York on the "Evolution of Host-Parasite Relationships". He began by analysing an ecological survey of such relations. The survey

was limited to biting and sucking lice, fleas and worms parasitic in vertebrates, because the taxonomy and host distribution of these parasites have been well studied, their life-cycles are usually complex and diverse and their host-relations show great diversity.

The host or host-group is comparable ecologically to an island, the parasites representing the endemic fauna, and the more isolated the island, or the more specialized the host, the higher is the degree of endemism of its fauna. There is a great deal of evidence showing that both morphological and physiological specialization of the parasites is a consequence of their adaptive evolution to distinct groups of hosts.

A reliable impression of host-distribution can be derived from histograms of the numbers of genera of parasites in particular host classes, and from the individual distribution of each group may be deduced its probable age.

Mollusca, for example, occur exclusively on birds and mammals, and have evolved more extensively on the former than on the latter. Monogenea are parasites on elasmobranchs, teleosts, amphibians and reptiles but are far more widely specialized on teleosts than on elasmobranchs and only very slightly on amphibians and reptiles. Cestodes occur throughout all the major groups of vertebrates—the greatest number of genera is found in birds and in elasmobranchs, whereas the largest number of genera of trematodes is found in teleosts even though trematodes have been reported from all the major groups of vertebrates.

Host-parasite relationships as expressed by the number of genera of parasites associated with a given group of hosts also imply that the age of the parasites, that is, the time when they first adopted parasitism as a way of life, varies considerably. For example fleas, lice and Mollusca are unknown from hosts other than birds and mammals and it is extremely unlikely that such parasites existed before their hosts themselves appeared in late Cretaceous times. Monogenea and cestodes were already most certainly associated with the precursors of modern albatrosses and appear to have accompanied the aquatic ancestors of the land-dwelling vertebrates. Moreover, ectoparasitic Monogenea have only been able to survive by seeking refuge within the mouth cavity, oesophagus and urinary bladder of their hosts and since their life-cycle restricts them to an aquatic habitat, they are associated with vertebrates such as amphibians and freshwater tortoises. On the other hand, tapeworms living invariably within the gut of their hosts have evolved together with the latter and as their life cycles also became adapted to terrestrial intermediate hosts, it is natural that these parasites occur in land-dwelling vertebrates, that is in reptiles, birds and mammals.

These parasites of vertebrates were discussed ecologically, separately as ectoparasites and as endoparasites, and as to whether the larval forms had a free-living stage or not. The ectoparasites with no free-living stage were the Mollusca and the Anoplura and with a free-living stage, the terrestrial Siphonoptera, and the aquatic Monogenea. The endoparasites were those with a gradual metamorphosis, the nematodes which might or might not have an intermediate host and those in the metamorphosis of which distinct stages occurred, the trematodes, cestodes and Acanthocephala, all of which had at least one intermediate host.

An analysis of the results from an ecological approach to host-parasite relationships clearly shows the presence of two factors responsible for host distribution, namely, (a) the physiological requirements of each of the stages of the life-cycle, (b) the degree of morphological differentiation of the in-

fective larval stage. These factors being inherent to the class to which the parasite belongs, must have been acquired genetically and are therefore subject to mutation and to evolutionary pressures.

Each successive stage of any life cycle does not necessarily have identical physiological requirements but the more highly specialized the latter the greater the degree of intimacy between the parasite and the host. In trematodes for example, host-specificity for the first intermediate host is more pronounced than in any of the subsequent stages, whereas in tapeworms the greatest degree of intimacy occurs with the definitive host. In trematodes and acanthocephalans the infective larval stage is already a completely formed young worm that only needs to mature and to grow to become adult. Since the distribution of these parasites in their definitive hosts mostly follows the ecological pattern, it is probable that the physiological requirements of the adult worms are not highly specialized. On the other hand the infective larvae of monogeneans and tapeworms on reaching the definitive host must undergo further metamorphosis before acquiring adult characters. The necessary conditions appear to be very strict and the more considerable the metamorphosis the greater the degree of host-specificity, the latter following the phylogenetical pattern. Although there is, as yet insufficient evidence for parasitic nematodes it seems, however, that there might be a specific mechanism that triggers the final moults of the infective larvae.

Free living flea larvae require strict conditions as to temperature and degree of humidity implying that their physiological requirements may be rather specialized. But the legendary mobility of adult fleas and their resistance to starvation enable them to survive but not necessarily to reproduce, by practising the art of host hopping.

During their entire life-cycle biting and sucking lice remain attached to the host. So it is not astonishing that their physiological requirements appear to be highly specialized as regards hair and feather structure. In birds their host distribution appears to reflect principally the latter.

Summing up the effects of both external and internal factors responsible for parasite relationships we find that parasites do not select their habitat but that the latter is imposed by ecology. The resulting distribution, however, also reveals another selective mechanism, namely, the degree of physiological and morphological adaptation of the parasites themselves.

Prof W E Kershaw (Liverpool School of Tropical Medicine), in discussing the evolving human flaria, suggested that it was more pertinent to consider their present evolution rather than what had happened in the past. This was possible because of precise information of these pathogenic human parasites which it had been necessary to obtain urgently in order to devise economic and practicable control measures. Their complicated life cycles involved man, possibly other animals, and usually multiple species of vectors each vector with its own sequence of environments. The parasite, therefore should be regarded as one component of a parasite-host-vector complex. The true evolving entity was therefore not the parasite but the complex which was evolving as were the separate components, and it was behaviour rather than structure which was critical.

Loa loa a parasite responsible for the recurrent and crippling so-called Calabar swelling occurs in West and Central Africa. There were two parasite-

host-vector complexes, an infection occurring in man and transmitted by two species of the vector genus, which bite during the day, and another occurring in three or more species of monkey which are adapted to different but related species of the vector which bite during twilight and at night. Both parasites were very closely related and differed only in their general dimensions and in their adaptation to different vectors. Each was well tolerated by the different vertebrate hosts and equally well transmitted by all the related vectors in the laboratory, but little interchange between these two populations occurred in Nature.

Malayan filariasis caused recurrent lymphatic inflammation and fever and often resulted later in the disabling permanent swelling of the limbs and the genitals known as elephantiasis, one form occurred in the north-west (periodic) and the other in the south and east of the Peninsula (non-periodic). The parasites responsible had only trivial structural differences, differing mostly in behaviour. In the 'periodic' form the larvae were rarely found in the blood during the day, being most numerous at night. In the 'non-periodic' form, the larvae were apparent during the day and night in similar numbers. The larvae of these two forms behaved differently in the blood, they had different groups of vectors, and though both could be transmitted easily to cats, one form is not so well adapted to animals and occurs naturally only in man, whereas the other form is well adapted to animals and occurs naturally in man, in several species of monkey, in the domestic cat and in the pangolin.

In addition to these two infections in man, one of which is shared with many animals, there was a further and separate parasite which behaves a little differently from the other two, was transmitted by vectors somewhat different from the others and occurred in a very large range of animals, including the dog, the domestic cat, two species of wild cats and the civet cat, the tiger, the pangolin, the moon-rat and the slow loris, and could be transmitted experimentally to man and to the domestic cat. It had so far been found in the State of Pahang.

Work in East Africa had disclosed a fourth parasite, occurring in animals but not so far in man, closely related in structure to the two forms of human filariasis in Malaya and to that described in the State of Pahang occurring in a large range of animals. There were four related parasite-host-vector complexes, one of which had separated from the other three and was so far believed to be restricted to East Africa, and three occurred in Malaya. These three in Malaya are now evidently undergoing further divergent evolution, though their overlap is still very considerable.

Onchocerciasis caused skin changes and was associated with blindness in Central America and in tropical Africa. In the Americas, the adult worms occurred in nodules in the head and neck and eye changes were common, while in Africa they occurred on the lower part of the trunk and the legs, and eye changes were less common and occurred mostly in old-standing infections, so that they were once thought to be due to different parasites. In Africa the distribution of the larvae in the skin had a very clear pattern both on the surface and in depth, and in early infections these larvae were limited to the legs. Only when exposure to the infection had been repeated for many years did the concentration of larvae rise and were they to be found in the upper parts of the

body. While similar precise information was lacking in the Americas it seemed likely that the larvae were most numerous in the head and neck. The vectors in Africa bit on the ankle and leg, and in America on the head and neck. These two different parasite-host-vector complexes have the same host and the same parasite, but differ in their manifestations because of the different behaviour of the two different groups of vectors.

The fundamental research undertaken to make it possible to devise economically practicable control measures has disclosed evolution in progress.

Dr C. A. Wright (British Museum, Natural History) discussed the relation between trematodes and molluscs. The problem of speciation in the digenetic trematodes had received little attention. Isolation of some kind is an essential factor in the evolution of new species, and it is suggested that the part played by the molluscan intermediate host is of considerable importance in the speciation of flukes. The effective geographical range of a parasite is that area where all of the hosts necessary to the completion of the life cycle occur together. The ecological requirements of most molluscs are such that a species is seldom uniformly distributed throughout its range but is broken up into separate populations between which there are varying degrees of isolation. These populations serve as the foci for the completion of fluke life-cycles and it is around these centres that the gene pools are formed from which new species may arise. There are three main factors in the maintenance of the purity of the gene pool, the geographical isolation of the locality, movement of the definitive host and the longevity of the adult parasite within that host. The third factor may partly offset the second for, if the parasite matures quickly, lays its eggs and dies, there is less chance of the eggs reaching other centres where the cycle could be completed even if the definitive host is very mobile.

The importance of host-restriction in the parallel evolution of host and parasite is of great significance, and the degree to which this phenomenon is shown in the relationship between larval flukes and their molluscan hosts is far greater than it is between the adult flukes and their vertebrate hosts. In those flukes which have a free-swimming miracidium there are at least two ways in which new fluke-mollusc relationships may occur. In the process of host-location by the miracidia the first stage is a response to physical stimuli which bring the larvae into the region of the host-habitat. Thus, the substitution of a different mollusc having the same ecological requirements as the normal host may result in the adoption of this new host if its tissues provide an acceptable environment for further development of the larvae. The last stage of the host-finding pattern by miracidia is a response to a chemical stimulus. Paper chromatography has shown the presence of species specific substances in the body-surface mucus of freshwater snails and it is possibly these substances which enable miracidia to discriminate between potential hosts. It has now been shown that there exist differences in the composition of the mucus of snails of the same species from different populations and this may have great significance in the evolution of new mollusc-fluke relationships.

Dr Theresa Clay (British Museum, Natural History) made some suggestions about the evolution of host-parasite relationships in the Mallophaga of birds. It was possible that the breaking up into

non breeding units by the birds during their evolution would result in isolated populations of Mallophaga and was analogous to the situation found on a group of continental islands the populations of which had become isolated by the disappearance of land connections. Later secondary infestations of Mallophaga from one host group to another are analogous to the trans-oceanic colonization of oceanic islands. Successive colonizations and the occupation of the different ecological niches on the body of the bird could explain the number of different genera and species of Mallophaga found on one host species. During the time that the Mallophaga were still partly free-living and before they had developed any close adaptation to life on the bird or to a particular bird species, inter change of host was presumably more frequent. Thus although birds within an order or sub-order are usually parasitized by related mallophagan faunas which have presumably evolved on these orders the origins of related mallophagan faunas on different orders are difficult to assess. In the affinities between mallophagan faunas of the birds¹, a diagram meant to demonstrate factually these affinities and not necessarily to suggest affinities between the host groups, the similarity of the mallophagan faunas of the Procellariiformes and those of the Charadriiformes, for example, may show no more than an ecological relationship members of both orders living in the same environment. The fact that in general the species on the two orders are now well differentiated suggests that if this distribution is due to secondary infestations, it could not have been recent and supports the theory that establishment on a new host took place mainly in the early days of the evolution of host and parasite.

Mr P F Mattingly (British Museum, Natural History) stated that the complete restriction of human and simian malaria to anopheline vectors suggests that this group may originally have evolved

mainly as feeders on mammals. Bird malaria on the other hand was carried exclusively by culicine mosquitoes which might thus have originated as feeders on birds. The fact that human filariasis was carried by both anopheline and culicine mosquitoes suggested that it may have entered the system comparatively recently. The comparative physiology and biochemistry of blood meal utilization in mosquitoes had been very inadequately studied. This was a particularly promising field for research which might throw light on many problems.

Prof G C Varley (Oxford) believed that host specificity needed careful definition. Not only must both host and parasite be accurately identified but also those cases where a parasite can only complete part of its development must be distinguished. Published lists unfortunately often gave equal emphasis to unique records and to regular parasite relationships.

Prof Baer considered that the relation between a parasite and a group of hosts related by ecology or phylogeny was biologically significant, whereas the relation between one parasite and one host meant little.

Prof Baer believed that the biochemical approach to species determination should be encouraged in the way that Dr Wright was applying it to snails, and that isolated proteins and carbohydrate fractions from hosts and parasites might be used.

Dr J Sandground (New York) described his experience with onchocerciasis in Guatemala and in the Gold Coast and referred to his demonstration some twenty years ago that the parasites in the New and Old World were identical. He believed that much more work remained to be done in onchocerciasis before the infection could be understood adequately and before control would be easy.

WILLIAM KERSHAW

¹ Clay, T. First Symposium on Host Specificity among Parasites of Vertebrates. Neuchâtel 120 (1957).

ANIMAL CLOCKS

THE significance of rhythmic activities in animal physiology is becoming increasingly evident. For this reason the symposium on 'animal clocks' held in York on September 4, by Section D (Zoology) of the British Association for the Advancement of Science, was well timed. During the morning sessions Dr L Harrison Matthews, section president, was in the chair.

The first speaker, Prof F A Brown, jun (North western University) described recent research carried out in his laboratory. In 1948 he had established that the frequency of the rhythm of colour change in fiddler crabs was independent of temperature over a 20 deg C range. Later it was shown that this 'indicator' process was itself regulated by a more fundamental rhythmic element and that two control centres were involved. Although the concept of an autonomous clock is retained by most investigators Prof Brown now postulated that the periodisms which comprise basic biological clock systems are imposed by environmental changes even in conditions hitherto presumed to be constant. This hypothesis he supported by a detailed statistical analysis of data obtained by means of an automatic recording respirometer from organisms as unrelated as fiddler crabs and potatoes which

had been hermetically sealed in constant conditions including pressure for several days at a time.

Although other speakers did not agree with this view, all must have been stimulated to look more carefully at their own data. Unfortunately, it has so far proved almost impossible to devise a really critical experiment that will differentiate between an innate clock mechanism and one derived from exogenous sources, since it appears possible by analogy, to alter the position of the hands of the clock relative to the works. Just as it is difficult to conceive of a distance judging mechanism independent of space, so a clock system presumably requires some fixed points of reference.

In a paper on the influence of the environment on the cyclical biting behaviour of mosquitoes Dr A J Haddow (director of the East African Virus Research Institute) pointed out that every species so far studied has shown a 24 hr periodicity. In some, this is merely nocturnal or diurnal but in others most of the activity is confined to one or two short and precisely delimited periods. These while usually very constant for a given environment may be entirely different in another. Further they may show very striking differences at different levels.

above ground within the same environment. At present, no single explanation fits all known cases.

The complexity of natural internal timing mechanisms was illustrated by Dr Janet Harker (Department of Zoology, Cambridge), who described a series of elegant experiments by which she had been able to slow down part of the mechanism. In cockroaches a hormone has now been discovered which increases the activity of the animal, and which is secreted in strict 24-hr cycles. This hormonal clock can be stopped by chilling the secretory cells while the rest of the body is kept at a normal temperature, and when this is done a second clock associated with the nervous system is revealed. When the secretory clock is allowed to start again, provided it has not got too far out of time with the nervous clock, it is reset by the latter. However, in normal conditions the secretory clock acts as the master-clock, and since, like the nervous clock, it is not affected by sudden short changes in light conditions, the diurnal activity rhythm of the animal is little upset by such changes. This may be important, in Nature, for animals which experience short periods of darkness during the day (for example, by going under a stone), or light at night (for example, bright moonlight or artificial light). If these minor changes in light conditions were to reset the clock, the animal would soon get out of time with day and night. On the other hand, the fact that the secretory cycle can be affected by the nervous system clock towards the beginning and end of the dark period, and the activity rhythm can be immediately reset at these times, suggests a way in which the animal can allow for changing day-length.

The morning session closed with an account by Dr C S Pittendrigh (Princeton University) of a coupled oscillator model for studying the behaviour of the innate circadian ('about a day') rhythm of cells and organisms. Its further utility was noted in explaining recent discoveries in thermo- and photoperiodism. Studies on the effects of single perturbations of the oscillator by light or temperature reflect the behaviour of a common underlying biological mechanism. In some organisms, the phase of a rhythm can be shifted by a light signal as short as 1/2,000 sec. It was concluded that the cell must comprise many diverse circadian oscillations, and disturbances of their mutual phase relations may lead to physiological stress or damage.

Prof G C Varley (University of Oxford) presided over the afternoon sessions in which plant clocks were described by Dr M B Wilkins (King's College, London), with special reference to his own observations on excised leaves of *Bryophyllum fedtschenkoi* placed in continuous darkness and temperature. These maintain a 22.4-hr rhythm in the rate of carbon dioxide output for several days. The clock controlling the rhythm is extremely sensitive to changes in external conditions of temperature and illumination to which the leaves are subjected. Continuous illumination inhibits the clock which recommences when darkness is restored, the phase of the subsequent rhythm being determined by the time at which the light was extinguished. The phase of a rhythm persisting in darkness is reset by applying a 3-hr light treatment to the leaves between the peaks but not at the crest of a peak. Red light inhibits the rhythm, but blue light has no effect. A rhythm can be induced in illuminated leaves by reducing the light intensity by at least 80 per cent, and it was later found that the phase of such a rhythm could

be reset by applying a 3-hr dark treatment at the crest of a peak, but not between the peaks. The rhythm is inhibited when the tissue is placed in an atmosphere of nitrogen and its period varies with temperature. It is apparently unaffected by solutions of mitotic inhibitors such as phenylurethane and colchicine.

Dr C G Butler (head of the Bee Research Department, Rothamsted Experimental Station) then surveyed the development of knowledge regarding the time-sense of the honey-bee since its fortuitous discovery in June 1905 by the famous naturalist, A Forel. It was not until more than twenty years later that Ingeborg Beling carried out her extensive experiments in which bees were trained to visit a feeding place at different times of day under constant conditions. Later workers have since obtained data which support the view that a honey-bee's time sense depends in some way upon metabolic rhythm, since it can be speeded up or slowed down by the use of appropriate drugs. Finally, bees trained in Paris to visit a feeding dish at a definite time each day have continued to maintain their feeding schedule under constant conditions after being flown to New York, thus demonstrating that the time sense of the insects is endogenous.

Dr A J Marshall (St Bartholomew's Hospital Medical College) introduced an exotic note when he discussed the possible influence of the internal rhythm of reproduction in the control of trans-equatorial migration of birds flying between Europe and Africa and Tasmania and the Aleutian Islands. He pointed out that although something akin to a clock was involved, it had to be likened, nevertheless, to a somewhat imprecise, chain-store variety in that it had to be 'corrected' by environmental factors at least once during each annual cycle. Work carried out by Dr D L Serventy and himself had made it clear that even when shearwater petrels (that breed on islands off the Southern Australian coast) were kept captive under widely varying conditions and day-length, they nevertheless came to breeding condition at the same time as the free birds that had made their astonishing circum-Pacific, trans-equatorial journey.

Next, Dr J L Cloudsley-Thompson (King's College, London) discussed the synchronization of animal clocks in general, pointing out that endogenous rhythms are frequently correlated with environmental changes although they are not necessarily a direct response to them. Thus, if cockroaches are subjected to alternating 12 hr periods of light and darkness, locomotion may actually begin shortly before the light is extinguished. We have therefore the concept of an innate rhythm synchronized by changes in environmental factors such as light, temperature and humidity which should be regarded as 'clues' rather than stimuli.

The field cricket, *Gryllus campestris*, placed in an actograph apparatus, can be seen to be active in the day-time with a rhythm that is endogenous and independent of temperature. When the 24 hr periodicity has died away, however, after weeks in constant conditions, it can be re-established by a single exposure to light or by a return to higher temperatures after a period at 5° C. The cricket's clock can be reset in this way, even when activity is completely suppressed by drought.

Although light intensity is the chief factor by which animal clocks are synchronized, regular temperature changes can also be effective. When night-

active animals such as white rats, deer mice and millipedes are placed in constant light, it is found that their rhythms tend to be delayed while those of day-active forms are accelerated. The converse often occurs in constant darkness. In this way, diurnal rhythms can be shifted as the days lengthen or draw in according to the season. Synchronization with environmental changes cannot be achieved both at dawn and dusk as the time of each of these is altering. The clue tends to be dusk in the case of nocturnal forms, dawn in that of day-active animals.

The symposium concluded with a paper by Dr Mary C. Lobban (Department of Physiology, Cambridge) who said that in most communities man's activities are geared to a 24-hr day. The clock which governs this periodicity is often difficult to reset, as those who travel great distances at the speed of modern aircraft well know. It is, however, possible to separate different physiological rhythms and to get them adapted to different degrees and at different rates. Recent work with indigenous Arctic peoples—Indians and Eskimos—indicates that environmental factors may influence physiological diurnal rhythms more than was hitherto thought. Temperature and physical exertion may well exert a profound effect in deciding whether an individual will become adapted successfully to a new time routine and even whether he will become adapted at all.

Both sessions were followed by lively discussions which served to emphasize the diversity of approaches to be found among workers on rhythmic phenomena. For example, Dr William Goody (London) noted that no definition of a clock had been given by any speaker; the papers were concerned with the forms of rhythms and their possible causes. The definition of a clock as some form of regularly repeated natural phenomenon implies the presence of an observer and each speaker had mentioned only those rhythmic processes which he had selected to be clock forms for him. Since it is possible to study innumerable time systems from the human time sense to the 'tides' inside single cells, the multiplicity and interaction of the mechanisms are evident. It might be wise to investigate organisms with nervous systems separ-

ately from plants. Though the cycles of some systems are related to the great events of astronomical observation, they will be modified by all other systems, perhaps giving rise to circadian cycles rather than exact 24 hr cycles. Final or simple rhythms of an organism, including those described, must represent the average effect of all the possible clock forms observable by biologists in that organism. Too much analytical work on a system in isolation might obscure the general principles which may one day explain the mysteries of the human time sense.

Mr P. F. Mattingly (London) pointed out that the study of arthropod-borne virus diseases had made it abundantly clear, despite the isolation of the virus in an intracellular environment, that its evolution has been conditioned by external factors no less than has that of the host. The integration of cyclical rhythms in animals is not merely a physiological problem but forms the basis of organic evolution itself.

Dr E. T. Burt (Newcastle upon Tyne) inquired whether different rhythmic activities might not profitably be regarded as portions of a continuous spectrum, but Dr Cloudsley Thompson replied that he believed there to be a hierarchy of mutually regulatory rhythmic patterns. Another speaker suggested that perhaps too much work had been devoted to arthropods since inter-cellular transference of hormones is not the same in these animals as in vertebrates. (An instance is afforded by the sex hormones, the inter-cellular movement of which is so much reduced among insects that mosaic individuals can be formed.)

Dr Sydney Smith (Cambridge) emphasized the dangers of lumping together a number of unrelated phenomena under ill-defined names such as rhythmic, or cellular activity—a trait as seductive as it is misleading. Finally, Dr Harker pointed out that under conditions of desiccation the distribution of hormones within the insect body becomes blocked owing to reduction in the amount of blood. This would explain the phenomenon observed in the field cricket.

J. L. CLOUDSLEY THOMPSON

THE CONTINUED PROGRESS OF SATELLITE 1958 δ_2 (SPUTNIK III)

By B. R. MAY and D. E. SMITH

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Ditton Park, Slough, Bucks

THE progress of the third Russian Earth satellite 1958 δ_2 , from launching on May 15, 1958, until October 31, has already been reviewed by D. G. King-Holmes.¹ From the latter date the responsibility of following the progress of the satellite and predicting its flight was taken over by the Radio Research Station, Slough.

For prediction purposes a period-time curve has been plotted, using radio and optical observations, and this is shown in Fig. 1. It is noticeable that the slope of the curve has been decreasing steadily throughout the period December–April. November 1 to December 20, 1958, of change of period was about

from December 20 to February 28 about 1.17 sec/day, and from February 28 to March 31 about 1.11 sec/day. This decrease in slope which arises from a lessening of atmospheric drag is very probably a consequence of the fact that the southerly latitude of perigee, the point in the orbit at which the satellite experiences the greatest atmospheric drag, has been increasing since October 24, the date on which it crossed the equator. This movement has resulted in a not-increase in the height of perigee above the Earth's surface since the rate at which the Earth's radius has been decreasing with time has been greater than the rate at which distance of the orbit has been d.

Table 1 ORBITAL ELEMENTS FOR SATELLITE 1958₄

| Date | Nodal period of revolution (min) | Semi major axis (km) | Eccentricity | Perigee distance (km) | Apogee distance (km) | Orbital inclination (deg) | Rate of rotation of orbital plane (deg/day) | Argument of perigee (deg) |
|----------|----------------------------------|----------------------|--------------|-----------------------|----------------------|---------------------------|---|---------------------------|
| 1958 | | | | | | | | |
| Nov 1 00 | 103 358 | 7205 8 | 0 0070 | 6585 7 | 8003 3 | 65 16 | 2 67 | 356 |
| | | | 0 0068 | 6580 4 | 8002 2 | | | |
| Dec 1 00 | 102 664 | 7203 18 | 0 0070 | 6587 3 | 7939 0 | 65 15 | 2 71 | 344 |
| | | | 0 0020 | 6588 6 | 7937 7 | | | |
| 1959 | | | | | | | | |
| Jan 1 00 | 102 013 | 7232 6 | 0 0804 | 6586 2 | 7870 0 | 65 14 | 2 74 | 331 |
| | | | 0 0801 | 6587 0 | 7877 3 | | | |
| Feb 1 00 | 101 407 | 7203 0 | 0 0850 | 6585 1 | 7822 7 | 65 13 | 2 78 | 310 |
| | | | 0 0856 | 6587 3 | 7820 4 | | | |
| Mar 1 00 | 100 791 | 7174 8 | 0 0823 | 6584 0 | 7765 2 | 65 13 | 2 82 | 308 |
| | | | 0 0920 | 6586 6 | 7763 0 | | | |
| Apr 1 00 | 100 202 | 7147 0 | 0 0780 | 6582 0 | 7711 3 | 65 12 | 2 84 | 298 |
| | | | 0 0785 | 6585 8 | 7708 3 | | | |
| May 1 00 | 99 647 | 7120 0 | 0 0757 | 6581 8 | 7660 1 | 65 11 | 2 88 | 286 |
| | | | 0 0752 | 6585 1 | 7656 8 | | | |
| Accuracy | ± 0.005 | ± 0.2 | ± 0.0005 | ± 1.0 | ± 1.0 | ± 0.01 | ± 0.02 | ± 1.0 |

Note Upper figures in columns 4, 5 and 6 were obtained assuming a scale height of 55.6 km (30 nautical miles), the lower figures correspond to a value of 37.1 km (20 nautical miles)

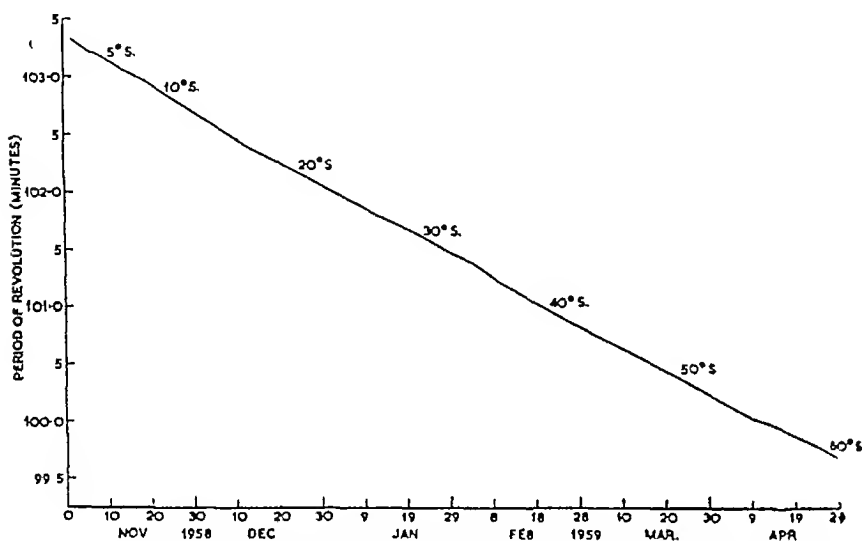


Fig 1 Nodal period of revolution of satellite 1958₄ (*Sputnik III*) Numbers on curve indicate latitude of perigee

of atmospheric drag follows from this increase in height. Some idea of the increase in perigee height with increasing southerly latitude can be obtained from the following figures: at latitudes 0°, 40° S and 60° S, the perigee heights were 210.9, 216.4 and 222.5 km, respectively, for a scale height of some 46 km (25 nautical miles). It is interesting to note that since March 25, 1959, the perigee of *Sputnik III* has been at a greater latitude than any other established satellite.

Superimposed upon the smooth curve are numerous irregularities implying changes in the effective cross-sectional area of the satellite, or as is more likely, irregularities in atmospheric density at perigee. Suggestions have been made as to the causes of those irregularities—discontinuities of density at the boundary of the light and dark sides of the Earth², solar disturbances³—though a discontinuity at about 28° S, corresponding to one detected at about 28° N by King-Hele⁴, has failed to make an appearance.

The irregularities in the period-time curve have made it difficult to forecast with any certainty the date of descent of the satellite. During December 1958 a theoretical date of descent of about December 15, 1959, was indicated, but at the present time the expected date is nearer January 5, 1960.

As an object for optical observations, the satellite has been comparatively faint since October 1958 due to its height, which has not been less than 460 km in the latitude of Great Britain. On only a very few occasions has it been observed visually at stellar magnitudes brighter than +3, and most observations have been made at magnitudes +5 to +7. During May when the satellite was visible two and three times each night, its brightness remained fairly constant (though of an unpredictable magnitude) on any one transit, in contrast with the flashing nature of its appearance earlier this year. The satellite is still transmitting on a frequency of between 20.004 and 20.005 Mc/s, though it has

been reported from Australia⁵ that the satellite does not now transmit a modulated signal when it is in the Earth's shadow. Radio observers in Great Britain have had little opportunity of verifying this since, on transits within radio-range, the satellite has not been in the Earth's shadow since April 28.

The initial elements of the orbit of the satellite, for epoch May 15.3, 1958, were: nodal period, 105.975 min; eccentricity, 0.111; perigee height, 226 km; apogee height, 1,879 km; and argument of perigee, 58°. The elements for the period November 1, 1958–May 1, 1959, are given in Table 1. The nodal periods have been taken from the period-time curve used for prediction purposes. The semi-major axis, eccentricity, perigee distance, apogee distance and the rate of rotation of the orbital plane have been calculated from the periods. The orbital inclination has been obtained by comparison with *Sputnik III* rocket (1958₁), and the argument of perigee from a mean curve plotted using values from various sources including the Smithsonian Astrophysical Observatory. As the value of the scale height at heights in the region of the perigee is uncertain, the eccentricity and the perigee and apogee distances have been calculated using two values of scale heights, 55.6 km

and 37.1 km, the limits within which the true value is thought to be

We should like to take this opportunity of thanking all those who have sent us observations on satellite 1958₁, both radio and optical

The work described above was carried out as part of the programme of the Radio Research Board and is published by permission of the Director of Radio

Research of the Department of Scientific and Industrial Research.

* King Hele D G *Nature* 182 1409 (1958)

* Groves G V *Nature* 182 1633 (1958)

* Nonweiler T R *Nature* 182 468 (1958)

* King Hele D G and Walker D M G *Nature* 182 800 (1958)

* Munro G H *Nature* 182 1540 (1959)

* King Hele D G and Walker D M C *J Brit Interplan Soc* 17 2 (1959-60)

OBITUARY

Sir Ian Heilbron, DSO, FRS

SIR IAN HEILBRON died in London at the age of seventy two, following a short illness on September 14. He was born in Glasgow in 1880 was educated at the High School and graduated from the Royal Technical College there. He had as he was fond of recalling decided upon chemistry as his career against family advice but his choice was soon confirmed under the inspiring guidance of the late Prof G G Henderson, for whom Heilbron acquired a life long admiration. It was at Henderson's suggestion that Heilbron spent a two years tenure of a Carnegie fellowship from 1900 with Hantzsch in Leipzig. Here, a close companion of the late Prof R Robson, Heilbron developed a lasting interest in the application of spectroscopy to structural organic chemistry, and this experience seems to have led to the emergence of one of his marked characteristics, namely, a constant readiness to extract all possible assistance in the study of natural compounds by applying new physical techniques such as molecular distillation, chromatography and countercurrent distribution. However, his academic career at the Royal Technical College Glasgow, where he was lecturer until 1914 and where he worked in purely synthetic organic chemistry, was interrupted by the First World War, in which he served with great distinction, eventually as assistant director of supplies in Salonika, and was awarded the DSO. After the War, he spent a short time with the then newly formed British Dyestuffs Corporation but soon embarked upon a brilliant academic career in which he successively held professorial chairs in Glasgow (1919-20), Liverpool (1920-33), Manchester (1933-39) and London (1938-49).

Heilbron's great and pioneering contributions to the study of natural compounds commenced in Liverpool. His early studies on the constituents of fish liver oils notably aqualone, led in turn to his introduction into Britain of micro methods to further his many investigations on the fat soluble vitamins A and D, with which was associated in due course still wider exploratory work on steroids and carotenoids generally. It is perhaps ironical that he himself rarely shared fully in the culminating synthetic triumphs which were often based on the difficult and arduous work which he had long ago instituted with such conspicuous acumen, courage and determination. However, outstanding as were his many direct contributions to knowledge as reflected for example, in some three hundred original publications, and his bringing into being with H M Bunbury the "Dictionary of Organic Compounds", his indirect contributions to chemistry in general

were perhaps unequalled. Repeatedly he equipped laboratories with unsurpassed vision so that each is now a thriving centre of research. Above all, he inspired a host of younger chemists many of whom now occupy leading positions in universities or industrial life in Britain and abroad.

The Second World War naturally brought Heilbron again to the service of his country ultimately as scientific adviser to the Ministry of Production, where he played an important part in introducing DDT, and as a result was knighted in 1946. All these duties discharged with a precision and penetration which constantly surprised his associates were assumed however, in addition to his academic work, which went on at an accelerated rather than a reduced rate and led later to a new spate of publications on such different topics as the chemistry of the steroids, acetylenic compounds and penicillin. Moreover, by this time his unique experience was widely sought in such capacities as chairman of the Colonial Insecticides Committee, as a member of the Advisory Council of the Royal Military College of Science and of the Advisory Council to the Committee of the Privy Council for Scientific and Industrial Research, and in reorganizing the International Union of Pure and Applied Chemistry. While in the midst of these activities he relinquished his academic post at the Imperial College of Science and Technology, London, to become director of the Brewing Industry Research Foundation (1949-58) which owes so much to his versatility, energy and genius.

Heilbron's scientific life began when the study of chemistry and particularly of natural compounds was scarcely more than an academic pursuit, but he lived to see many of the methods and techniques which he had sponsored become general tools of research and many of his research projects develop into substantial segments of chemical industry. It is not surprising therefore, that he received wide recognition in the form of numerous awards and honorary degrees, both in Britain and overseas. Any mere catalogue of these achievements and distinctions could, however, convey little real impression of his great qualities as a man. Lucidity, constructive imagination and an almost intuitive insight into the complexities of scientific effort were among many similar characteristics which were almost immediately apparent to all with whom he came into contact. These somewhat closer, as in the departments which he directed, came also to recognize his generosity, scrupulous fairness and invariable feeling of fatherly concern for even the most junior members of his staff. To those privileged to know him still better his quick sense of humour, keen appreciation of the arts and above all, the spontaneous assured wisdom

with which his lively mind abounded, made him an unforgettable and delightful personality. He is survived by two sons, but the sudden death of his wife, Elda, in 1954 was a sad blow which affected him far more deeply than many who knew him may have realized.

A. H. COOK

My close friendship with Ian Heilbron dates from near the end of the First World War and arose from many common interests and activities. These included consultation with industrial research groups, membership of committees under government auspices and tenure at different times of the chairs of organic chemistry at the Universities of Liverpool and Manchester. Heilbron was, of course, an illustrious organic chemist whose reputation was world-wide and whose original work could justly be described as pioneering. As Dr Cook has pointed out, he did not always enjoy the full fruits of his labours. Others stood on his shoulders and were thus enabled to reach higher. A part of his work was in fields of potential commercial importance and doubtless for this reason some of his discoveries were impatiently exploited.

Heilbron had much courage of his very firmly held convictions, and did not fail in finding words to express them. He caused many a breath of fresh air to pass over the conference tables, especially when he thought progress was too slow or where he detected evidence of red-tape mentality.

His contributions in the Second World War were extremely valuable. If he had not been a scientist he could have become a most successful business man and his executive activity was characterized by promptitude and efficiency. Every laboratory which came under his charge was greatly improved, not merely by new construction but also by better considered organization of existing facilities. His attention to detail in these connexions was very characteristic. As an investigator he also excelled in planning the campaign and was instrumental in the introduction of important novel techniques.

In private life his friends found him quite charming, an excellent host and a greatly appreciated guest. He was fastidious and had a most sensitive appreciation of the fine arts. Above all he was a warm-hearted, generous man who devoted himself to public service and to the progress of science.

R. ROBINSON

NEWS and VIEWS

Astronomy at St Andrews Prof E F Freundlich

PROF E FINLAY FREUNDLICH, who four years ago retired from the Napier chair of astronomy at St Andrews, relinquishes now also his directorship of the University Observatory. Prof Freundlich started his astronomical life some forty years ago at the Berlin Observatory. Much of his work was determined by an early association with Einstein which made him pursue the question of observational tests of the theory of relativity. In order to investigate the predicted red-shift of spectrum lines, Freundlich created in the early 'twenties at Potsdam the well-known Einstein Institute with its tower telescope. The new solar installation, among the best of the time, produced new observational evidence on the 'limb' effect, and also important pioneer work on line profiles. Freundlich's main contribution to the field of relativity astronomy is undoubtedly his eclipse work on the deflection of light at the Sun's limb. His results of 1929 are still among the best obtained on this extremely difficult problem, and his conclusion that the observed deflection exceeds the theoretical value is now generally accepted. Prof Freundlich left Germany in 1933 and after a few years in Istanbul and Prague settled in St Andrews in 1939. Here he became interested in the design of a large Schmidt-Cassegrain telescope. A 19-in pilot model was successfully set up in 1950, and the main parts of the full-size 37 in telescope are now nearing completion. In the University, Freundlich instituted an honours course in astronomy, in which he paid particular attention to his favourite subject of celestial mechanics. It is pleasing to know that when Prof Freundlich returns to his native Rhineland, an association with the University of Mainz will allow him to retain an active interest in astronomy.

Prof D W N Stibbs

DR D W N STIBBS succeeds Prof E Finlay Freundlich in the Napier chair of astronomy at

St Andrews. A graduate of the University of Sydney in physics in 1942, Dr Stibbs gained his early astronomical training at the Commonwealth Observatory under the Astronomer Royal, Dr R v d R Woolley, afterwards they were co-authors of the well known monograph "The Outer Layers of a Star". Engaged as lecturer in mathematical physics at Armidale in 1942, Dr Stibbs was seconded from there to work for the Royal Australian Air Force on the influence of the ionosphere on radio direction-finding. He returned to Canberra after the War and was appointed Radcliffe Travelling Fellow in Astronomy in 1951, and worked first at the Radcliffe Observatory, Pretoria, and afterwards at Oxford where he gained his D Phil in 1954. In 1955 he joined the Theoretical Physics Division at the Atomic Weapons Research Establishment, Aldermaston, where he has been engaged in theoretical research on the interaction between radiation and matter under stellar conditions. He is probably best known for his fundamental work on the motions of the southern galactic Cepheids as determined from his own consummately planned observations at the Radcliffe Observatory. In a discussion of the motion of these stars and of those earlier observed by Joy at Mt Wilson, Dr Stibbs revealed a marked discrepancy in the neighbourhood of the galactic centre between the rotation of the Cepheid System and the neutral hydrogen clouds.

California Institute of Technology

Dr Richard P Feynman

DR RICHARD P FEYNMAN has been appointed Richard Chaco Tolman professor of theoretical physics at the California Institute of Technology. The trustees created the new chair in physics in honour of the memory of the late Dr Richard Tolman, an internationally known theoretical physicist and chemist who for years was dean of graduate studies at the Institute. Dr Feynman is considered to be one of the world's outstanding theoretical physicists for his contributions to the understanding of atomic

structures and quantum mechanics. Recently, in collaboration with Dr Murray Gell Mann, of the California Institute of Technology, he developed a theory of weak interactions, which govern the electron and positron in radioactivity. Dr Feynman graduated from the Massachusetts Institute of Technology and received his Ph.D. at Princeton University. As a scientist with the Manhattan Project, he is credited with making important contributions toward developing the atomic bomb. In 1954 he won the Albert Einstein award, one of America's highest scientific honours.

Ministry of Supply Director of Materials Research and Development

THE retirement of Dr H. Sutton in August from his present post as director of Materials Research and Development (Air) marks the end of the full time service of a most distinguished metallurgist who has given the whole of his professional life to the public service. Dr Sutton was educated at King's School, Worcester, took his first degree in chemistry at the University of Manchester, later the degree of M.Sc. and in 1935 he received the degree of D.Sc. In the First World War he served as research assistant to Prof. C. A. Edwards, who was then the regional controller and adviser in Manchester to the Ministry of Munitions. His departure therefore severs one of the rare personal links of the present Ministry of Supply with one of its predecessors, the Ministry of Munitions. Joining the Royal Aircraft Establishment at Farnborough in 1918 he was appointed the head of its Department of Metallurgy. In 1925 a post he retained until 1943 when he was transferred to the headquarters post which he has built up largely through his own personal and professional qualities, to the important position it now holds in the field of British metallurgy, especially in relation to aeronautics.

Dr Sutton was a pioneer in the work on the formulation and fabrication of light metal alloys without which aircraft in their present form would not be known. He was also early in foreseeing some of the special dangers to which they are subject in relation to crack formation, brittleness and the like. In later years, while never discarding his first interests in aluminium based alloys, he has been forward in promoting work on titanium and other possible more novel metals. At the same time as the scope of his duties has widened, he has seen to it that much attention has been given to the non-metallic materials that play so important a part in the construction of modern aircraft. A prolific author of papers on metallurgical subjects published in most of the metallurgical journals, he has been honoured during his career by the award of the Simms Gold Medal and the Silver Medal of the Royal Aeronautical Society. He is a Fellow of the Royal Aeronautical Society, a founder Fellow of the Institution of Metallurgists and a member of all the relevant professional societies. His professional advice has been widely sought by committees in government and industry and he has been unsparing in forwarding those subjects to which he has devoted his life.

The Council for Nature

At the recent annual general meeting of the Council for Nature the following resolutions were passed:

"The Council for Nature fully shares the great concern of naturalists in Britain at the threats to the remaining undeveloped areas of the country's coast

line by industrial and other developments and considers that the importance of these areas both for scientific study and for the conservation of wild life no less than for the preservation of amenity and opportunities for recreation calls for a halt to the process of spoliation. The Council therefore urges that a meeting of the national bodies interested in the matter should be convened by the Nature Conservancy at an early date with a view to pressing for vigorous action including a review of the principles at present governing the siting of nuclear power stations.

"The Council for Nature welcomes the public spirited action of a large firm of manufacturers in withdrawing recently their supplies of arsenical spray. The Council, while recognizing the need for the use of toxic sprays (subject to proper safeguards) urges the Government to control the wholesale application of agricultural sprays the cumulative effect of which is still unknown, but which have been, or may be damaging to so many plants and animals, including such useful insects as bees. The Council urges further that the use of arsenical sprays should be prohibited or restricted forthwith, and that the Government and its agencies should give high priority to the research needed into the long term effect of toxic sprays on the complex life of the countryside."

Canadian Institute of Oceanography

THE Canadian Government as well as the universities are showing rapidly growing interest in the scientific study of the oceans. An annual grant of 90,000 dollars to Dalhousie University was made by the National Research Council of Canada for the establishment of an Institute within the University to teach and promote research (see *Nature*, 183, 1101, 1959). The Department of Mines and Technical Surveys has now announced its intention to set up a new three-million dollar laboratory in Bedford Basin at the head of Halifax Harbour only a few miles from the University. The project means the building up in the neighbourhood of Halifax and Dartmouth of a strong centre for marine sciences. It will include the Atlantic and sub-Arctic sections of the Canadian Hydrographic Service, the oceanographers, hydrographers and geologists who work in the Arctic and the Atlantic Oceanographical Group of the Fisheries Research Board. Ten new ships to serve them are already being planned and the first, the C.G.S. *Hudson* costing seven million dollars is expected to be commissioned in 1961. The main purpose of the new laboratory which will be called the Bedford Institute of Oceanography, is to study the physics of the water and the sea bed, but provision is made for close co-operation and liaison among all aspects of the subject and with the rapidly growing effort on the Pacific coast and work on the Great Lakes. In making the announcement the Ministry of Mines and Technical Surveys stressed the importance of a better understanding of the oceans to science, defence, commerce, and development of the country's resources.

Reconstruction of Brazilian Library

AN appeal for help to reconstruct the library of the Brazilian Centre for Physics Research, damaged in a recent fire, has been launched by Unesco and the International Atomic Energy Agency. At a meeting of Unesco's Executive Board in Paris in June Prof. P. de B. Carniero stated that the Centre's collection of works on nuclear physics and higher mathematics, the only one of its kind in Latin America, has been

almost entirely destroyed. The Executive Board responded to the appeal by recommending a number of measures to provide international aid from Unesco, the International Atomic Energy Agency and the U.N. Technical Assistance Administration. The library has been added to the list of projects for which Unesco gift coupons may be given. Universities, libraries, technical institutes, non-government organizations, and governments of Unesco's Member States have also been asked to contribute. Organizations or individuals wishing to help in the restoration of the library may write to Centro Brasileiro de Pesquisas Físicas, 71 avenida Venâncio Braus, Rio de Janeiro, Brazil. All offers of books, micro films, extracts or other documentation should be made directly to the Centre. Gifts of money may be sent in the form of Unesco Gift Coupons, about which information may be obtained from the Public Liaison Division, Unesco, Place de Fontenay, Paris 70.

Grants for U.K. Students

THE 1959 Grants Year Book, the fourth to be issued by the National Union of Students (1959 Grants Year Book. Local Education Authority Awards to Students. Pp. 107. London: National Union of Students, 1959. 2s. 6d.), comprises a detailed guide to the values of awards paid by the Ministry of Education and the Local Education Authorities to students taking courses of higher education and to the regulations governing those awards. These details are arranged by counties and county boroughs and there are appended notes on university and technical college awards, on training college awards, postgraduate awards of the Department of Scientific and Industrial Research, and other bodies. An account of the new system recently introduced in Northern Ireland is included, and there is a general survey of awards, 1958-59, based on information received since November 1958. An introduction to the Year Book urges the importance of further expansion of the teacher training colleges and stresses the need for a national scale of minor awards assessed on the same basis and principles as the major awards to eliminate the present wide variation in minor awards for technical and similar courses. Attention is directed to the wide variations between the local education authorities in number of awards shown by the Ministry of Education's published statistics.

Research in Dairying

It is not often realized that the milk produced in the United Kingdom nowadays amounts to about 2,200 million gallons a year and is worth about £1 million a day. An industry of such magnitude and importance surely deserves a first-class research service. The fact that it has got such a service can be seen from the annual report of the National Institute for Research in Dairying for 1958 (pp. 154. Shinfield: National Institute for Research in Dairying, University of Reading, 1959. 4s.). It is clear from the report that the Institute is making a very thorough study of the scientific principles on which the art of dairying is based, by doing research work of a high quality on fundamental problems, such as digestion and metabolism in the ruminant, the biochemistry and physiology of milk secretion, and also on problems of an immediately practical nature such as those concerned with the growing of crops for feeding dairy cattle, the milking technique itself and many technical and engineering problems

associated with the handling and processing of milk and the manufacture of milk products. The report contains an informative description of the work that is being done in each department of the Institute, and some of the more significant of the recent findings are summarized in a brief outline which gives information on about thirty of the many different items under investigation. A well-deserved tribute is paid to Prof. H. D. Kay, who retired last year after being director of the Institute for more than twenty-five years, and also to the Earl of Iveagh, who has resigned from the board after a long period of service in which he did so much for the welfare of the Institute and its staff. The report includes a detailed list of 182 papers that were published in the period under review.

Mathematical Games

AMONG the many aspects of Japanese culture that have recently engaged the interest of Americans is 'origami', the ancient Japanese art of paper-folding. Several books on the subject are now available in English, an origami workshop flourishes in Manhattan and the country's first paper-folding exhibit was open to the public at Cooper Union's Museum for the Arts of Decoration in New York (*Scientific American*, 201, No. 1, July 1959).

The origins of origami are lost in early Oriental history. Folded-paper birds appear as kimono decorations in eighteenth-century Japanese prints but the art is many centuries older in both China and Japan. At one time it was considered an accomplishment of refined Japanese ladies, now its chief practitioners seem to be goisha girls and Japanese children who learn it in school. During the past twenty years there has been a marked upsurge of interest in origami in Spain and South America. Traditionally, origami is the art of folding realistic animals, birds, fish and other objects from a single sheet of paper, without cutting, pasting or decorating. The attraction of origami lies in the extraordinary realism that can be obtained with nothing more than a square of paper and pair of deft hands. A sheet is folded along geometrical lines. Suddenly it is transformed into a delicate piece of miniature semi-abstract sculpture of considerable beauty.

In view of the geometrical aspect of paper folding, it is not surprising that many mathematicians have been fascinated by this art. Lewis Carroll, for example, was an enthusiastic paper-folder. The literature of recreational mathematics includes many booklets and articles on folded-paper models, including those curious toys called flexagons. The folding of regular polygons, though not part of classic origami, is a challenging classroom exercise. The equilateral triangle, square, hexagon and octagon are quite easy to fold, but the pentagon offers special difficulties. Paper can also be folded to produce tangents that have as their envelope various low-order curves. The parabola is particularly easy to demonstrate. Closely related to this folding procedure an interesting problem in elementary calculus can be demonstrated. The most remarkable of all origami constructions is, however, the bird that flaps its wings. A number of origami animals have action features: a fish that opens its mouth, a frog that hops when its back is stroked, and so on.

International Combustion Symposium

THE report of the Seventh Symposium (International) on Combustion, the first of the Inter-

national Combustion Symposia to be held outside the United States has been published (Pp xxvi+959 London Butterworths Scientific Publications 1959 22s) It contains 124 original papers presented during August 29-September 3, 1958, at Oxford For who have a serious interest in combustion will fail to profit from a study of its pages The largest of the eleven groups of papers concerns the chemistry of combustion reactions and there are three important groups devoted respectively to deflagration, detonation and combustion in flowing systems Smaller sections are concerned with spectroscopy, ionization and turbulence in flames, the last containing particularly welcome contributions to a difficult and until recently, neglected subject The section on ignition and limits of inflammability attracted mainly papers on the former subject, while that on the interaction of flames with surfaces proves to be a repository for papers on a variety of loosely related topics The section on special fuels is disappointingly short and the final group of papers on instrumentation is characteristically miscellaneous

The editors and publishers are to be commended on at least two counts For the first time the volume appeared with a delay of little more than six months after the meetings Furthermore, there is for the first time a rational and almost complete record of the discussions One suggestion still remaining to be implemented is that the papers should be provided with a uniform type of summary or abstract Will the Eighth Symposium book display every virtue of its kind? The present volume has not fallen far short of doing so

Computer Applications

The report of the proceedings of the fifth annual Computer Applications Symposium held in Chicago during October 29-30 1958, has now been published (pp x+153 Chicago, Ill: Armour Research Foundation of Illinois Institute of Technology, 1959 3 dollars) It covers the whole range of applications of computers and some two thirds of the papers are concerned with data processing or computer organization, even though sometimes labelled as engineering and scientific, as for example, the papers by R A Haertle on "Use of a Computer in the 'AC' Spark Plug Division of General Motors", and by E M Chastain and J C McCall on "Computer Sharing by a Group of Consulting Engineering Firms" At first reading it would appear that the United States is much ahead of Britain technically in dealing with data processing and large-scale scientific work, but perhaps it is in the attitude of mind towards application of the computer to this type of work that Britain is really behind The breadth of vision shown in papers such as that of Col Elliott, dealing with the data processing for air material command, and the willingness to attempt the 'blue skies' approach indicated both there and in the paper by R D Whisler on work at Johnson's Wax, is very impressive It contrasts markedly with the timid and hesitating steps being taken in Britain and is a measure of the confidence now felt in the United States in the capacity of computers to carry through data processing economically On the technical side, one or two papers are of particular interest, such as that of R W Hamming on 'Frontiers of Computer Technology', and that of W F Bauer on 'The Future of Automatic Programming' On the whole, it is an interesting report, but not of special

interest to the general scientific reader, except to demonstrate the very wide field over which computers are now applied

Guatemalan Flora

The Flora of Guatemala is continued with a part devoted to a number of families of Gymnosperms and Monocotyledons, including the large Cyperaceae, Palmaeaceae, Araceae and Bromeliaceae (Chicago Natural History Museum. Fieldiana Botany Vol 24, Part 1 Flora of Guatemala By Paul C Standley and Julian A Steyermark. Pp ix+478 (121 figures) (Chicago, Ill Chicago Natural History Museum, 1958) 8 dollars) There is a number of helpful illustrations It must be remembered that this work also deals with the flowering plants (and their vernacular names) of British Honduras, 'since on both geographic and botanical grounds it is essentially a part of Guatemala' This part opens with a plan of the Flora and mentions certain areas of Guatemala which still need further exploration

Space Projectiles

The Russian journal *Priroda* has recently published a series of articles dealing with various types of space projectiles launched in the Soviet Union and the type and methods of observations connected with these projectiles Thus Y L Alpert (10, 71 1958) discusses the study of the ionosphere V L Krasovskiy (12, 71, 1958)—the study of the upper atmosphere, A E Chudakov (12 88 1958)—the study of photons, N A Dobrotin (1, 57 1959)—the study of cosmic rays N S Yakhontova (4, 5 1959) presents an account of the small artificial planet launched in January, and, finally, V L Kurt (5 74; 1959) discusses the artificial luminous sodium comet

New Radioisotope Training Programme

The Atomic Energy Commission of the United States has announced a new programme which will provide students of undergraduate colleges with the opportunity for specialized training in the techniques of using radioisotopes The new programme will utilize a mobile training laboratory which can be moved to the college campus for presentation of a short (two week) concentrated course on the basic techniques of handling radioisotopes The laboratory will be similar to one presented last year to the International Atomic Energy Agency by the United States Further information is available from University Relations Division, Oak Ridge Institute of Nuclear Studies, P O Box 117 Oak Ridge Tennessee

Animal Health Trust Awards, 1959-60

The Animal Health Trust has announced the following senior awards for the period 1959-60 *Wellcome Fellowships* Mr P H Lainont to undertake investigation of enteroviruses of the pig and their possible role in disease at the Department of Animal Pathology, Cambridge, under Prof W I Bovordridge, Mr I R Falconer to study thyroid-ovarian-pituitary interrelationship at the Department of Biological Chemistry, University of Aberdeen, under Dr H A Robertson *Vitameco Fellowship* This new award was founded to commemorate the 70th birthday of Lord Rank and his close association with Vitamins Ltd, by whom it was given The first recipient is Mr D B Ross, who is to continue work on some

of the more fundamental aspects of magnesium metabolism, particularly intestinal absorption. Initially Mr Ross will work at the Department of Animal Pathology, Cambridge *Research Training Scholarship*. Mr W A G Charleston to undertake an investigation into the mechanics of the quadrupedal vertebral column, with special reference to the dog and the cat, under Prof C W Ottway at the Department of Veterinary Anatomy, University of Bristol. Eight Evans Final Year Scholarships have also been awarded.

The International Nickel Company of Canada, Ltd, Fellowship

THE establishment of a fellowship to honour the visit of H M the Queen and H R H Prince Philip, Duke of Edinburgh, to the nickel mines in the Sudbury area has been announced by the International Nickel Company of Canada, Ltd, and the Canada Council (the latter being a body established by the Canadian Government for the encouragement of the arts, humanities and social sciences). The fellowship will be called 'The Queen Elizabeth II Fellowship (The International Nickel Company of Canada, Limited, Royal Tour, 1959)'. The award will be a postdoctoral fellowship tenable for two years. Research can be undertaken in the chemistry or physics of metals, geophysics, geology, metallurgy, mineralogy, or mining. Candidates must be Canadian citizens and holders of a doctor's degree and the fellowship must be held at a Canadian university. The International Nickel Company has deposited 15,000 dollars with the Canada Council, which will supervise all arrangements for the fellowship.

The Night Sky in November

FULL Moon occurs on Nov 15d 09h 42m UT and New Moon on Nov 30d 08h 46m. The following conjunctions with the Moon take place: Nov 4d 16h, Saturn 5° S, Nov 27d 02h, Venus 0.6° N. In addition to these conjunctions with the Moon, Mercury is in conjunction with Jupiter on Nov 7d 10h, Mercury being 3.4° S, Mercury with Antares on Nov 10d 05h, Mercury being 2.0° N, Jupiter with Antares on Nov 15d 16h, Jupiter being 5.2° N, Mercury with Jupiter on Nov 17d 06h, Mercury being 2.1° S, Mercury with Antares on Nov 17d 21h, Mercury being 3.3° N, and Venus with Spica on Nov 30d 05h, Venus being 4.5° N. Mercury is too close to the Sun for observation. Venus is a morning star, rising at 2h 35m, 2h 55m and 3h 25m on November 1, 15 and 30, respectively, its stellar magnitude is -4.0 . Its distance increases during the month from 55 to 77 million miles and the visible portion of the apparent disk increases from 0.443 to 0.598. Mars and Jupiter are too close to the Sun for observation. Saturn sets about 2 hr after the Sun, and will be visible low in the southwest after sunset, conditions are not favourable for observation. Occultations of stars brighter than magnitude 6 are as follows, observations being made at Greenwich: Nov 4d 17h 47.6m, γ Sgr (D), Nov 5d 17h 23.7m, ρ Sgr (D), Nov 14d 3h 53.9m, ξ Ari (D), Nov 16d 18h 32.0m, α Tau (D), Nov 16d 19h 28.9m, α Tau (R). D and R refer to disappearance and reappearance, respectively. The Taurid meteors are active during the first fortnight of the month, conditions being moderately favourable, the radiant is near R.A. 3h 36m, Dec $+14^\circ$. The Leonids are active during November

15-17, but conditions are unfavourable for observation.

Announcements

THE first Polarographic Society Medal has been awarded to Prof J Heyrovsky for his discovery of the polarographic method in the nineteen-twenties and for the subsequent major contributions to the subject by himself and his students.

DR W M HAMPTON, of Chance Brothers, Ltd, will deliver the Fifth Chance Memorial Lecture of the Society of Chemical Industry under the title "The Development of Furnaces for Glass Melting". The Lecture will be delivered on February 9 in Birmingham.

DR AINSLEY IGGO, of the Department of Physiology, University of Edinburgh, has been appointed by the Royal Society to a Locke Research Fellowship. Dr Iggo will continue his research at Edinburgh on unmyelinated afferent nerve fibres: their peripheral specificity and their central connexions.

PROF A L HODGKIN, Royal Society research professor in the University of Cambridge, and Prof R Milnes Walker, professor of surgery in the University of Bristol, have been appointed members of the Medical Research Council in succession to Prof R C Garry and Mr H J Seddon, who are retiring after their normal four-year term of service. The Committee of Privy Council has also recently appointed Sir Hugh Lunstead as the House of Commons member of the Council in succession to the late Richard Fort.

THE Bibliography of Scientific Publications of South and South-East Asia for June 1959 (No 6, Vol 5) compiled jointly by the Unesco Science Co-operation Offices for these areas and published by Indoc, National Physical Laboratory, New Delhi, lists by subject a further 102 titles.

THE Committee on Fire Research and the Fire Research Conference of the Division of Engineering and Industrial Research of the U.S. National Academy of Sciences-National Research Council is planning a two-day international symposium on the theme "The Use of Models in Fire Research", to be held at the National Academy of Sciences in Washington, D.C., during November 9-10. Further information can be obtained from Mr D W Thornhill, Executive Secretary, Committee on Fire Research and Fire Research Conference, National Academy of Sciences, 2101 Constitution Avenue, Washington 25, D.C.

AWARDS for study in statistics by persons whose primary field is not statistics but one of the physical, biological or social sciences to which statistics can be applied are offered by the Department of Statistics of the University of Chicago. The awards range from 3,600 dollars to 5,000 dollars on a nine months basis or 4,400 dollars to 6,000 dollars on a basis of eleven months. The closing date for application for the academic year 1960-61 is February 15, 1960. Further information can be obtained from the Department of Statistics, Eckhart Hall, University of Chicago, Chicago 37, Illinois.

ERRATUM In the communication entitled "Incorporation of DL-[2- 14 C] Mevalonic Acid Lactone into Polyisoprene", by R G O Kekwick, B L Archer *et al.*, in *Nature* of July 25, on p 270, col 1, line 1, for "active" read "inactive".

THE NATIONAL PHYSICAL LABORATORY

THE National Physical Laboratory held two open days on May 27-28, when about 3 600 guests from industry, the universities and Government departments viewed 150 exhibits covering the main items of the current research programmes. As last year, the exhibits were chosen to illustrate certain selected topics, but arrangements were made for visitors to discuss with specialist members of the staff items of work not on display.

The nine scientific divisions of the Laboratory function largely as independent units, but in a number of cases the programmes involve close collaboration between divisions. This is particularly the case with the work of Mathematics Division, much of the work of which consists of providing advice and computing facilities to other divisions. Excellent examples of the fruitfulness of such collaboration were seen in the work on machine tool control by the use of diffraction gratings, shown by the Light Division, and in a new infra-red spectrometer exhibited by the Basic Physics Division.

The measurement of fundamental standards has always been one of the basic responsibilities of the Laboratory and a reorganization of Divisions in 1958 brought such measurements mainly within the fields of the Standards and Applied Physics Divisions with the newly created Basic Physics Division concerned with more fundamental research in some newer fields.

In an experiment designed to measure the gyro magnetic ratio of the proton, apparatus for which was exhibited the Standards Division is extending its field of endeavouring to relate measurement to atomic constants. A magnetic field about twenty times the strength of the Earth's field is produced by means of a known electric current in wire coils of known dimensions. At the centre of the coil system a spherical container is filled with water the source of the protons. The latter are polarized in a direction perpendicular to the known field by a current maintained for a few seconds in a coil surrounding the sphere. When this polarizing field is removed the protons return to a state of equilibrium over a period of about 2 sec, during which time an e.m.f. is induced in the polarizing coil now used as a pick-up coil. The frequency of this e.m.f., about 40 kc/s, is measured, and from it and the known applied field the gyromagnetic ratio is calculated. This constant is of importance for defining stronger magnetic fields which may then be used for the determination of e/m for fundamental particles.

The tendency to relate all standards to more fundamental quantities is also seen in the use of monochromatic radiation as a fundamental standard of length. The precise intercomparison of wave lengths has thus become of increased importance and a high resolution spectrometer for this purpose was shown. It uses the method of air pressure variation to scan the fringes of a Fabry-Perot interferometer but, since the instrument is illuminated with light of the two wave lengths to be compared in very rapid alternation it is not necessary to measure the absolute pressure of the air very exactly. In synchronism with the rotating 'chopper shutter' the

output of the receiving photomultiplier is switched to two amplifiers. Errors due to changes of source intensity are eliminated by an additional photocell measuring the ratio of transmitted to incident light. The variation in intensity of the centre fringe with pressure for the two sources being compared is recorded on a chart recorder. Arrangements are also fitted for digitizing the records on punched tape which can then be fed to a computer for Fourier analysis to obtain data on phase shifts at the semi reflecting surfaces and other information. The instrument will be used for comparisons of standard wave-lengths, measurements of isotope shifts and work with sources at liquid helium temperatures.

Another new field of standardization, undertaken in the Applied Physics Division, is that of neutron sources, required to produce known neutron fluxes for work in problems of reactor design. The strengths of the sources are compared by suspending them overnight by a fine thread at the centre of a large spherical container filled with manganese sulphate solution. A correction is applied for the neutrons escaping from the vessel. The amount of manganese 56 produced is determined by β -decay measurements, which are compared with those obtained after the addition of a known amount of active manganese to the same container. It is also hoped to obtain a confirmatory measurement from the amount of helium produced in three sources over a period of time. Six British sources have been compared with a Canadian standard.

The same Division has several rooms specially designed for the measurement of sound, but this is a field in which subjective measurements are of more than usual importance. The results of extensive experiments on the loudness of directional sound fields, as measured by pressure at the listener's ear, were shown. Such measurements however do not indicate the total loudness to a listener owing to the additive effects of both ears. Charts were also shown for a group of observers showing that the directional arrival for maximum loudness varies in a complicated way with frequency. An approximate binaural summation theory has been developed from which some calculations of loudness have been made. These compare fairly well with the results of direct measurements.

The newer programmes in the Basic Physics Division are only now coming into operation. An interesting infra-red spectrometer of novel type for study of the wave-length region $50\mu-1\text{ mm}$, was shown. This region is of particular importance in the theory of superconductors and of radiation from the Earth's atmosphere. A Michelson interferometer is used to scan the spectrum, the output intensity being received by a Golay cell. The resulting interferogram is then translated into a spectrum by digitizing the information and feeding to a computer. The instrument has considerable advantages over a conventional infra-red spectrometer in speed. In a typical example the range $100-300\mu$ was observed in 25 min with a resolution of 0.4 cm^{-1} and computed in 5 min. It is hoped that with further development corresponding advantages in resolution will also be obtained.

The same Division also showed an ultrasonic goniometer. In this device the critical angle of reflexion of an ultrasonic wave (5 mc/s) incident upon an area of about 1 cm² of the surface of the specimen is measured. In metals of marked elastic anisotropy, any preferred orientation introduced during fabrication can be detected from the change in this critical angle. It is, for example, in some cases possible to determine the rolling direction of a plate. By varying the frequency of the incident wave (2-15 mc/s) some information on the depth of surface effects in texture can be obtained.

In the Metallurgy Division results of importance in the fundamental theory of metals are being obtained from transmission electronmicrographs of thin iron foils. Strip, 0.02 in. thick and representative of bulk material, is thinned by electropolishing to 2-3000 Å, at which thickness electrons can penetrate it. The idea that in alpha iron two dislocations with <111> Burgers vectors unite to form one <100> dislocation with a saving of energy has been confirmed by the observation of a hexagonal network formed by the interaction of two dislocation systems. Distortion in parts of this network, shown in some of the photographs exhibited, can also be explained in terms of the interaction of stranger dislocations. Photographs were also shown of precipitates, about one hundred atoms thick, growing from a supersaturated alloy in dendritic form on dislocations.

The recording of creep strain data is often a major item in the programme of a large metallurgical laboratory, and a new electrical recording extensometer, developed in the Division, promises to simplify this problem. The movements of the extensometer are measured by the changes in inductance in a linear differential transformer fitted to the extensometer limbs. The transducer is built into a bridge circuit, in which an electronic detector is used to determine the balance conditions, and measurements are independent of zero drift or changes in amplification. Long-term stability, of great importance in tests lasting 10,000 hr or more, is dependent only on the stability of the transducer and resistors. Other advantages of the equipment, the sensitivity of which is comparable with that of a mirror extensometer, are the possibility of measurements over a large range of strain without readjustment, and the application of automation to the recording of the data.

Other Divisions of the Laboratory are concerned more with developments in applied science, with particular reference to problems of interest to industry, and Control Mechanisms and Electronics Division demonstrated a technique for the manufacture of radial coded plates for recording digitally the instantaneous position of a revolving shaft. The individual code zones are generated circumferentially in succession, by optical reduction from a 35-mm film in conjunction with a dividing machine, and the precision of the latter is the limiting factor in the angular resolution obtained. This process is much quicker, particularly for complicated code systems, than earlier methods of programming a set of events, for example, lamp flashes, to produce one element of all the code zones simultaneously in a radial direction. An example was shown of an eighteen-code system with a resolution of 0.01° and a total radial width of 0.1 in.

An application of radial diffraction gratings was shown in a system for measuring the torque in a rotating shaft. Each end carried a radial grating in

conjunction with a similar stationary grating, producing an alternating signal by interruption of an optical beam. Any torque on the shaft is manifested as a phase difference between the signals from the two ends, such a system is sensitive to a few seconds of arc.

In addition to the work on the use of diffraction gratings in machine-tool control, several novel uses of the interferometric principle were exhibited by the Light Division, a Kösters prism being used as a compact Michelson interferometer. When used to measure the angle of tilt of a reflecting surface by the alignment of white light fringes such a system is sensitive to 1/10 sec of arc. The instrument, with both coarse and fine adjustments to facilitate setting, has possible applications in engineering metrology. The Kösters prism is also used as a reverse shearing interferometer for testing the revolution symmetry and asphericity of large mirrors. In another method, in which no test plate or comparison system is needed, such larger systems are examined by the superposition of the scattered light from two identical plastic scattering screens. The interference colours seen on the mirror indicate directly to a millionth of an inch how far each point of the surface is above or below that of an imaginary perfect sphere.

The work of the Aerodynamics and Ship Divisions is from the nature of their subjects rather more specialized than that of other divisions. Perhaps the field of greatest topical interest on display in Aero dynamics Division was that concerned with the new aerodynamic problems that occur in hypersonic flow (that is, at speeds greater than about five times that of sound), particularly those associated with the temperature of several thousand degrees centigrade that arise from aerodynamic heating. The Division is developing a shock tunnel, in which the flow duration is about a millisecond, and a 'hotshot', in which about twenty times this flow duration can be obtained. Two small shock tubes were shown in which spectrographic and microwave techniques are being developed for temperature measurements and for studying the effects of dissociation and ionization.

Also of current interest is the design of slender wings, the planform and section shape of which combine to give the required low drag at cruising speeds of about twice the speed of sound, together with satisfactory stability characteristics and good landing and take off performance. Vortex-type flow separations from sharp edges are being studied in transonic

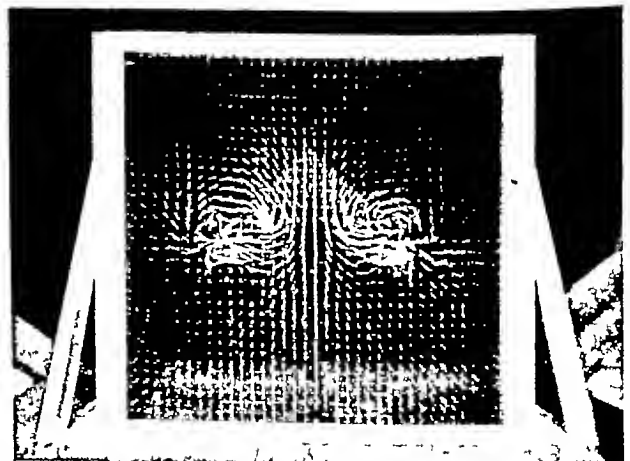


Fig 1 Vortex wake behind a swept back wing at low speeds as shown by a tuft grid placed behind the model

and supersonic flow and appear to behave in a remarkably similar way to those at low speeds (Fig 1) The work shown included detailed quantitative explorations in a low speed tunnel and flow visualization experiments on a wing oscillating in a water tunnel in which qualitative observations were being made on the flow in those dynamic conditions

Results were also displayed from an extensive series of investigations into the aerodynamic design of swept wings for aircraft to cruise in the Mach number range 0.8-1.2. A special design of wing section has been developed to delay the drag rise that occurs at transonic speeds and methods of combining a high drag rise Mach number with a large drag rise/buffet margin are being sought To enable drag rise and buffet boundaries to be predicted a semi-empirical theory has been developed for calculating pressure distributions in two-dimensional transonic flow The effects of wing planform, camber and twist have also been studied, together with the design of the junction between wing and fuselage with the object of maintaining the full sweep of the leading edge over the whole of the wing span One of the biggest problems is to reduce the required body 'waxing' to an amount acceptable for civil aircraft

Research displayed on boundary layer and shear flows included theoretical and experimental investigations into the mechanics of transition following

the non linear growth of small disturbances, measurements of surface friction, and studies of turbulent boundary layer development wall jets pipe flow, and the flow up an abrupt step at a Mach number of 2.5

As part of a long term programme of research into ship vibration, the Ship Division demonstrated apparatus for determining the characteristics of the oscillatory pressure distribution around model propellers A large dynamometer for propellers up to 24 in in diameter measures torque and thrust electrically by movement of a balanced armature transducer, connected to a bearing in a helical slot on the shaft in one case and to a flexible coupling allowing only axial movement in the other A new 12 in open dynamometer was also displayed this has a capacity of 5 lb/ft torque and 50 lb thrust at 0 to 2000 r.p.m., torque being measured by balancing the reaction on the motor casing and thrust by balancing the axial load on the shaft Both components are measured by dead weight and spring systems, recording on a built in chart recorder

On the Lathweg water tunnel, techniques for automatic data recording and analysis have been installed Measurements of the physical quantities are converted into either rotation of a shaft or into voltage; shaft digitizers or digital voltmeters then turn these into coded electrical pulses suitable for feeding to computers

THE BRITISH GLASS INDUSTRY RESEARCH ASSOCIATION

NEW LABORATORIES

THE official opening of the newly built laboratories of the British Glass Industry Research Association by the Right Hon the Earl of Halifax, Chancellor of the University of Sheffield, which took place on June 6, marked a noteworthy stage in the development of industrial research for the British glass industry Co-operative research has been continuously expanding since the inauguration by W E S Turner of a Department of Glass Manufacture in the University of Sheffield in the autumn of 1915 Prof Turner then a lecturer in chemistry in the University, pioneered the establishment of a centre of organized scientific research into the physical and chemical properties of glass, to provide technical and scientific advice to the industry, and to include facilities for teaching Under his influence and professorship (he occupied the chair from its inauguration in 1920 until his retirement in 1945) the Department of Glass Technology, as it was renamed became known and respected throughout the world by those interested in the manufacture and use of glass

In his early endeavour to found the Department of Glass Manufacture, Turner received great encouragement from his professor, the late W P Wynne who loaned him a small chemical laboratory for his investigations and a tiny attic to house his glass melting furnace He also received the enthusiastic support of glass manufacturers—particularly those of south Yorkshire and of Lancashire With increase of work and staff, Turner expanded his Department to occupy first a section of the applied science building of the University, and when this became insufficient, the site of a derelict glassworks in the Attercliffe district of the city The latter site was occupied

until 1938 when, with the financial support of the glass industry, the present Department was built by addition to a large house occupying extensive grounds adjoining the main University territory

After the Second World War it became apparent that the requirements of industrial investigations and that part of the research work which formed their immediate background, involved so much time that staff could not efficiently conduct them concurrently with teaching and long term research duties Prof H Moore who succeeded Prof Turner on his retirement in 1945, therefore advocated the establishment of a research association as a separate entity, the function of which would be to attack the industrial and development problems, leaving the University Department free to concentrate upon fundamental research and the education of glass technologists On the retirement of Prof Moore in 1955 this plan was adopted, Prof R W Douglas being appointed to the chair of glass technology, and Dr R G Newton as director of the newly formed Research Association From this time until the occupation of its new building in January 1959, the Research Association's staff was successfully accommodated in the University Department's building, despite the rapid expansion of both organizations The foregoing will have indicated the close connexion between the University, the Research Association and the glass industry the new buildings of the Research Association, built to the design of Prof Stephen Welsh now stand adjacent to the University Department which will enable the close connections of the past to be maintained in the future

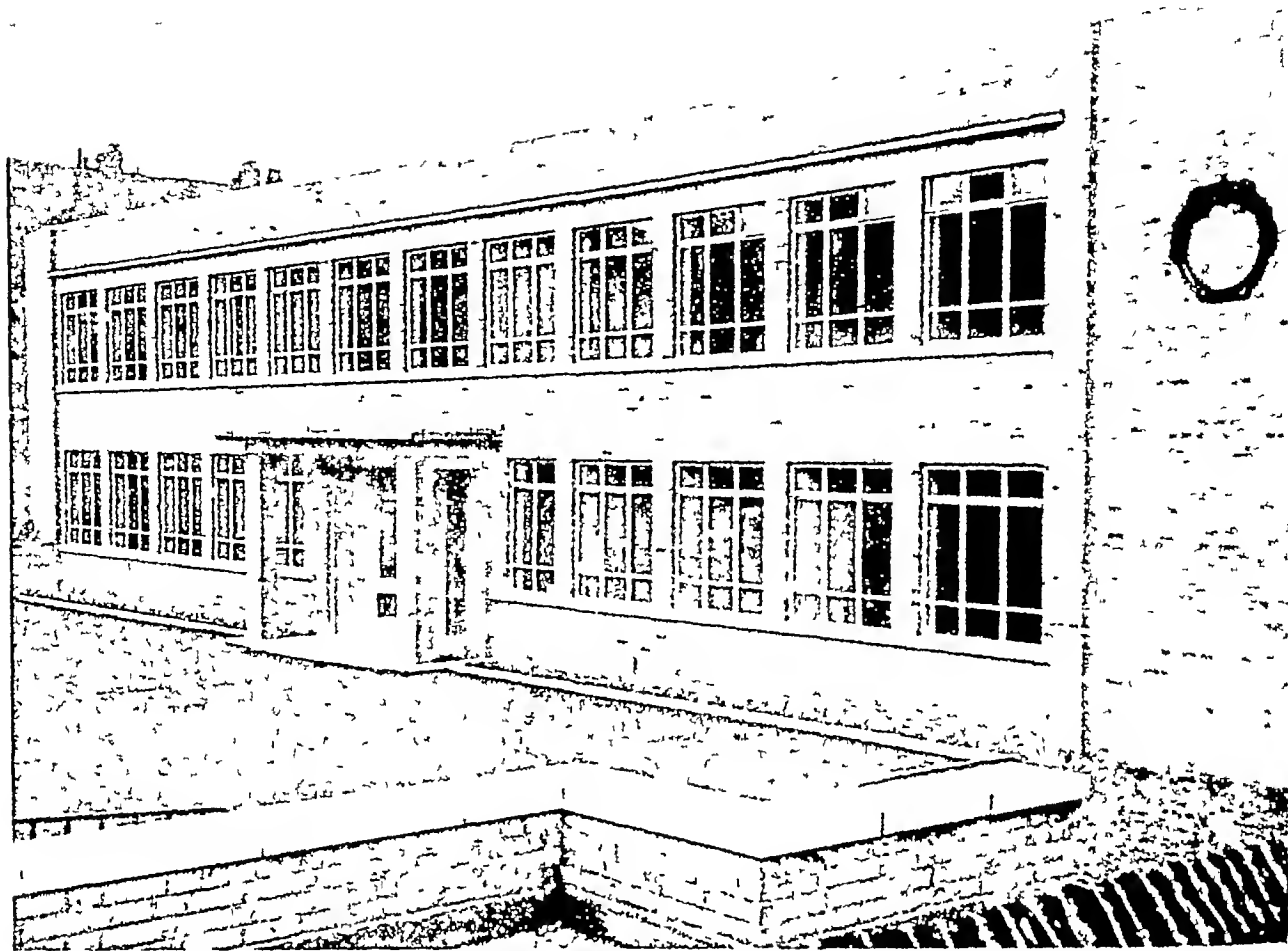


Fig 1 The British Glass Industry Research Association Laboratories

The British Glass Industry Research Association is supported by eighty-nine subscribing member firms, forty-seven of which are engaged in glass melting, the remainder being closely associated with glass manufacture through the supply of raw materials or are connected with the manipulation of fabricated glass, as, for example, the formation of articles from glass tubing. The strong backing of the British Glass Industry Research Association by industry is denoted not only by the fact that approximately half its income is derived from members' subscriptions but also from the fact that the forty-seven members previously noted as being concerned with the actual melting of glass together melt 98 per cent of the total glass melted in the United Kingdom. Strong financial support is also provided to the Association by the Department of Scientific and Industrial Research.

Following the opening ceremony, members and guests of the Association were invited to tour the new building and inspect numerous exhibits which illustrated the type of work being carried out by the Research Association. The laboratories are sectionalized to conform so far as possible with the type of problem to be dealt with. The two-story building, which has a total superficial area of 20,000 sq ft, is of 'L'-shaped plan, the ground-floor housing administrative offices, a section dealing with fuel, furnace and instrumentation problems, laboratories for the study of glass technological problems, a refractories section, and a furnace room with its associated batch mixing shop. The furnace room is sited at the extreme end of the wing and occupies a single story only so that heat and noise will not

impede the work of other sections. The first floor is occupied by a reference library and information section, with associated reading rooms and meeting room, work study section, drawing office, and with the physical and chemical laboratories. Each of the latter two sections is subdivided into main and subsidiary laboratories. In the chemical section, for example, a separate division has been made to enable the durability of glass to various attacking media to be studied without the influence of the general atmosphere of the main chemical laboratory. Muffles and lead-lined fume cupboards for decomposition with hydrofluoric acid have also been segregated, and a separate division for spectrographic work has been provided.

A semi-basement extending beneath approximately half the ground-floor area contains an excellently equipped workshop, a pot room and a pot drying-room for the manufacture of small melting pots and other refractory articles. The remainder of the basement area is given to storage space, boiler-house, and a glass grinding, cutting and polishing unit.

Numerous demonstrations illustrating the type of work done by individual sections were presented, of which only a limited number may be mentioned within the compass of this short review. The fuel, furnace and instrumentation section demonstrated methods of surface temperature measurement and the estimating and recording of oxygen content of waste gas from furnaces, together with results of furnace heat surveys carried out at member-firms' factories with the view of assessing furnace performance under varying conditions. The physics section demonstrated laboratory apparatus for the deter-

nation of tensile strength and thermal expansion, the latter by instrumental recording of the rate of expansion, thus eliminating the necessity for lengthy periods of direct observation. This section also demonstrated a pressure test rig for glass panels in which deflexions from fifty individual points on the glass surface were simultaneously displayed on scale instruments and one photographed at second intervals during the loading cycle. The performance of different types of refractory materials for glass furnace construction had been the subject of investigation by the refractories section, and a demonstration of a corrosion-erosion test rig was given. The glass technology section showed a novel rotating hearth furnace designed to give identical thermal treatment simultaneously to a number of experimental glass batch mixtures. This apparatus is to be used for study of the influence of raw materials on the rate of founding of glass. The chemical section in addition to numerous examples of analytical techniques in silicate analysis, demonstrated apparatus for the determination of the durability of glass to aqueous attack, and gave an excellent demonstration of the analysis of gaseous inclusions in glass. The demonstration showed methods of extraction of minute bubbles of gas from solid glass and of their analysis to the component gases carbon dioxide, carbon mon-

oxide, sulphur dioxide, sulphur trioxide and oxygen. Such studies have an important bearing on the problem of melting high quality glass at maximum rate. The work study section illustrated the use of one second interval cine photography for the study of manual operators in factories, and has shown that this technique can prove of value when a number of individual manual operations have to be co-ordinated with each other or with the operation of a machine.

Speakers at the official luncheon marking the opening ceremony reviewed the origin and future objectives of the British Glass Industry Research Association. Dr L. H. A. Pilkington, chairman of the Council of the Association, directed attention to the man power deployed on research in glass technology at the present time, estimating this to be some 200-250, and forecasting that the figure would increase to 750-900 within a five-year period. Although smaller in numbers than a force of some 750 at present employed in research by four of the largest glass manufacturing firms of the United States, these men managed to keep us abreast of developments in many fields and definitely ahead in some. Mr A. W. Clark, chairman of the Glass Manufacturers' Federation, referred to the value of research associations to smaller firms the resources of which could not justify individual research units.

COIL SPRING FEDERATION RESEARCH ORGANISATION NEW LABORATORIES

THE Coil Spring Federation Research Organisation, which has been in existence for fourteen years, has for the majority of this time confined its research activities to extra mural work in universities, although the long term aim of the spring industry has always been to operate its own research and development laboratories while maintaining the close links it has established with universities. This has now been achieved by the setting up of a new research centre the construction of which has been financed from reserves set aside for the purpose.

The two-story laboratory block recently completed in Doncaster Street, Sheffield, is probably the most comprehensive of its kind for research into all forms of springs and spring materials.

The ground floor, in addition to the usual reception facilities, contains laboratories for heavy fatigue testing, general mechanical testing, experimental heat treatment and electroplating. In the fatigue testing laboratory are housed 12½ b.p. machines capable of applying a dynamic load of 0 tons, which are used for fatigue testing heavy coil springs up to eighteen springs may be tested at one time. Other machines used for fatigue testing springs of the internal combustion engine type are capable of infinitely variable speeds of compression of up to 4 000 per min. Fatigue tests in repeated torsion are carried out on torsion bars and are used to produce data from which an assessment of the effects of composition, heat treatment and surface condition can be made prior to the manufacture of experimental helical springs. A special feature of this laboratory is the sound proofing and anti-vibration features incorporated in both the suspended ceiling and the floor.

The mechanical testing laboratory houses a variety of conventional machines used for determining the properties of both specimens and springs, covering the range of material diameters 0.004-2.0 in. One machine, for example, is capable of developing a maximum torque of 120 000 in lb and is used to investigate the effects of hardenability on the static torsional properties of large diameter spring steel bars.

Many researches relate to the load-deflexion characteristics of springs and the Organisation has a comprehensive range of machines, capable of applying static loads from a few ounces up to 30 tons. The determination of fatigue characteristics of drawn wires of diameters 0.01-0.25 in. is provided for by high speed rotating beam fatigue machines which can complete up to 100 million cycles in as little time as one week. The study of corrosion and protection of spring materials and the effects of hydrogen embrittlement due to electroplating has had an important place in the Organisation's programme for many years. The work is being continued in a new laboratory specially fitted out for this purpose: the plant in it has been presented by Messrs Canning Ltd., the Birmingham manufacturers of electroplating equipment. Facilities are available for electroplating copper, zinc, tin, cadmium and nickel. The experimental heat-treatment laboratory is equipped with fully instrumented electric furnaces for general heat treatment, and high temperature heat treatment under various types of protective atmosphere.

The laboratories contain a number of machine tools and a shot-peening unit which automatically rotates the object under treatment while at the same

time traversing it with the shot stream. It is being used in a fundamental study of the effects of shot-peening and optimization of it, together with an assessment of possible methods of measuring intensity.

The first floor is devoted to light laboratories (containing small static testing machines, general scientific instruments and equipment), administrative offices, and a conference room. The materials testing laboratory contains machines for determining macro-hardness, tensile and torsional properties of wires and load-deflexion characteristics of small springs. Metallographic facilities are provided in specially

fitted rooms for rough sample preparation, fine polishing and etching, microscopical examination and photography. The microscope room contains a high powered binocular bench microscope, projection microscope and micro-hardness testing equipment.

The Organisation is studying spring materials for elevated temperature applications, in particular the stress-temperature relaxation properties of springs made from a very wide range of alloys. A battery of spring creep testing machines is installed which will enable the behaviour of springs to be determined up to 850°C.

CHEMISTRY OF PROPELLANTS

A MEETING was recently held in Paris (June 8-12) under the auspices of the Combustion and Propulsion Panel of the Advisory Group for Aeronautical Research and Development, with "Chemistry of Propellants" as the main topic. It was felt that such a meeting could contribute to a useful exchange of research information and discussion of current problems among North Atlantic Treaty Organization countries. Its importance can be judged by the attendance of nearly two hundred observers from eleven countries, nominated through their Advisory Group for Aeronautical Research and Development national delegates.

The meeting was opened by Dr von Karman, who was supported by Dr Seitz, the science adviser to the North Atlantic Council, and his recent predecessor, Dr N F Ramsey. Later in the week Dr G B Kistiakowsky, the new scientific adviser to the President of the United States, attended and took part in the proceedings. These could be classified under three main headings, namely, propellants or associated features for liquid rockets, solid rockets and air-breathing engines, and the papers presented covered reviews of existing knowledge, reports of recent work and assessments of future problems.

The first technical session was introduced by a paper by S Greenfield (United States), who reported on an experimental evaluation of liquid-propellant data. This was based on a research programme to compare differences in behaviour of various hydrocarbon fuels when burned with liquid oxygen. The fuels were pure samples of each of the chemical types such as paraffins, aromatics and olefins together with a reference fuel specified as JP-5. The main results covered liquid film heat transfer coefficients and their variation with heat flux and combustion stability, specific impulse variations with mixture ratio, and effect of aromatics on available energy in fuel-rich gases suitable for turbo-pump operation. An interesting feature of this work was the precise measurements achieved and the important influence of combustion chamber length (or L^*) on performance. The conclusion was drawn that naphthenics are beneficial in a mixed fuel, but normal paraffins are of doubtful value.

This paper was, to some extent, complementary to another by R J Thompson (United States) covering theoretical performance evaluation. This work was carried out on an electronic data-processing machine and presented a vast tabulation of thermodynamic functions and propellant parameters which were discussed and illustrated. The main propellant com-

bination discussed was liquid oxygen and kerosene, although data on fluorine-liquid hydrogen were also used to illustrate the calculations. Additionally, thermodynamic properties as functions of temperature for eleven of the more important elementary monatomic gases were given. It is certain that these two papers will be of great use in future studies of propellants.

The next paper in this group was by D L Armstrong (United States) and reviewed the characteristics of liquid propellants desired and achieved in rocket engines. The important physical properties included vapour pressure, density, viscosity, specific heat, boiling and freezing points, and other features which were tabulated and discussed. Chemical properties were also enumerated and mention was made of reactivity, self-ignition, combustion kinetics, stability and corrosion. The author also gave some indication of performance, manufacturing processes and suggested propellants for various missions, but much more detailed and relevant papers on these aspects were presented by W G Parker and G Ruston (Great Britain) on the merits of utilizing high-energy propellants, and S H Dole and M A Margolis (United States) on the sources, availability and estimated cost of propellants. The former took a slightly unusual line in dismissing the majority of the exotic propellants from consideration, first, because of the unfavourable properties such as extreme reactivity and toxicity, and secondly, because the advantages of higher specific impulse become less marked beyond values of about 320 sec. Their conclusions were that liquid hydrogen was worth developing because of its probable use in nuclear rockets, but it should be in combination with nitric acid or hydrogen peroxide rather than liquid oxygen. The accidental combination of hydrogen and oxygen liquid or vapour could be too great a hazard to risk. The paper on costs pointed out that prices of many propellants would be significantly altered if production demands increased, but even allowing for this, it was clear that the cryogenics would give a better performance than the storable liquids for a given cost. Costs should, however, include the overall system cost, and some curves were given showing flight vehicle cost against total impulse required for solid propellant, storable and cryogenic. At the higher values of total impulse, the cost of using these propellants was in descending order. This was strongly challenged by protagonists of solid propellants during the discussion.

The papers on solid propellants were given by R Stemberger (United States) on the properties of

double base forms with a corresponding one by P Tavernier and J Bousson (France) on composite forms and one on burning rate control by G H Young (Great Britain). All these appeared to suffer from the limitations imposed by 'security', but the first two gave useful accounts of the standard materials and processes in manufacture. It was interesting to compare these and from this point of view they were an informative contribution. Steinberger, however, included a good deal more on the life expectancy of double base propellants. This is not surprising in view of the much longer experience of them which exists. The paper by Young covered some of the same ground and, rather than a discussion of burning rate control was limited to descriptions of methods of measuring burning rate and the range of burning rates achieved. The difficulties imposed on this author by the classified nature of his subject were obvious and it was generally agreed that it could only receive suitable treatment at a closed session.

The papers on air burning fuels included one on properties and preparation of ramjet fuels by M Barrere and G François (France) one on performance evaluation by E Perchonok (United States), one on deposits in jet engines by R Broitwieser (United States) and a final one on physico-chemical reactions during nozzle flow by J F Morris (United States). The first two covered the main features found necessary in the special conditions of ramjet operation and collected much data which will be useful for future reference. Both papers dwelt on the use of solid fuels in slurry form and the attractions of boron hydrides and other compounds but the American paper emphasized some additional considerations if ramjets are to be operated at hypersonic speeds. For example the need for regenerative cooling of engine walls will limit the use of JP-4 fuel to speeds of $M=6$. The high gas temperatures resulting from these speeds also have an important effect on dissociation conditions and thrust available. With frozen gas exit flow, the thrust may be reduced as much as 58 per cent at $M=8$ compared with equilibrium flow. This problem was treated by Morris, who reviewed the background of relaxation rate theory and discussed the gaps in knowledge which will enable predictions of non-equilibrium flow of both internal and external gas for hypersonic vehicles. The long list of references appended to this paper calls for special mention as it extends to more than four hundred. The other paper in this group emphasized the problems of solid deposits in engines

and pointed out that these became more serious with some of the high-energy fuels now being considered. Boron oxide is one combustion product which may form on engine surfaces in large quantities. Some measurements on convergent-divergent nozzles showed losses in total stream momentum of more than 5 per cent within 20 sec of initiating combustion. Other sensitive components are turbine stator blades and combustion chambers. Two mechanisms of deposition were discussed consisting of diffusion of particles less than $\frac{1}{2}\mu$ diameter and of impact by particles of 5μ and larger. The former was analysed theoretically and compared with measured deposition rates. Although good agreement was claimed, this analysis received some criticism during the discussion.

In addition to the papers, a round table discussion on basic problems in propulsion was held with Dr von Karman in the chair. The discussion was initiated by A D Baxtor (Great Britain), who summarized the merits of liquid propellant rocket engines and outlined some of the remaining lines which require research. These included physical problems such as heat transfer and combustion chamber design parameters and chemical problems associated with propellant stability, ignition delays and reaction rates. H W Ritchey (United States) then presented a similar case for solid propellants and was followed by three speakers giving views on futuristic possibilities. G B Kistiakowsky (United States) spoke on solid propellant horizons, J W Bond (United States) on electromagnetic and nuclear thermal propulsion, and A Ferri (United States) on composite launchers. The last was a stimulating argument in favour of air breathing engines as the first stage in multi stage rocket vehicles. One of the advantages would be the ability to fit aerodynamic lifting surfaces and fly the launcher back to the take off point. The discussion was so successful that it was continued at the final session of the meeting, ranging over a broad field. Points brought out were the convergence of design features in solid and liquid propellant engines, the question as to how vital improved specific impulse was, the problems of size in rockets and the future of nuclear rockets.

This discussion was a fitting climax to a successful meeting and no doubt, when the edited proceedings are published, they will be found to provide a valuable addition to the literature, not only because of the data included but equally because of the excellent bibliographies attached to most papers. A D BAXTOR

CLAY MINERALS

TWO series of meetings on clay minerals were held in Yorkshire during April. The first at Sheffield was arranged by the Clay Minerals Group of the Mineralogical Society. Two sessions on April 16, in the Metallurgy Department of the University, were devoted to the reading of scientific papers, while on April 18 visits were made to the works of Thomas Marshall at Loxley and General Refractories at Wharfedale. The chair at the scientific sessions was occupied by Dr A F Hallmond (London), chairman of the Group, in the morning, and by Prof J White (Sheffield) in the afternoon.

Several papers concerned the industrial application of clay minerals. In the first of these, E H

Steger (London) discussed various problems in civil engineering in which clays are implicated and dealt particularly with soil stabilization by injection of a suitable clay suspension into sands, etc. The factors necessary to give good results are broadly known, but much work on fundamental aspects is still required. In the discussion, the difficulty of replicating laboratory findings in the field was widely referred to.

Divergent views upon the relationship between the mineralogical constitution and the firing properties of clays were expressed by Prof G W Brindley and S Udagawa (Pennsylvania) and by Dr R W Nuree (Watford). The former described how, by 'synthetic' clays from mixtures of appropriate pure

minerals over a range of compositions, it is possible to make some forecasts regarding the behaviour of natural clays from a rapid check of their mineralogical composition. This technique enables immediate rejection of completely unsuitable clays, but those which appear of possible use still have to be tested individually. Dr Nurse, on the other hand, could find no correlation between firing properties and mineralogical composition for a series of clays of various geological ages.

The use of thermal expansion measurements in indicating the mineralogy of clays¹ was considered by D. A. Holdridge (Stoke-on-Trent), who showed its application in quartz determinations. The significance of the same test after firing was also discussed.

Dr R. F. Youell (Leeds) described how X-ray data on heat-treated silicates, which he had obtained earlier, were explicable on the basis of silicon-containing spinel structures². He particularly referred to the composition of the spinel phases and the occurrence of ordered transformations. In discussion, the propriety of using the term 'silicate' for a silicon-containing spinel was questioned and the frequency of occurrence of ordered transformations was stressed.

Three general papers were also read. In the first B. D. Mitchell and Dr R. C. Mackenzie (Aberdeen) described a relatively inexpensive controlled atmosphere differential thermal analysis apparatus and illustrated its applicability to investigations in nitrogen, oxygen and steam, while in the other two Dr H. G. Midgley (Watford)—this paper was read in his absence by Dr R. W. Nurse—and W. Windle and E. K. Cundy (St Austell) described occurrences of sepiolite and zinnwaldite, respectively, in Cornwall, chemical, X-ray and other data were given.

This meeting not only brought to notice relatively new uses of clays in industry (such as their use in soil stabilization) but also raised the practical question of the value of mineralogical analysis in assessing clays. Difficulties encountered in relating the mineralogy of a clay to its firing properties could, for example, be due either to incomplete mineralogical data or to effects being not truly additive: the observations reported rather suggest the latter.

The Sheffield meeting was followed by one at Leeds during April 17–18 arranged by the X-ray analysis Group of the Institute of Physics. This meeting included a session on clay minerals as well as one on biological fibres, only the former is reported here.

No outstanding advance in structural investigations of the common natural clay minerals was forthcoming

at the meeting. Prof G. W. Brindley, in an introductory address, pointed to the value of electron diffraction techniques in such investigations. He was able to report a very promising approach to the problem of thermal changes in kaolinite by his collaborator, M. Nakamura, using small single crystals. This work suggests that the 'spinel' phase is really a silica-alumina crystallization structurally similar to spinel³, and appears to have furnished clear evidence that the much-discussed metakaolin is not amorphous, but is an intermediate stage in the formation of spinel, having a substantial degree of crystallinity.

The dehydration products of kaolinite were also discussed by F. Vaughan (Stoke-on-Trent). D. A. Holdridge showed the possibilities of thermal expansion measurements for studying phase changes on firing. Quartz content, notably, can be estimated by this means.

Interesting structural studies on sepiolite were reported by Dr J. Goodyear and Dr W. J. Duffin (Sheffield) and on iddingsite by G. Brown and Dr I. Stephen (Harpenden). H. P. Rooksby (Wembley) reported on further detailed work on iron and aluminium oxides.

The question of surface structure in clays is one of fundamental importance, about which there is still much uncertainty. An extensive, many-sided approach to this problem is being made by Prof J. J. Fripiat and collaborators in Belgium under the auspices of Institut National pour l'Étude Agronomique du Congo Belge. Among the techniques under study are measurement of surface hydroxyl groups by exchange with heavy water vapour, and methylation and acetylation for determining acidic groups.

Dr D. M. C. MacEwan (Dundee) reported on an extensive series of calculations on diffraction effects from mixed-layer structures, now being carried out with electronic calculators. The resulting curves will be published as a special monograph by the Spanish Consejo Superior de Investigaciones Científicas.

Study of a German 'fireclay mineral' by Prof A. L. Roberts and Dr W. E. Worrall (Leeds) provided further support for Schofield's theory of the existence of isomorphous substitution in kaolins.

R. C. MACKENZIE

D. M. C. MACEWAN

¹ of Brough, J., and Robertson, R. H. S., *Clay Min. Bull.*, 3, 221 (1953).

² Steadman, R., and Youell, R. F., *Nature*, 180, 1066 (1957). Brindley, G. W., and Nakamura, M., *Nature*, 181, 1333 (1958).

THE COUNCIL FOR SCIENTIFIC AND INDUSTRIAL RESEARCH

THE second report of the Council for Scientific and Industrial Research covers the year 1958 in which the Department's gross expenditure was £9,453,652, compared with £8,255,561 in the previous year, and reduced to £8,357,913 by various receipts (£464,713 being from the National Physical Laboratory) for work done for Government departments or for industry, the net increase on 1957 being £1,108,070. Grants to students amounted to £444,958, the number of students in training being 1,681 and in 1957, 1,301, of whom 781 in 1958 and 653 in 1957 were new. The advanced course studentships increased from 152 in 1957 to 201, of which 184 were new, and of 26 research

fellowships (18 in 1957), 14 were new. Grants for special researches totalled £475,754, numbering 230 compared with £363,884 and 193 in 1957, and of these 147 were new. Of these grants 106 were in physics, 45 in chemistry, 32 in biology and biochemistry, 24 in other engineering, 11 in geology, 7 in mathematics, 6 in chemical engineering and metallurgy, and 3 in electrical engineering. Chemistry claimed 593 of research students, physics 360, biology and biochemistry 208, mathematics 144, chemical engineering and metallurgy 110, other engineering 100, geology 99, electrical engineering 50, and human sciences 17.

Expenditure on the National Chemical Laboratory decreased slightly, from £100 404 in 1957 to £155,010, and there were also slight decreases in expenditure on fuel research (£330,502-£326,899) and fire research (£38,745-£37,174), but with these exceptions expenditure increased on all branches of the Department's work, the biggest increases being in road research (£500,813 compared with £441 702 in 1957), the National Physical Laboratory (£737,958 compared with £638,031) headquarters administration (£377,905 compared with £307,430) mechanical engineering research (£507,104 compared with £454 810) and the Geological Survey and Museum (£328,320 compared with £282 370). Expenditure for other sections in 1958 was as follows, the 1957 figures being given in brackets: budding research £541 371 (£521,005) forest products research, £135 645 (£128,256), hydraulics research, £100 050 (£91,067), pest infestation,

£89 309 (£83 341), radio research £150 398 (£135,057) and water pollution research, £103 882 (£90,020). Besides the National Physical Laboratory considerable payments for work done for other Government departments and industry were received in respect of fire research (£143,330), the National Chemical Laboratory (£104,716), the Geological Survey and Museum (£97 527) road research (£59 182), hydraulics research (£44 710), building research (£33 879) and mechanical engineering research. Contributions to European nuclear research increased from £20,000 to £1,100,000 and of the grants for special researches authorized during the session October 1 1957, to September 30, 1958 by far the largest is the £355 000 over four years from January 1 1958 to Prof C O Butler of the Imperial College of Science and Technology for the construction of a large liquid hydrogen bubble chamber.

ROTHAMSTED EXPERIMENTAL STATION

REPORT FOR 1958

THE report of the Rothamsted Experimental Station for 1958* is a book of 283 pages containing accounts of the work of some twenty separate departments. It follows the pattern of previous years in that it is introduced by a general report by the Director in which the more interesting departmental results are commented upon. This is particularly valuable in that it enables the reader to appreciate something of the scope and cohesion of the Rothamsted work and those who frame the Station policy are to be commended on the blend of science and practice that characterizes the research programmes. Their reward is the use made of their results in the practical world of farming in Britain and overseas.

The Chemistry Department has studied the action of organic matter in the soil, and popular conceptions of this may have to be somewhat modified in that in heavy soil, as at Rothamsted its beneficial action appears to be derived solely from its nutrient content and no measurable effect from physical sources was found. By contrast, in lighter soils organic matter is apparently necessary to maintain structure. Work has continued on the main plant nutrients in soil and, in particular, attempts are being made to evolve a more accurate method of assessing available phosphate. Soil analysts would welcome progress in this matter.

The Physics Department has studied the electrical charges on clay, soil aeration, soil water, and the effect of crop rotation on soil structure. This last experiment showed that using beet and carrots as the test crops the effect from modification of structure due to rotation was largely confined to the period during and immediately following seed germination. This again may surprise practical growers. Studies in agricultural meteorology have continued and progress has been made with the analysis of temperature, humidity and ventilation data in spring wheat collected during the three summers 1955-57. A detailed survey is promised in a later report. The microbiological studies of the Pedology Department have been continued on native and foreign soils and the results as they accumulate, may well lead to a sounder basis for soil classification.

Microbiological investigations have dealt with the decomposition of cellulose and some of the newer chemicals used in agriculture. Many of these have proved to be subject to attack and therefore will be removed from the soil in time, a point of considerable practical importance. Aspects of nodule formation on legumes have also received attention. Although it has long been known that nitrate at the concentrations usually employed in nutritional work will depress nodulation, it was found that as little as 2.5 p.p.m. of nitrate nitrogen would delay nodulation of white clover by two days. A similar effect was given by nitrite but not by ammonium salts, asparagine, or urea, all of which are assimilated by the host plant at about the same rate.

The Botany Department at Rothamsted has been interested for some time in the development and use of methods of growth analysis and these are now producing information on various aspects of crop growth. Gibberellic acid was found to increase the yield of potatoes in the year under review. This effect was only observed when nitrogen was high, and spraying actually reduced yields when this element was low. Additional data suggest that the effectiveness of gibberellic acid depends also upon the time and frequency of application. Weed studies reported upon include an evaluation of competition effects between crop and weed plants and the possible excretion of toxic substances by *Agropyron repens*. No evidence of this was found in living material; the leachate from water cultures of this grass, in fact, actually increased the dry weight and leaf area of tomato and kale plants.

The blackening of potatoes on boiling was the subject of a biochemical study that supported the belief that this discoloration is due to a complex of ferric iron and dihydroxy phenols. Boiling is believed to liberate ferrous iron which combines with the dihydroxy phenols in the potato to give relatively colourless ferrous complexes which blacken when oxidized in the air to ferric complexes. Other work in this Department concerned mitochondria, the enzymic breakdown of chlorophyll in plant tissues and the properties, particularly the infectivity, of tobacco mosaic virus fragments.

* Rothamsted Experimental Station Report for 1958. Pp 283 (Harpden: Rothamsted Experimental Station 1959) 10s.

Research in plant pathology covers a wide field. Progress has been made in devising staining methods for preparations of plant viruses for electron microscopy at high resolution. This is new work, but enough progress has been made to encourage the hope that the methods will contribute usefully to the further elucidation of particle structure. The increasing importance of cereal viruses in agriculture adds to their interest, and useful information on infectivity and host ranges has been obtained. Experiments on initial field establishment of potato blight (*Phytophthora infestans*) have shown that this may occur without the normal stem-infecting stage. It is likely, however, that infection from contaminated soil can only occur in a wet season such as 1958. Trials on the susceptibility to wilt (*Fusarium oxysporum f. pisi*) of pea varieties commonly grown in Britain have shown that resistance exists, but the parasite itself is so variable that the breeding of resistant varieties will not be easy.

The Nematology Department has conducted studies on the changes in eelworm populations under different rotations and individual crops. These together with concurrent observations on the movement of eelworms in soil and over plants should interest those concerned with the control of these pests in the field. Frit flies, gall midges, wheat bulb fly, slugs and earthworms are included in the wide range of animals

studied by the Entomology Department. A short section deals with the ecology of the natural enemies of aphids. The Bee Department, as a result of improved methods of assay, has learned more of the nature and function of 'queen substance' produced in the mandibular glands of queen honey bees. It has been shown that 'queen substance' contains an inhibitor which, when fed to queen honey bees, can prevent them from queen rearing and which can also inhibit ovary development in queenless worker honey bees.

As a result of the disastrous epidemic of virus yellows of sugar beet in 1957, the staff of the Dunholme Field Station organized a survey of crops and issued spray warnings when needed. As a result, 100,000 acres were sprayed with very satisfactory results when compared with unsprayed areas in September. The value of spraying against aphids to check the spread of virus yellows is now firmly established.

This account has necessarily omitted much worthy of mention, but it is impossible, in a short review, to do justice to all the work described in this report and the selection of items for particular mention here is obviously open to criticism. The extremely useful list of publications for the year 1958 each with an abstract of the contents, with which the report closes, is a fitting indication of the value of Rothamsted to biology and agriculture alike. J. H. WESTERN

AUSTRALIAN DEFENCE STANDARDS LABORATORIES REPORT, 1957

THE main sections of the annual report of the Australian Defence Standards Laboratories for the year ended June 30, 1957 (Pp. iv+60. Melbourne, Victoria: Defence Standards Laboratories, Department of Supply, 1959), are devoted to a statement of the functions of, and scope of work undertaken by, the Laboratories and descriptions of some of the more important projects and investigations carried out by the Divisions of Chemistry, Metallurgy and Physics.

In the Metallurgy Division work has continued on the production and investigation of chromium-base high-temperature alloys. The ultimate aim is to develop alloys suitable for use in gas turbines operating at rotor blade temperatures of 950°C or higher. The plant for the production of pure chromium has operated satisfactorily and a total of 475 lb of metal was produced during the year. It has been shown that ductile chromium can be made from suitably pure electrolytic chromium. Investigations included experiments on the tensile properties of annealed chromium, the influence of pre-strain on ductility, precipitation hardening effects and creep behaviour. A fractographic study, augmented by X-ray diffraction tests, was made of the cleavage surfaces in cast chromium. In addition, work has been done on titanium alloys, cathodic protection of ships and naval structures, and the mechanism of polishing and the nature of mechanically polished metal surfaces.

The activities of the Physics Division are discussed under the headings of chemical physics, radiological physics, the development and testing of electrical and electronic components for use by the armed services, and metrology. The study by the micro-

wave interferometric technique of the propagation of detonation has been most fruitful. Radiation alarm systems and other safeguards against the mishandling of radioactive sources have been developed and work has continued on the determination of the energy and angular distributions of the radiation intensity in air at various distances from a point radioactive source. Facilities for the precise calibration of end standards of length have been improved, and standardizations of lengths up to 40 in based on the wavelength of light can now be made. A technique has been developed for determining the mean diameters of capillary tubes by the mercury content method to an accuracy of 0.00004 in.

The Chemistry Division has been active in a variety of fields, including the determination of gases in metals and alloys, the microdetermination of silicon, infra-red spectroscopy, adsorption, and organic and polymer chemistry.

The annual report lists the various personnel of the Laboratories and their status, and gives details of the publications by members of the staff during the year under review. Papers were presented by members of the staff to the thirty-second meeting of the Australian and New Zealand Association for the Advancement of Science held at Dunedin during January 1957 and to the Institute of Physics Conference on Contemporary Optics in Sydney during September 1956. Noteworthy visitors to the Laboratories during the year were Sir Owen Wansbrough-Jones, chief scientist of the British Ministry of Supply, and Sir Leslie Martin, chairman of the Australian Defence Research and Development Policy Committee.

THE IMPERIAL CANCER RESEARCH FUND

THE fifty-sixth annual report of the Imperial Cancer Research Fund*, for 1957-58, describes the lines of investigation in progress in the laboratories at Mill Hill and Lincoln's Inn Fields. They can be sub-divided as follows:

(1) *Tumours induced by viruses*

Work continues on the virus aetiology of cancer by studying the mechanism whereby the virus gains access to the cell it infects, the virus's mode of replication and its specificity. Attempts are being made to grow the mouse leukaemia inducing virus in tissue cultures of embryo fibroblasts, and by reciprocal transplantation experiments to find whether the cellular elements in such transplants survive or whether virus is liberated to produce a new tumour by infection of the host's own cells.

(2) *Tissue culture studies of tumour cells*

The reaction of tumour cells to environmental changes is being studied by observing the effect of variation in the tension of carbon dioxide on cells of the mouse sarcoma 37.

The activities of individual cells in culture of the various mouse tumours are being examined by time-lapse cinematography. BP/80 and BAS/50 ascites tumour cells show 'tails' which may attach to the glass and which have great tensile strength and elasticity. The undulating surface membranes of these cells show very active pinocytosis and unusually large volumes of culture medium may be injected in this way.

(3) *Preservation of tumours in the frozen state*

The frozen tumour bank preserves tumours in an unaltered genetic state and these can therefore be used to check the respective inbred strains of mice for any genetic divergence which affects histocompatibility. In this way it has been shown with a strain A specific tumour, not only that A/G mice are genetically distinct from true A but that the genetic change occurred prior to 1932.

(4) *Heterotransplantation of human tumours*

Human sarcoma tissue is being maintained by subcutaneous, intramuscular or intraperitoneal trans-

plantation in cortisone treated hamsters, subcutaneously in cortisone treated mice and in the anterior chamber of the eye in normal guinea pigs. The attempts to grow human lung cancer in guinea pig anterior chamber or in organ cultures were unsuccessful, but 25 per cent of human embryonic lung tissue grafts survived 22-49 days in mice treated with cortisone.

Other human embryonic tissues such as bone and bowel, some human adult tissue, for example skin and transitional epithelium, and human prostatic carcinoma and adult rodent lung and prostate have all been maintained in fluid media. Organ cultures of mouse prostate have been employed to study the direct action of oestrogens and androgens on glands from mice of different ages. The oestrogens produced epithelial atrophy and testosterone a stimulation.

(5) *Hormone-dependent breast cancer*

About 60 per cent of human breast cancers cease to proliferate if they are totally deprived of the hormones which control cell multiplication in the normal breast. At present the operative technique of cutting off the supply of hormones is by the surgical removal of the ovaries, both adrenals and the pituitary. This somewhat drastic treatment may give spectacular growth regression and clinical improvement, but unfortunately these have proved to be temporary.

(6) *A pregnancy-dependent mouse tumour*

The spontaneous mammary tumour BR6 has the peculiarity of always first appearing during pregnancy and mostly regressing after parturition. The tumour incidence is very high (in excess of 97 per cent in more than 400 mice that lived longer than six months, had more than two litters and where the mothers had developed tumours). Under certain conditions some females not only remain tumour free but give rise to tumour free sub lines which "appear from transplantation experiments to be genetically different from the tumour prone line and one aspect of this genetic difference may be a greater androgen production by the males of the tumour prone line".

I. HIGGINS

* Imperial Cancer Research Fund. Fifty-sixth Annual Report, 1957-1958. Pp. 59 (London: Imperial Cancer Research Fund 1959).

BEHAVIOUR OF SEA URCHINS

MANY of the habits of sea urchins were observed by A. N. Sinclair during day and night diving in the waters around Sydney with members of the Underwater Research Group of New South Wales. An aqualung and a waterproof torch were used (*Austral Mus. Mag.*, 13, No 1, March 16, 1959).

When diving in daylight Sinclair was impressed by the numbers of the large rough spined sea urchin *Centrostephanus rodgersii*. Many of these were seen in hollows carved in the sandstone rocks, and often the hollows were deep enough to contain the whole urchin, but were never as deep comparatively, as the sharply etched hollows carved by the smaller urchins *Helocidaris erythrogramma*. Other urchins appeared to be motionless, with the spines sticking

out at right angles to the body surface in a typical 'hedgehog', or defence, position.

It was found that after darkness set in the urchins became active. Within an hour or two of sunset numbers of *Centrostephanus* were seen 'out walking' on the rocks but they did not seem to favour walking on the sand. The spines at such times were generally arranged in groups or cones. If a torch was shone on the urchin for a short time no reaction to the light could be observed, but if the urchin was touched it immediately assumed the 'hedgehog' position seen in daylight.

Results of marking specimens of *O. rodgersii* in Clovelly Bay, Sydney had shown that the urchins moved up to 3 or 4 ft. from their rock holes within

two hours of sunset and returned to their own holes by the next morning, though often each was lying turned round from its original position.

During daylight it was common to see vacant rock holes, which, by the absence of weed growth, appeared to have been recently vacated. Usually, however, these holes were again occupied within a week, but tagging techniques had been inadequate to reveal whether the occupants were the original ones or newcomers.

Unlike most of the finer-spined urchins, the slate pencil urchin, *Phyllanthus parvispinus*, appeared not to live in holes, preferring crevices between rocks. In more than 200 sightings of these urchins, only one had been seen in a spherical rock hole. Most were in crevices, during daylight, but were so securely wedged in that they could only be moved by breaking spines. Other haunts of the slate pencil urchin were on the floor of forests of weed or kelp. Like *C. rodgersi* these urchins seemed to prefer deeper water and were more numerous in 20–30 ft of water. Although each slate pencil urchin did not have its own particular rock hole, it returned to a particular locality.

The slate pencil urchins went out 'walking' at night, often covering 1 ft in 20 min, and were seen attacking whelks bigger than themselves.

The commonest urchin at shallow levels within about 6 ft of the surface was *Heiodidaris erythrogramma*. This was the dominant species, and practically the only urchin present in the intertidal zone. It lived in crevices and holes in the rock, which could be almost honeycombed. It appeared to dig

holes much deeper in relation to its size than any other species. This urchin appeared in many colours: greens, reds, browns and purples, a new one being revealed at almost every dive. The spines were smooth and relatively short. One of the most interesting combinations of spine shape and colour in this urchin was in the blue or mauve specimens.

Tripneustes gratilla, a wanderer from tropic seas, apparently had the distinctive habit of being unconcerned with the need for shelter. It was usually found on the walls of caves or in the open many yards from the nearest shelter. It was a large-bodied urchin with very short white spines tipped red or mauve. The rounded body had a plain darkish colour, or was white with five darker major bands and five secondary bands. Some of these urchins carried small pieces of shell or weed, presumably for sheltering from the light. *T. gratilla* was usually seen at depths of 10 ft or more.

Most of the useful observations made by diving were of an ecological, rather than a systematic, nature, and an observation ledge had been carefully watched at frequent intervals during the past seven months, however, other observation points will be established after a twelve months period has been completed. A handicap to observation was that many local residents had developed a taste for eating sea urchins and the colony risked extinction.

In summer the colony comprised twenty *C. rodgersi*, one *H. tuberculata*, and one *P. parvispinus*. By early July the numbers of *C. rodgersi* had fallen to fourteen, and later in the month had been reduced to ten.

JOURNAL OF APPLIED POLYMER SCIENCE

THE study of polymeric systems originated largely from technological considerations, but has now grown into a scientific subject in its own right, with its own techniques and outlook. This change has occurred in a very short time, and its rate of growth can be illustrated by the increasing size of the *Journal of Polymer Science*, which attracts contributions from both chemists and physicists interested in the preparation and properties of these interesting materials. From the original *Polymer Bulletin*, published in 1945 with 158 pages, it has progressed stepwise: 1946–50, 598 to 800 pages; 1951–54, 1460 to 1,864 pages; 1955–57, 2,432 to 2,420 pages; 1958, 4,256 pages. This seven-fold increase in thirteen years shows no sign of slowing down, and the publishers have therefore decided, as a transition measure, to split the journal, the original journal to continue, but in addition to publish the *Journal of Applied Polymer Science**. The latter is intended to deal with the properties of industrially significant materials, leaving articles of a definitely basic character to the original *Journal*.

It is difficult to see how this distinction can be maintained. The first number of the *Journal* includes papers on such basic matters as thermal expansion and transition temperatures, impact

strength and spherulite growth, and anisotropic properties of strained viscoelastic fluids. Perhaps a better grouping of subject-matter would be—preparative techniques, physical properties, characterization and constants, and applications.

The present tendency for publication of specialist journals, as distinct from the journals of learned societies of wider scope, must be taken as an inevitable consequence of increased specialization. Although it may facilitate the task of the scientist wishing to keep together papers on his own research subject, it has made it almost impossible for him to pay for the subscriptions. The stage has been reached where even the smaller scientific libraries cannot hope to purchase more than a small fraction of these specialist journals. This situation is likely to worsen, and the research man will have to visit large central libraries, or rely on abstracts to track down new papers of interest to him. Perhaps one solution is for the smaller libraries to pool some of their resources on a local basis, by arranging regular circulation through several laboratories. In any event one would like to see an extension of the system of reduced rates for personal copies. The increased cost cannot be blamed on the publisher, the cost per page has remained constant at 2.5 cents since 1952. The new *Journal* is somewhat larger in page size than the earlier publication, and this has improved the presentation and layout.

* *Journal of Applied Polymer Science* Vol. 1, No. 1, January–February, 1959. Pp. 127. Published bi-monthly covering two volumes annually. Subscription price 17.50 dollars per volume (New York and London: Interscience Publishers Inc., 1959).

MEASUREMENT OF COSMIC NOISE AT LOW FREQUENCIES ABOVE THE IONOSPHERE

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THE Canadian Defence Research Board, in co-operation with the National Aeronautics and Space Administration is at present designing a 2-15 Mc/s swept-frequency ionosphere sounder to be launched as an Earth satellite by a United States vehicle. The preliminary design objective calls for operation over a one year period in an elliptical orbit with a perigee and apogee of 300 and 1,200 miles, respectively. Power will be derived from the Sun via solar cells and nickel-cadmium rechargeable batteries.

System studies have shown that cosmic noise is likely to be an important factor in determining the minimum sounding power for a satisfactory signal to noise ratio. Published figures for cosmic noise at 3 Mc/s give brightness temperatures varying between 7×10^4 °K and 120×10^4 °K.^{1,2} Measurements on the Earth's surface particularly at such low frequencies, inevitably involve assumptions concerning transmission losses through the ionosphere and for frequencies less than approximately 15 Mc/s the accuracy of existing data on cosmic noise is questionable.³ A direct measurement of this noise using either a rocket or satellite is therefore indicated, and the results obtained would have the added merit of being of considerable interest in the field of radio astronomy.

Ground based radiometers have been described by several authors⁴⁻⁶ and design techniques appropriate to the ground environment are by now well established. By comparison, a radiometer for use in a sounding rocket or a satellite is severely limited in its dimensions, weight, and power consumption. In addition, it must also survive the mechanical and thermal shocks associated with a rapid ascent through the Earth's atmosphere.

It is found that the successful instrumentation of such a radiometer depends critically on the design of a suitable low frequency aerial and reference noise source. The use of one or more Hertzian dipoles on a space vehicle, poses a formidable aerial calibration problem which becomes increasingly serious as the frequency is reduced. This approach was therefore abandoned in favour of the magnetic dipole which is easier to calibrate since it is relatively unaffected by the proximity of the ground or other conducting surfaces.

Optimum utilization of a given volume of ferrite has been investigated, and it is of interest to consider the design and efficiency of a pair of loop aerials at 3 Mc/s using 300 gm of ferrite.

Two 18 cm \times 3 cm \times 1 cm rectangular cores, each made up of three plates of ferrite were spaced so that each winding covered 80 per cent of the length of its ferrite core. The calculated radiation resistance of each aerial was

$$4 \times 10^{-4} \Omega$$

and was found to be negligibly small compared with the equivalent series resistance due to core and copper losses

For a bandwidth of 80 kc/sec and with the two aerials connected in series, the power available at the input terminals of the receiver is

$$4E^2 \times 10^{-14} \text{ watts}$$

where E is in $\mu\text{V/metre}$. This power is 30 db below that available from a matched, lossless half wave dipole.

Transistor receivers with equivalent input noise temperatures of 300° K at 3 Mc/s have been constructed and if the brightness temperature of the cosmic noise is 120×10^4 °K, the signal to noise ratio of the receiver output will be 11 db. This includes an additional aerial loss of 3 db due to the random polarization of the noise.

Errors due to changes in the gain and band width of the receiver are reduced by continuously switching the receiver input between the aerials and a reference noise source. At the output terminals of the receiver the ratio of the switched power levels is

$$\frac{G(P_N + P_{A1})}{GP_{N2}} = \frac{P_N + P_{A1}}{P_{N2}}$$

and is independent of the receiver gain (P_A is the noise power from the aerials, P_{N1} is the equivalent input noise power due to the receiver when connected to the aerials, P_{N2} is the input noise power due to the receiver and reference noise source when the aerials are disconnected, and G is the power gain of the receiver). The addition of an AGC loop increases the dynamic range of the receiver to approximately 50 db and converts the output into a voltage suitable for telemetering to the ground. If the AGC time constant is short compared with the period of rotation of the rocket or satellite the existence of directional properties in the cosmic noise may be observed.

The overall accuracy of the instrument depends largely on the stability of the reference noise level and the accuracy with which the aerials can be calibrated on the ground. An avalanche diode is used as a reference noise source and its case temperature is monitored on a separate telemetry channel. Laboratory tests on this radiometer indicate an overall probable error of less than ± 2 db in the measured cosmic noise intensity.

Errors due to atmospheric and man made interference (including radiation from ground based transmitters) will be negligible at frequencies less than the minimum penetration frequency of the F_2 layer. Since the radiometer will be operating in an ionized medium the electron density in its immediate vicinity will set a lower limit to the frequency at which cosmic noise can be measured. In practice, this low frequency cut off will be modified by the Earth's magnetic field and may also be higher than the local plasma frequency if regions of increased electron density exist above the radiometer. At very high altitudes it is possible that the Van Allen belts may play a significant part in filtering out the low frequency end of the cosmic noise spectrum.

A prototype radiometer is undergoing vehicle acceptance tests and the final instrument is expected to make the first measurements of cosmic noise above the ionosphere at 3 Mc/s in the near future.

The sensitivity and accuracy of the radiometer could be improved by having a controllable noise source and using the receiver as a null detector, a technique widely used on the ground. A silicon diode operating in the avalanche mode generates noise, the level of which can be controlled by varying the diode current flowing through the diode⁸. Thus, one has a semiconductor analogue of a temperature-limited diode, and radiometers of the type described by Ryle⁹ become practicable for space vehicles.

The experiment will be extended at a later date to observe changes in the cosmic noise-level with frequency using a swept-frequency receiver. By observing the wave-length at which the noise level starts to increase rapidly, plasma frequencies, and therefore electron densities, can be deduced at various heights over different parts of the world from a satellite travelling in an elliptical orbit.

¹ National Bureau of Standards Circular No. 557 (1955)

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SURFACE TOPOGRAPHY OF THE ANTARCTIC ICE SHEET

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IT has been reported by Lister and by Pratt^{1,2} that the surface of the Antarctic ice sheet over much of the route of the Trans-Antarctic Expedition consists of a series of undulations with wave-lengths of 5–30 km and a mean amplitude of about 20 m. In this respect the surface differs markedly from that of the Greenland ice sheet, which, except near the margins, is generally much more uniform^{3,4}. The question then arises as to whether the undulations seen in Antarctica are due to some effect of wind, which causes the snow to accumulate preferentially in certain places, or whether they are the result of unevenness in the rock bed upon which the ice sheet lies. The following analysis leads to the conclusion that the latter explanation is the right one, and that we may hope to discover much about the topography of the bed simply by an inspection of the surface.

Owing to the higher temperature of the lower layers of ice, and the large effect of temperature on the creep rate of ice, the outward motion of the ice sheet probably takes place almost entirely by sliding on the rock bed (combined with rapid shearing in a very thin layer at the bottom)⁵. The velocity of sliding u will depend on the shear stress τ at the interface, the effective roughness of the bed, and the temperature (and possibly on the hydrostatic pressure). At a given place on the bed let us assume that

$$u = \left(\frac{\tau}{A}\right)^m \quad (1)$$

where A and m are constants. According to Weertman's calculation⁶, which is appropriate where the ice in contact with the rock is at the pressure melting-point (which may be the case in parts of Antarctica), the value of m is 2 or 2.5 – is given approximately⁶ by $\rho g h \alpha$, where ρ is the mean density, h is the thickness, and α is the (small) slope of the upper surface averaged over a distance $\sim h$. Hence

$$u = \left(\frac{\rho g h \alpha}{A}\right)^m \quad (2)$$

u at a point is thus determined by the slope of the upper surface and the thickness at that point. On the other hand, in a steady state, where the accumulation of snow on the upper surface is just balanced by the outward flow, u is also determined by the rate of accumulation of snow, integrated between the place

under consideration and the 'centre' of the ice sheet. This makes it possible, in principle, to calculate the steady-state profile of the upper surface, and with certain simplifying assumptions, such as uniform roughness of the bed, some analytical solutions can be derived⁴.

Our present concern, however, is with departures from the steady state, and here the appropriate analysis has already been performed by Weertman⁷. He uses equation (2) and considers an ice sheet moving down a uniform plane bed of slope β in the direction Ox ; the assumption of uniform slope is not in fact necessary, and we may put β a function of x without altering the result. (The effect of non-uniform roughness is treated in ref. 4.) In the steady state, the thickness is $h_0(x)$, the velocity is $u_0(x)$, and the thickness of ice added at the upper surface per unit time is $a(x)$. We put $dh_0/dx = -\varphi_0$ (φ_0 is positive) and $\alpha_0 = \varphi_0 + \beta$, so that α_0 is the steady-state slope of the upper surface. Let there now be a departure $h_1(x, t)$ from the steady-state thickness, where $h_1 \ll h_0$, $\partial h_1/\partial x \ll \varphi_0$, $\partial h_1/\partial x \ll \alpha_0$, $\partial^2 h_1/\partial x^2 \ll dx_0/dx$. Weertman then shows, solely from equation (2) and an equation of continuity, that the subsequent history of this perturbation is given by

$$\frac{\partial h_1}{\partial t} = -Bh_1 - C \frac{\partial h_1}{\partial x} + D \frac{\partial^2 h_1}{\partial x^2} \quad (3)$$

B , C and D being fixed by the steady-state parameters as follows

$$\left. \begin{aligned} B &= (m+1)(\varphi_0 u_0 + a)/h_0 \\ C &= \{(m+1)(\alpha_0 + \varphi_0)u_0 - (m-1)a\}/\alpha_0 \\ D &= mu_0 h_0/\alpha_0 \end{aligned} \right\}$$

The three terms on the right in equation (3) have simple meanings⁷. The term $-Bh_1$ represents an exponential decay with a time constant B^{-1} . Putting $m = 2.5$, $h_0 = 3,000$ m, $u_0 = 20$ m/yr, $\varphi_0 = 3 \times 10^{-3}$, $a = 0.1$ m/yr gives $B^{-1} = 5,000$ yr. This term is concerned with departures from the equilibrium thickness, rather than from the equilibrium slope. It shows that such departures, extending, as we shall see, over long distances comparable with the size of the whole ice sheet, can persist for several thousand years—long, that is, compared with the period for which the rate of accumulation can be

considered steady. The term $-G\partial h/\partial x$ represents a travelling wave of constant h , moving with a velocity C . This wave is akin to the kinematic waves of Lighthill and Whitham.¹ Putting $\alpha = \varphi_0$ and the other values as before gives $C = 0.0 \text{ m}/\text{yr}$. (We may note in passing that for small α , C can be negative—that is, the wave can travel upstream. This happens up to distances of about 200 km from the centre.) The term $D\partial^2 h/\partial x^2$, which is the one of primary interest in the present application, represents an outward spreading and broadening of an initial disturbance in accordance with the diffusion equation. The characteristic time for the diffusion process will depend on the length of the waves. If there are surface waves of wave length λ , the characteristic time will be $(B + \frac{4\pi^2 D}{\lambda^2})^{-1}$. Putting in numerical values

as before and taking $\lambda = 12 \text{ km}$ (the mean observed wave length), we find the time to be 0.07 yr (B is negligible here). Thus surface waves as short as 12 km will disappear in a matter of months. In order to survive for one year a wave would need to have $\lambda > 40 \text{ km}$, and for 10 years, $\lambda > 140 \text{ km}$. A wave with $\lambda/2$ equal to the width of the ice sheet say, 3 km, and waves with $\lambda \ll 3 \text{ km}$ —as a result, for example—will not be eliminated by the above mechanism. Thus we conclude that departures from the equilibrium form of the ice sheet cannot survive for longer than one year if their wave lengths are between about 3 (or less) and 40 km.

The physical reason for this result may be explained as follows. The upstream side of a crest will have a smaller slope than normal, and the downstream side will have a greater slope. This causes a greater shear stress on the bed, and therefore a greater velocity, on the downstream side. The crest is therefore stretched and flattened. If, however, the crest is narrow compared with the depth of the ice sheet, as in a strugli, the changes of slope do not affect the shear stress on the bed, and so the crest survives. At the other extreme, if the crest is very extensive the additional curvature of the surface is so slight that a long time is needed to eliminate it. Between these two extremes there is a range of wave lengths where the crests disappear in times less than one year.

It follows from this analysis that, if comparatively long lived undulations are observed in the range of wave lengths where waves are quickly eliminated, they cannot be departures from the equilibrium profile but are the result of the topography of the bed. This conclusion, from purely mechanical reasoning, will apply to the surface waves with $\lambda \sim 12 \text{ km}$ seen in Antarctica provided the waves cannot build up by preferential accumulation in very short times. According to the above figures they could only be due to preferential accumulation if they were built up within a few months—and this seems exceedingly unlikely in view of the measurements of annual accumulation interpreted from cores drilled on the waves by the Trans-Antarctic Expedition during the crossing.¹⁴ Incidentally, if our conclusion that the waves are the result of bed topography is correct, one might expect to find the accumulation rather greater in the sheltered hollows than on the exposed crests, and this does appear to be the case.¹⁵

We must now ask how the topography of the bed will influence the surface. If m were infinite, equation

(1) shows that the velocity of sliding would be zero up to a critical shear stress A , and when $\tau = A$ u could take any value. Putting m infinite in fact leads to the older theory² in which τ was regarded as constant everywhere on the bed of an ice sheet. In this approximation therefore h is proportional to $1/\alpha$. Using this approximation, Bourgoin⁴ has succeeded in making a detailed correlation between the very slight relief of the surface of the Greenland ice sheet and the relief of the bed measured by seismic sounding. He found that an unevenness of the surface of as little as 10 m between two points 30 km apart denoted the presence of a hill in the bed rock about 350 m high. This theory can now be improved by using the more general relation (1) in which m is finite and which allows for changes in τ . It is then found⁴ that a hill on the bed of height p , where $p \ll h$, produces (a) a change in height of the surface which is an order of magnitude less than p , (b) a change $\Delta\alpha$ in surface slope where

$$\frac{\Delta\alpha}{\alpha} = \frac{m+1}{m} \frac{p}{h} \approx 1.4 \frac{p}{h} \quad (4)$$

and (c) a change $\Delta\tau$ of shear stress on the bed where

$$\frac{\Delta\tau}{\tau} = \frac{1}{m} \frac{p}{h} \approx 0.4 \frac{p}{h} \quad (5)$$

Thus a mountain 300 m high covered by ice 3 000 m thick shows itself as a change in height of the surface small compared with 300 m (as verified by Bourgoin's work), a change in surface slope of 14 per cent and a change of shear stress on the bed of 4 per cent. The smallness of this last figure is the reason for the success of the older theory in which τ was regarded as constant.

In order to deduce the height of a buried mountain from the change of slope of the surface that it produces we write (4) as

$$p \approx \frac{m}{m+1} \frac{h\Delta\alpha}{\alpha} \approx 0.7 \frac{h\Delta\alpha}{\alpha} \quad (6)$$

The value of p deduced by putting m infinite is $h\Delta\alpha/\alpha$. Thus with the new theory, which allows τ to vary, we deduce values of p which are 70 per cent of those deduced on the older theory. Generally speaking the accuracy of the seismic methods used in Greenland (and Antarctica) is not yet sufficient to check this change in the theoretical prediction.

The fluctuations of surface slope observed in Antarctica are comparable with the average slope itself, and it follows from (4) that the heights of the submerged mountains are a large fraction of the total thickness of the ice sheet. We are thus left with the conclusion that the surface waves in Antarctica small as they are, reflect a very considerable relief of the rock bed—a relief which is already becoming apparent from the seismic and gravity work. Greenland is very different there the bed is comparatively uniform in the regions so far studied, and this shows itself in the extreme uniformity of the surface.

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NUCLEOTIDE-PEPTIDE COMPOUNDS OF *SACCHAROMYCES CEREVISIAE*

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Synthetic 'Active' Nucleotide-Peptide Compounds

THE recent demonstration¹ of the presence in strains of *Saccharomyces cerevisiae* of nucleotide-peptide compounds containing an active carboxyl group in the peptide moiety and the isolation of individual compounds of this nature², which may function as protein precursors, made it clearly desirable to prepare model 'active' compounds.

Methods already available³⁻⁶ for the synthesis of the related amino-acid adenylates have therefore been applied to the elaboration of certain nucleotide-peptide compounds. For example, application of the method of Berg³, as modified by Kingdon *et al.*⁴ to the condensation by means of dicyclohexyl carbodiimide in aqueous pyridine of adenylic acid with leucylglycine, has yielded a mixed nucleotide-peptide anhydride, although only in small yield. The crude product was obtained from the reaction mixture by precipitating it by means of acetone, extracting the dried precipitate with weak acetate buffer at pH 4.0 and removing contaminating adenylic acid and polymers by adsorption of these impurities on 'Dowex-1' (formate). It was further purified by chromatography on Whatman 3MM paper in the solvent system, *n* propanol-ethyl acetate-water (7:1:2, v/v), elution with cold water and evaporation of the resulting solution in the cold.

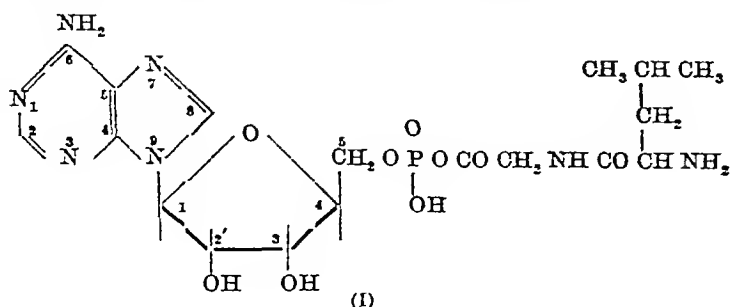
The product had an *R_F* value of 0.20 in the above chromatographic solvent and was therefore well differentiated from unchanged leucylglycine having an *R_F* value of 0.32. It gave a characteristic red coloration with ninhydrin reagent on paper and a strong red-brown coloration due to the formation of a ferric hydroxamate on treatment with hydroxylamine followed by ferric chloride under the conditions recommended by Koningsberger *et al.*¹ These colour reactions and the behaviour of the compound on 'Dowex-1' (formate) resemble closely those given by the corresponding products from yeast. With the latter, the synthetic compound shares also the further characteristic properties of migrating towards the cathode on electrophoresis on paper in acetate buffer at pH 4.0 and of having an ultra-violet absorption spectrum of the type given by the corresponding nucleoside. From a consideration of its properties, the mode of synthesis and the fact that the compound yielded on hydrolysis equimolar proportions of

adenine, ribose, phosphoric acid, leucine and glycine, it may be deduced that the nucleotide-peptide has the structure (1). This resembles closely certain of the yeast constituents which, however, contain uracil in place of adenine, and it is of interest to record that replacement in the above synthesis of adenylic acid by uridylic acid results in the formation of a product of very similar properties with the exception that it is less readily desorbed from 'Dowex-1' (formate). Again, the substitution of the tripeptide DL-leucylglycylglycine for the above dipeptide yields analogous products, and present efforts are therefore being made to extend the synthesis to certain of the naturally occurring nucleotide-peptide compounds.

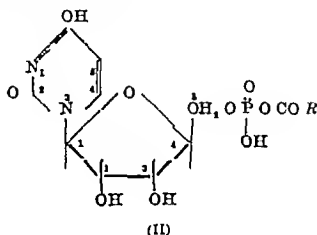
A Second Nucleotide-Peptide Compound from Brewers' Yeast: Isolation and Structural Observations

THE initial discovery² of a nucleotide-peptide compound in cold ethanol extracts of a brewer's yeast and the possibility that such compounds might play a part in protein synthesis prompted a search for other substances of this nature. It has now been observed that extraction of *Saccharomyces cerevisiae* (No. 240 of the British National Collection of Yeast Cultures) by means of hot aqueous ethanol, following inactivation of the cells with cold ethanol and ether, yields a mixture containing several nucleotide-peptide compounds. Treatment of the extract with 'Dowex-1' (chloride) resulted in adsorption of certain of these compounds among others on the resin, while desorption of some of the adsorbed material was achieved by treatment of the resin with acetate buffer solution at pH 5.0. The concentrate thus obtained was freed from various nucleotides, peptides and amino-acids by successive adsorption of these compounds on 'Dowex-1' (formate) and 'Amberlite CG 50' (acid form) and was then subjected to electrophoresis in acetate buffer at pH 4.0 on Whatman No. 3 paper. Elution by means of cold water of that material on the final electropherogram which had the properties of (a) migrating towards the cathode, (b) reacting with hydroxylamine to form a hydroxamic acid^{1,2}, and (c) yielding a coloration with ninhydrin, gave a preparation, which on freeze-drying and freeing from salt by solution in wet ethanol, followed by precipitation with ether, yielded a homogeneous nucleotide-peptide.

The product migrated as a single narrow band on electrophoresis as above and formed one well-defined chromatographic zone in the solvent systems composed (a) of butanol, acetic acid and water (4:1:1, v/v), and (b) of ethyl acetate, propanol and water (1:7:2, v/v). As indicated above, it formed a hydroxamic acid on reacting with hydroxylamine under the conditions described by Koningsberger *et al.*



al¹ and it gave a red coloration on heating with anhydride. In acid solution, its absorption spectrum displayed maxima at 235 and 265 mμ, the peaks corresponding presumably to the absorption due to the peptide and nucleotide moieties, respectively. The molecule was broken down into its constituent parts by treatment with cold alkalis, for example, sodium hydroxide, aqueous ammonia or hydroxylamine, the nucleotide portion displaying the chromatographic¹, electrophoretic and light absorption properties characteristic of uridine 5' phosphate. The peptide hydroxamic acid formed by treatment of the original nucleotide peptide with hydroxylamine behaved chromatographically as a single substance which on hydrolysis with acid yielded only arginine and α-alanine as judged by chromatography and colour reactions⁸. The treatment with alkalis naturally resulted in the loss of reactivity towards hydroxylamine.



where R represents a tetrapeptide residue consisting of two arginine and two α-alanine units.

The presence of a uridylic acid residue in the nucleotide-peptide compound was confirmed by hydrolysing the latter material (a) with formic acid to produce uracil, itself estimated by ion-exchange chromatography⁹, (b) phosphate¹⁰ (1 mole), and (c) ribose (1 mole)^{11,12}. The composition of the

peptide was ascertained by hydrolysis with hydrochloric acid followed by chromatography on paper. The arginine and α-alanine were eluted by means of dilute acid and estimated by the colorimetric method of Yemm and Cocking¹³, whereupon it was found that the molecule contained two residues each of the above amino acids. The evidence indicates that the nucleotide-peptide now described is a mixed anhydride (II) of uridine 5' phosphate with a tetrapeptide containing two units of α-alanine and two units of arginine. The site of the 'active anhydride' grouping at the 5' position of the uridine 5' phosphate is indicated (a) by the loss of reactivity towards hydroxylamine coincident with fission of the molecule by means of alkalis, (b) the formation of a peptide-hydroxamic acid and (c) by the fact that the compound itself is immediately attacked by periodate thus demonstrating the lack of substituents on the 2 and 3 positions. The close structural relationship between the nucleotide-peptide here described and the mixed 5' phosphoanhydrides of adenosine 5' phosphate with various single amino acids, taken together with the fact that the latter anhydrides are held to be implicated in protein synthesis, suggests that the peptide derivatives also might play a part in cell growth.

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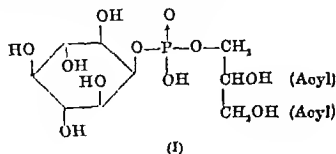
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SYNTHESIS AND PROPERTIES OF 1-GLYCERYL-2-MYO-INOSITYL PHOSPHATE

THE simplest member of the glycerinosityl phosphatides¹ is considered to be a diacyl derivative of 1-glyceryl 2-myo-inosityl phosphate (I)¹⁻⁴, since on hydrolysis it yields glycerol, myo-inositol, glycerol phosphate, myo-inosityl phosphate and fatty acids, the ratio fatty acids: glycerol: inositol, phosphorus being 2:1:1:1.



Although there is strong evidence for formula (I), doubt still exists concerning the position of the phosphate group because of its tendency to migrate to adjacent hydroxyl sites under the conditions of hydrolysis^{5,6}. We have therefore synthesized

1-glyceryl 2-myo-inosityl phosphate for comparison with the natural product. This was kindly undertaken by Dr J N Hawthorne, who found our synthetic product identical with his own specimen isolated from ox liver and with a specimen synthesized by a different route (see second communication).

T. MALKIN

Synthesis of 1-Glyceryl-2-myo-inosityl Phosphate

3,4,5,6-TETRAACETYL-myo-INOSITOL⁷ in pyridine when treated with 1.25 moles of acetyl chloride in benzene yielded 1,3,4,5,6-pentacetyl myo-inositol in 78 per cent yield, shown by mixed m.p. 172–74°C and mixed m.p. of p-nitrobenzoyl esters 232–25°C to be identical with the pentacetate obtained by the stereospecific reduction of pentacetyl-acylo-inositol⁸⁻¹⁰. This pentacetate, when treated with phenylphosphorodichloride 1.1 moles in lutidine at 40°C for 48 hr followed by addition of 1:2 isopropylidene

glycerol, 5 moles, at 50°C, and stirring for 36 hr, gave 1 2-*isopropylidene*-glyceryl-pentacetyl-2-*myo*-inosityl-phenylphosphate, as colourless crystals from ethanol, m p 140–42°C, in 52 per cent yield (found C, 51.0, H, 5.7, P, 4.7. $C_{28}H_{37}O_{16}P$ requires C, 50.9, H, 5.6, P, 4.7 per cent). Hydrogenolysis in ethanol or ethyl acetate, in the presence of Adams's catalyst, removed the phenyl group, and the resultant acidity was sufficient to cause the loss of the *isopropylidene* group, on dissolution in water and standing overnight. Evaporation of the solvent at < 40°C gave the glyceryl-pentacetyl-inosityl-phosphate as a deliquescent glass, which was characterized as the *cyclohexylamine* salt, m p 204°C (found C, 46.2, H, 6.7, N, 2.2, P, 4.7 per cent, $C_{28}H_{42}O_{16}PN$ requires C, 46.6, H, 6.5, N, 2.2, P, 4.8 per cent). Sodium methylate in methanol converted the pentacetyl compound into sodium glyceryl-*myo*-inosityl-phosphate, which was separated in a centrifuge and converted into the free acid by passing an aqueous solution down a column of 'IR 120' resin. Evaporation to dryness at < 40°C gave a deliquescent glass, which was quite unsuitable for characterization or for handling. Sodium, potassium and barium salts were made by passing an aqueous solution of the phosphate down a column of 'IR 120' resin in the appropriate basic form. Both the former are very deliquescent, but the latter is less so and can be handled reasonably well. The removal of protecting groups is carried out with an overall yield of 70–75 per cent.

Since most of the natural glyceryl phosphatides occur in the L-form, we have carried out the same synthesis, using D-*isopropylidene* glycerol¹¹, which yields the L-glyceryl phosphate, but although various optically active intermediates were obtained, the final glyceryl-inosityl-phosphate was inactive. Racemization is, of course, to be expected, once the protecting *isopropylidene* group is removed, because of the phosphate equilibrium between the 1 2-positions of the glycerol, and this appears to be particularly rapid, when all the protecting groups are removed. It is, however, perhaps too early to discuss this aspect of the work in detail, as so little is yet known about the activity of the natural compounds.

L-*isopropylidene*-glyceryl-1 3 4 5 6-pentacetyl-*myo*-inosityl-phenyl-phosphate was made as described for the DL-compound. The m p and mixed m p with the DL-compound are surprisingly the same (140–42°C), $[\alpha]_D^{20} + 2.34^\circ$ C in chloroform, $[\alpha]_D^{20} + 2.4$ in ethyl acetate.

Hydrogenolysis of the above and neutralization with N/10 sodium hydroxide (phenolphthalein) gave sodium L-*isopropylidene*-glyceryl-1 3 4 5 6-pentacetyl *myo*-inosityl-phosphate, $[\alpha]_D^{20} + 3.25^\circ$ C, in chloroform (found C, 43.3, H, 5.2, P, 5.0. $C_{28}H_{32}O_{16}PNa$ requires C, 43.5, H, 5.2, P, 5.0 per cent). Thus, on deacetylation, gave sodium L-*isopropylidene*-glyceryl *myo*-inosityl-phosphate as a deliquescent white powder, $[\alpha]_D^{20} - 1.04^\circ$ C in water.

For comparison with the natural products, we sent the barium salt of glyceryl-*myo*-inosityl phosphate, prepared from D-*isopropylidene* glycerol, to Dr J N Hawthorne. Our own hydrolysis and paper chromatographic comparisons showed it to be identical with that obtained from inactive *isopropylidene* glycerol.

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1-Glyceryl-2-*myo*-inosityl Phosphate: Alternative Synthesis and Behaviour on Hydrolysis

By a mild alkaline hydrolysis of liver phosphatidyl inositol (Formula I, previous communication) the two fatty acids have been selectively removed, and glyceryl-*myo*-inosityl phosphate prepared. After purification on an ion-exchange column, it has been broken down to a mixture of glycerophosphate and inositol monophosphate by hydrolysis with 0.5 N sodium hydroxide at 100°C for 40 min.¹² For comparison with glyceryl-*myo*-inosityl phosphate prepared in this way, a synthetic sample was required. 1-Glyceryl-2-*myo*-inosityl phosphate was chosen for this work.

The method of phosphorylation used in the present synthesis is that which has been developed by Gilham and Khorana¹³ a phosphate monoester and an alcohol, under the influence of dicyclohexylcarbodiimide in anhydrous pyridine, condense together to give a phosphate diester. (This work began before the method of Gilham and Khorana appeared. We are grateful to Dr Khorana for sending details in advance of publication.) This method has not previously been applied to the syntheses of phospholipids or their intermediates.

The alcohol used in the present work was DL-*isopropylidene* glycerol¹¹ and the phosphate monoester was 1 3 4 5 6-penta-acetyl-*myo*-inositol-2 phosphate. This latter compound was prepared by a modification of Iselin's five stage synthesis.⁸ *myo*-inositol was oxidized by *Acetobacter suboxydans* to scyllo-inosose. This was acetylated to its penta-acetate with acetic anhydride containing 0.3 per cent perchloric acid. The catalytic reduction of this compound is difficult¹⁰, presumably because the carbonyl group is sterically hindered and it was eventually found necessary to carry out the hydrogenation in glacial acetic acid. The reaction is not completely stereospecific in this solvent and a mixture of *myo*-inositol and scyllitol penta-acetates is formed. The mixture was phosphorylated with diphenyl phosphorochloridate in pyridine at 80°C for 20 hr. The product, recrystallized from dry ethanol, had m p 183–88°C. The yield was 66 per cent. The phenyl groups were removed by hydrogenolysis in dry ethanol with Adams's catalyst, and the contaminating scyllitol isomer was then removed by fractional crystallization from the concentrated ethanol solution at room temperature, the penta acetyl scyllitol phosphate had m p 249–51°C, yield 5 per cent, the penta acetyl inositol phosphate had m p 230–32°C after recrystallizing from dry ethanol, yield 64 per cent.

DL-*isopropylidene* glycerol (0.5 ml) and penta acetyl inositol-2-phosphoric acid (0.2 mmole) were allowed to react together in anhydrous pyridine (5 ml) with dicyclohexylcarbodiimide (1.5 mmoles) for 2 days at room temperature. Water was added and the precipitated dicyclohexylurea removed by centrifugation. The *isopropylidene* group was removed by stirring with a large excess of 'Zeo-Karb 225' (H⁺-form) overnight. The solution was concentrated to a small volume *in vacuo* at a bath temperature of less than 40°C and the acetyls removed as their hydroxamates. Hydroxylamine was prepared by reaction of its hydrochloride with the calculated amount of sodium metal in dry methanol and added in excess to the phosphate solution. It was allowed to react for 20 min.

The reaction mixture contained 25–30 per cent glyceryl *myo* inositol phosphate, free inositol mono-phosphate, and a third component which is probably *bis* inositol pyrophosphate. These compounds were separated by chromatography on Dowex 1¹ using borate-formate mixtures for elution.¹² The synthetic glyceryl-*myo* inositol phosphate was eluted at the same formate concentration as the natural material. Determination of glycerol by the chromotropic acid method¹³ showed a glycerol to phosphorus molar ratio of 1.0(03)/1.

The synthetic product was subjected to the same alkaline hydrolysis that has been used for the glyceryl *myo* inositol phosphate isolated from the inosinate. The hydrolysate, complexed with borate in the usual manner, was analysed into its components on a Nalcote SAR¹⁴ column.¹⁵ No phosphate was now eluted with the glyceryl *myo* inositol phosphate eluting agent but two peaks appeared in the positions where inositol monophosphate and glycerophosphate are known to occur. Only the second, corresponding to glycerophosphate contained glycerol 31 per cent of the phosphorus was present in the inositol phosphate peak.

For comparison, the barium salt of glyceryl *myo* inositol phosphoric acid prepared in the Bristol laboratories was hydrolysed by the same method. Analysis by the chromotropic acid method showed that it contained the theoretical amount of glycerol. The inositol monophosphate and glycerophosphate produced by hydrolysis were separated on a column as above. In two analyses 31 and 35 per cent of the phosphate in the hydrolysate was in the form of inositol monophosphate.

This hydrolytic pattern agrees well with that obtained with glyceryl *myo* inositol phosphate prepared from the liver phosphatidyl inositol.¹⁶ In addition Hanahan and Olley¹⁷ found that alkaline hydrolysis of the lipid itself gave a 35 per cent phosphorus in the form of inositol phosphate. It is likely, therefore, that the natural product has a similar configuration, involving inositol 2 or 1 phosphate. A decision between these two should be possible since only the 1-compound is optically active.¹⁸

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FUNCTIONAL ORGANIZATION OF THE RESPIRATORY CHAIN IN LIVER MITOCHONDRIA

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THE question of whether the mitochondrion is compartmentalized into separate respiratory chains serving the individual cytochrome-linked dehydrogenases and acting independently of each other or whether all or most of these dehydrogenases are structurally and functionally linked to a common electron transport system, has been an open and much debated one. In the past, two major approaches have been used to explore this question. One entails the isolation of mitochondrial fragments capable of oxidizing only one substrate at significant rates (such as a reduced diphosphopyridine nucleotide oxidase preparation¹) and the other the measurement of the extent of reduction of the various cytochrome components in anaerobiosis in intact mitochondria.² Elsewhere³, we have discussed the limitations of these methods and the consequent uncertainties of the conclusions derived from their application. A series of alternative methods have been employed by Ringer and Singer^{4,5} to a study of the respiratory chain in brain mitochondria and some of the same methods have been applied by Wu and Tsou⁶ to Keilin-Hartree preparations of pig heart in their study of the interrelation of succinate and reduced diphosphopyridine nucleotide oxidases.

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The following possibilities have been considered in the present study. (1) There may be a separate and distinct cytochrome chain serving each cytochrome reducing dehydrogenase in mitochondria, with no interconnection between the chains. (2) Two or more dehydrogenases may be attached to any given chain but there is no functional interconnection between the chains. (3) Two or more dehydrogenases may be linked to a given cytochrome chain, and there is intercommunication (that is, electron transport) among all the chains in a given mitochondrion. The third alternative recognizes the least degree of specialization for the electron transport system. Both alternatives (2) and (3) pose the further question as to the point in the chain at which a bifurcation to the various dehydrogenases might occur. In the present investigation these alternatives were examined in sucrose mitochondria of rat liver, using the succinic and choline oxidase systems as indicators, since both specific dehydrogenases have been isolated and sufficiently characterized to permit the conclusion that they are flavoproteins. The techniques employed in order to decide among the aforementioned possibilities included (a) a study of the rate of the cross reaction in anaerobiosis between the two dehydrogenases and of the effect of inhibitors thereon;

Table 1 COMPETITION OF SUCCINIC AND CHOLINE DEHYDROGENASES FOR THE RESPIRATORY CHAIN

| Experiment | Electron acceptor | Substrate | Oxygen uptake (μ atoms) | Fumarate formed (μ moles) |
|------------|--|---------------------|------------------------------|--------------------------------|
| 1 | Respiratory chain cyt <i>a</i> , limiting (3.3 mM azide) | Succinate | 40.0 | 36.0 |
| | | Choline | 20.0 | |
| 2 | Phenazine methosulphate | Succinate* | 51.2 | |
| | | Choline | 55.4 | |
| 3 | Respiratory chain, cyt <i>b</i> → <i>c</i> , limiting (9.3 × 10 ⁻⁴ M quinoxaline oxide) | Succinate* | 22.2 | 22.8 |
| | | Choline | 12.5 | |
| 3 | | Succinate + choline | 36.1 | 24.6 |

* Succinic dehydrogenase activity depressed by titration with malonate to the level of choline dehydrogenase

Conditions: Manometric assays at 30°, pH 7.6 in the presence of 0.02 M succinate and/or 0.017 M choline and sucrose mitochondria of rat liver. The reaction period and the amount of mitochondria were varied in the different experiments, but the results are expressed for a 15-min period and 1 ml mitochondrial suspension. The latter contained 25.2 mgm protein in experiments 1 and 2, and 25.9 mgm in experiment 3. In experiments 1 and 3, 0.5 mgm cyt *c* was added. Fumarate was determined, after deproteinization, with crystalline fumarase and the malle enzyme of *L. arabinosus* (ref. 9)

(b) comparison of the quantitative effect of the titration of mitochondria with respiratory chain inhibitors on the two enzyme systems, (c) a study of the effect of depletion and re-addition of a specific component of the respiratory chain on the two activities, (d) competition experiments between the two enzyme systems for specific components of the respiratory chain

The investigations of Slater⁶ and of Wu and Tsou⁷ of the reduced diphosphopyridine nucleotide and succinic oxidases of heart and of Ringler and Singer^{8,4} of the succinic and α -glycerophosphoric oxidases of brain have ruled out the possibility that separate and specific cytochrome chains serve these dehydrogenases in the tissues mentioned, but did not permit distinguishing between alternatives (2) and (3). In contrast, the results of a comparison of the behaviour of choline and succinic oxidases in rat liver did not seem to be readily reconcilable with the operation of a common respiratory chain and suggested that at least a part of their cytochrome chains may operate independently of each other. Thus, anaerobically, no oxidation of choline by fumarate could be detected, the oxidation of choline and succinate via the complete chain was additive, not competitive, addition of cytochrome *c* to partially depleted mitochondria stimulated succinate oxidation three- to four-fold but did not affect choline oxidation, and titration with azide, cyanide, antimycin *a*, and 2-*n*-heptyl-4-hydroxyquinoline N-oxide (quinoxaline oxide) inhibited succinate oxidation at much lower concentrations than choline oxidation (Fig 1). Further, amytal completely inhibited choline respiration without inhibiting succinate oxidation.

Since during the steady state both choline and succinate reduce all the known cytochromes of liver mitochondria (*b*, *c* + *c*₁, *a*, *a*₃), although to different extents⁸, and since the differential effects of amytal were readily explained, without postulating separate pathways, by the finding that this inhibitor acts between choline dehydrogenase flavoprotein and cytochrome *b*⁸, it was desirable to establish whether the differential effects on choline and succinic oxidases might not be the results of the greater activity of succinic than of choline dehydrogenase and of the consequently greater demand it puts on the respira-

tory chain. In order to test this possibility, succinic dehydrogenase activity was depressed by malonate to a point where it equalled choline dehydrogenase activity. Under these conditions, external cytochrome *c* no longer stimulated either succinic or choline oxidase, since the residual cytochrome *c* in washed sucrose mitochondria was sufficient to support this lowered rate of respiration. Similarly, when succinic and choline dehydrogenase activities were equalized by malonate titration, the titration curves of choline and succinic oxidases (and of the corresponding cytochrome *c* reductases) with all the respiratory chain inhibitors mentioned coincided.

Since the activity of choline oxidase in rat liver mitochondria is only 20–25 per cent as high as that of succinic oxidase, it seemed possible that the turnover-rate of the slowest member of the cytochrome chain in liver mitochondria (supplemented with cytochrome *c*) may exceed the combined activity of the two oxidases and that, therefore, in order to demonstrate a competition between the two oxidases it is necessary to depress the turnover of one of the components of the respiratory chain. Indeed, when the turnover of cytochrome *a*₃ was depressed by titration with azide, the mutual competition of choline and succinic oxidases could be readily demonstrated (Table 1, exp. 1). Significantly, as in the mutual competition of succinic and α -glycerophosphoric dehydrogenases in brain mitochondria, when the two substrates are simultaneously oxidized, the rate is less than that of the faster of the two oxidations. The reasons for this have been discussed elsewhere⁴. That the depression of succinate oxidation is the direct result of the operation of choline dehydrogenase is shown by the fact that the addition of 3 mM amytal, under these conditions, completely inhibits choline oxidation and re-establishes the rate of succinate oxidation and fumarate formation to the level found with succinate alone present. When the respiratory chain is by-passed by intercepting electrons with phenazine methosulphate (exp. 2), the competition disappears and a strict additiveness is obtained. It may be concluded that the electrons originating from these two dehydrogenases flow through a common transport system, at least at the level of cytochrome oxidase.

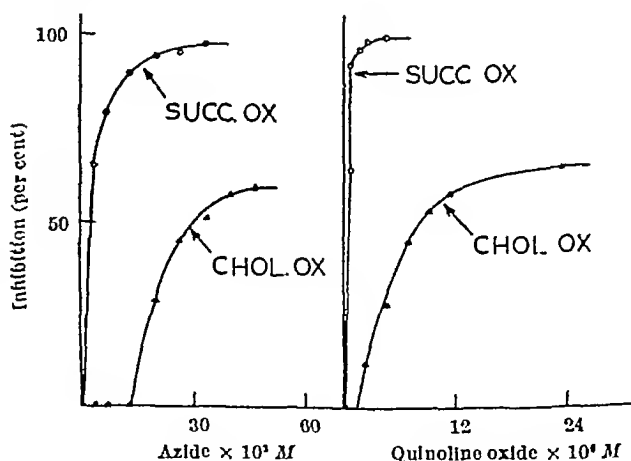


Fig 1 Titration of succinic oxidase and choline oxidase activities of sucrose mitochondria of rat liver with respiratory chain inhibitors. Manometric assay of uptake of oxygen at 30° as in Table 1. The inhibitions were calculated from the linear rate of respiration in the interval 6–20 min after addition of the substrate. The initial rate of respiration (0–5 min), before the inhibitor-resistant oxidation of choline is manifest (cf. below), gives similar differences in the titration of the two oxidases, but the inhibition of both enzymes reaches completion.

When antimycin or quinoline oxide was used to limit the rate of the cytochrome $b \rightarrow c_1$ step, instead of competition, additive rates were obtained (exp. 3). This is interpreted to mean that the cytochrome b moieties serving succinate and choline dehydrogenases are not the same nor in direct intercommunication. Further support for this conclusion came from a detailed study of the azide, CN^- , antimycin and quinoline oxide resistant oxidation of choline (Fig. 1). Using an oxygen electrode, it was demonstrated that immediately following the addition of choline to mito chondria, treated with any of these inhibitors in excess the oxidation is completely inhibited, but after 3-5 min at 30°C or after 10-20 min at room temperature a respiration resistant to all these inhibitors begins. The cytochrome b linked to choline dehydrogenase (but not that linked to succinate dehydrogenase) appears to be the site of the 'leak' and the resistance to inhibitors is thought to represent a conversion of this cytochrome b to an auto oxidizable form for the following reasons: (1) Choline dehydrogenase is not auto oxidizable. (2) Amytal inhibition of choline oxidation is complete but antimycin or quinoline oxide inhibition is not. Thus the 'leak' is between flavoprotein and cytochrome c_1 . (3) Choline cytochrome c reductase is completely blocked by all three of these inhibitors. (4) The auto-oxidizable component through which succinate and choline oxidations occur with excess azide or CN^- present is the same, since under these conditions the rate of respiration per mgm. mitochondria is equal whether succinate, choline, or both are present. Thus, the two dehydrogenases compete for the leak. (5) That the b component linked to choline dehydrogenase (and not that serving succinate dehydrogenase) is the site of the leak is indicated by the fact that while choline oxidation is partially resistant to antimycin and quinolineoxide (agents which inhibit the $b \rightarrow c_1$ step), succinate oxidation is completely inhibited by these compounds.

The auto oxidization or reduced cytochrome b in certain types of heart muscle preparations in the presence of cyanide was first observed by Keilin¹⁰. Recently Chance¹¹ questioned the evidence for the direct reaction of cytochrome b with oxygen at a significant rate. In view of the slow rate of the development of the cyanide and azide resistant respiration in liver mitochondria, the auto oxidation of cytochrome b possibly may escape detection in spectrophotometric experiments of very

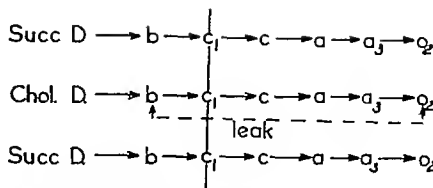


Fig. 2 Schematic representation of the interrelations of succinate and choline oxidases in rat liver mitochondria

short duration, as employed by the Philadelphia group¹².

The findings suggest that the respiratory chains of liver mitochondria, at least so far as the succinate and choline oxidase systems are concerned are not compartmentalized, but are interlinked at and above the oxidation level of cytochrome c_1 , although the b components do not appear to be on a common path (Fig. 2). Intercommunication between the chains (alternative (3) above) is indicated by the fact that the quantitative effect of titration with an inhibitor such as azide or cyanide, depends on the relative turnover rates of the dehydrogenase and the cytochrome component being titrated, respectively and may be altered by depressing the activity of the dehydrogenase. Neither mechanism (1) nor (2) is compatible with this behaviour but it is to be expected from the third one.

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IS THE MULTIMAMMATE RAT A NATURAL RESERVOIR OF BORRELIA DUTTONI?

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FOR about two years now the Entomological Department of the South African Institute for Medical Research, Johannesburg, has been carrying out transmission experiments and epidemiological investigations on relapsing fever (*Borrelia duttoni*) in Bechuanaland in collaboration with the Medical Department of that Protectorate.

With the help of Dr. E. L. Szilamp, medical officer in Maun a strain of *Borrelia duttoni* was isolated from tamarins (*Ornithodoros moubata*) collected in a hut in Maun inhabited by a native suffering from

an acute attack of relapsing fever. Eleven specimens of *O. moubata* were collected on December 5 1958 and were injected into six white mice on December 17. All the mice became positive between December 23 and 29, 1958.

Thus Maun strain was then used for a great number of transmission experiments on which a report will be given in a later paper. Up to now quite a few interesting results have been obtained but one is of special interest and is reported in this preliminary note. In our search for the natural

reservoirs of African relapsing fever, which I expect to find among wild rodents, we also injected several specimens of the indigenous multimammate rat (*Rattus natalensis* = *Mastomys coucha*) with the 'Maun' strain and found that this wild rat is very highly susceptible to *Borrelia duttoni* although, judging from the general appearance and behaviour of the animals, there are no obvious clinical symptoms. The same is true for the white mouse, but in the multimammate rat the parasitaemia of the blood is much higher, and persists, almost without interruption, for a longer period. A photomicrograph of a blood smear of a white mouse at the peak of the blood-parasitaemia (ninth day after subcutaneous injection) is shown in Fig 1, and one of a blood-smear from a multimammate rat at a corresponding peak (eleventh day after injection) is given in Fig 2.

The course of the infection in the above-mentioned white mouse was as follows. It was infected on June 2, 1959, with an emulsion of eggs laid by an infected *O. moubata*. The first few spirochaetes were detected in the blood-smear on June 10. The next day the smear was positive (Fig 1), and it did not reach this degree of parasitaemia again. On June 13, only a few spirochaetes were present in the field. On the two following days the blood smears were negative. On June 17 the result was recorded as ++. A few spirochaetes were again detected in the smear on June 20, 24 and 27. On the intervening days, and after June 27, all smears were found to be negative.

The specimen of multimammate rat was injected on June 2 with a brain emulsion from a white mouse. On June 9, the first spirochaetes appeared in the blood and were recorded as ++. The next day no spirochaetes could be detected in the smear. They re-appeared on June 11 and increased steadily until June 15, when they reached the peak shown in Fig 2. The rat then remained highly positive until June 27. On the following two days the blood was negative, then another peak was reached on July 3. The rat was then still in the best condition of health, and its progress is to be followed up. Similar results were obtained with other specimens of the multimammate rat.

These results, which are to be consolidated by further experiments, have suggested several interesting problems. One is that the multimammate rat used in this Institute for some time for many investigations on plague, cancer and bilharzia, is evidently a much better experimental animal for investigations on relapsing fever than the white mouse. It may perhaps prove to be an ideal biological test-animal.

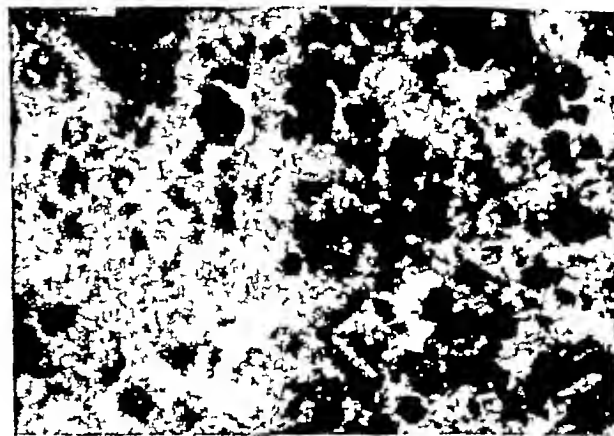


Fig 2 Blood smear of multimammate rat on the eleventh day after subcutaneous infection with *Borrelia duttoni*.

for silent infections in humans, where spirochaetes are so rare in the blood that they cannot be detected by the usual laboratory methods.

Another problem is an epidemiological one. It is now almost certain that the natives get their tamps from the burrows of wart-hogs. All the wart-hog burrows which I have been able to check in the Bechuanaland Protectorate have been highly infested with tamps which, according to Dr G. A. Walton (by letter) are, with scarcely any doubt, morphologically and physiologically identical with those found in the huts in Maun and other places in the Bechuanaland Protectorate and the Northern Transvaal. But the ticks collected by us from burrows in these areas, and also those collected by other authors in Central Africa, have never been found infected with *Borrelia*. Further, the wart-hog itself has never been found infected and is refractory when infected experimentally (comp. Geigy and Mooser¹). Evidently the wart-hog is not a natural reservoir of African relapsing fever, and the ticks may acquire their infection from another animal. Incidentally, the 'wild' *Ornithodoros moubata* from the burrows of wart-hogs can easily be infected experimentally with *Borrelia duttoni*.

The multimammate rat is a wild rodent which lives in close contact with man in Africa and in the native villages it plays the same part as the house rat (*Rattus rattus*) and the Norwegian rat (*Rattus norvegicus*) in the towns in Africa and in human habitations throughout Europe and Asia. Tamps brought to the huts by native hunters, for example, sooner or later come into contact with the multimammate rats there. Is this rat perhaps the natural reservoir, or one of them, of *Borrelia duttoni*? We have not yet looked for natural infections in this rat, but the experimental picture shows that it would be an ideal reservoir, as it remains highly positive for a long time without its general condition of health being influenced. This problem is being investigated more thoroughly.

I wish to thank Prof J. F. Murray and Dr B. de Meillon of this Institute for their interest and help, Mr D. H. S. Davis, Medical Ecology Centre, Union Health Department, for providing the wild rodents, and Drs B. T. Squires, B. O. Wilkin and E. L. Szlam of the Medical Department, Bechuanaland Protectorate, for their support. The photomicrographs were prepared by Mr M. Ulrich of the Photographic Department, South African Institute for Medical Research.

¹ Geigy, R., and Mooser, H., *J. Trop. Med. Hyg.*, 58, 199 (1955).

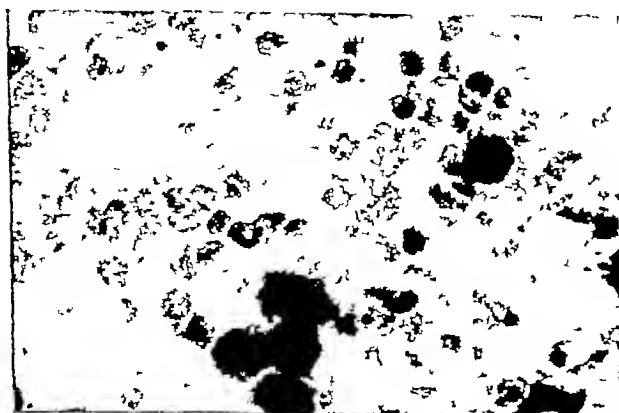


Fig 1 Blood smear of white mouse on the ninth day after subcutaneous infection with *Borrelia duttoni*.

CHEMISTRY AND TAXONOMY IN THE DIPTEROCARPACEAE

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AND

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LIVING specimens of the Dipterocarpaceae are not apparently available in Great Britain, and it has so far not been possible to include them in surveys of the phenolic constituents of plants.¹⁻³ Recently, however, through the kindness of the Director Forest Research Institute, Kepong (Selangor), fresh leaves of twenty eight species of dipterocarps have been received from Malaya, and these have been examined by the methods previously described (*loc cit*). The results are interesting because the species were selected from a large collection so as to be representative not only of all the available genera but also of the recognized groups of *Shorea*, the largest genus in this family, which, because of its valuable timber and other economic products, has received a great deal of attention from the forestry officers and official taxonomists in the Indomalaysian countries.

Consideration of the phenolic constituents of the leaves of a large number of Dicotyledons has indicated¹ that three characters are particularly valuable from the taxonomic point of view: presence or absence of leuco-anthocyanins, presence or absence of vicinal trihydroxy groupings in the phenolic constituents, and the presence or absence of the polyhydroxy and hydroxymethoxy aromatic acids, caffeic, ellagic, ferulic and sinapic acids. It is often of value also to note other constituents, not necessarily identified, which are present in some, but absent from other, species in the same or different genera as indicators of possible relation between the species possessing them.

The results of the chromatographic examination of the hydrolysates of the leaves of the 28 species are given in Table 1. The constituents recorded are,

from left to right, in order of increasing *R_F* in aqueous acetic acid-hydrochloric acid (Forestal solvent), *M* = myricetin, *D* = delphinidin (formed from leuco delphinidin), *E* = ellagic acid, *Q* = quercetin, *Cy* = cyanidin (formed from leucocyanidin), *K* = kaempferol, *Caff* = caffeic acid, *S* = sinapic acid, *F* = ferulic acid. In the last column are recorded other constituents visible in the ultra violet with their *R_F* values in Forestal solvent and their appearance in ultra violet before and after (→) fuming in ammonia vapour. The abbreviations used are: *bl* = blue, *brn* = brown, *gr* = green, *v* = violet, *y* = yellow, *br* = bright, *d* = deep, *dl* = dark, *f* = faint, *l* = light, *v* = very. Sinapic acid and ferulic acid are identified on a separate chromatogram run in toluene-acetic acid.⁴

The genera are listed in the order given by Symington.¹ The species are listed in alphabetical order within the genus, except for *Shorea* which is divided into groups according to the same author. Symington considered these groups to be natural subdivisions of the genus, perhaps worthy of generic status, but was not prepared to give them definite botanical names or status until the whole genus was revised taxonomically. This revision has still not been made for it awaits the collection and description of the rich Bornean dipterocarp flora. Desch⁵ working on the timbers of *Shorea* independently established four groups based mainly on gross timber characters which correspond closely to Symington's subdivisions. The groups are named *B* = balau, *Y*, *W* and *R* = yellow, white and red meranti respectively within each there is considerable homogeneity in characters of the living trees including the colour of the wood and sliced bark and the dead leaves.

Table 1

| Species | Div | M | D | E | Q | Cy | K | Caff | S | F | Other constituents |
|--|-----|-----|---|----|-----|-----|---|------|-----|-----|--------------------------------------|
| <i>Shorea foeniculifera</i> Sym | B | - | + | + | - | ? | - | - | (+) | - | → d purple-orm. of gallic acid, 0.61 |
| <i>kuatleri</i> King | B | - | - | ? | + | + | + | - | (+) | - | → dull y, 0.73 |
| <i>marcelliana</i> King | B | (+) | - | + | + | + | + | - | (+) | - | bl 1 → br, gr 0.60 |
| <i>maxima</i> (King) Sym | F | - | - | + | - | ? | + | ? | (+) | - | bl 1 → v, br, dl, gr 0.73 |
| <i>multiflora</i> (Burr.) Sym. | F | - | - | ++ | + | (+) | + | ? | - | - | intense br, dl 0.60 ? 0.8 |
| <i>bracteolata</i> Dyer | W | - | - | + | + | (+) | + | + | - | - | |
| <i>curatili</i> Dyer ex King | R | + | + | ? | + | (+) | + | + | - | - | |
| <i>keudragana</i> (King) King | R | - | - | + | - | - | - | - | - | - | → y 0.7 |
| <i>ex Forx</i> | R | - | - | + | - | - | - | - | - | - | |
| <i>leprosa</i> Miq | R | - | + | ? | ++ | ++ | - | - | - | - | → f y 0.7 |
| <i>singhacang</i> (Miq) Burck | R | - | + | + | + | + | + | + | - | - | bl 1 → br, gr 0.6 |
| <i>Hopea beccarifera</i> Burck | + | - | + | + | + | + | + | + | + | + | |
| <i>mongaiensis</i> Miq | + | - | + | + | + | + | + | + | + | + | |
| <i>nitida</i> Ridl | + | - | - | + | + | - | - | - | (+) | - | v, d, dl → v, br, dl 0.63 |
| <i>odorata</i> Roxb | + | - | - | + | + | - | - | ++ | - | - | v, d, dl → v, br, dl 0.63 |
| <i>sangkal</i> Korth | + | - | - | + | + | - | - | ++ | - | - | |
| <i>subulata</i> Sym | + | - | - | + | (+) | - | - | + | - | - | intense br, dl 0.72 |
| <i>Balanocarpus kintali</i> King | + | - | + | + | + | + | + | ++ | - | - | |
| <i>Dipterocarpus bawdi</i> Korth | + | + | + | + | + | + | + | + | - | - | |
| <i>costatus</i> V. Sl. | ++ | + | + | ? | + | - | - | - | - | - | |
| <i>crinitus</i> Dyer | + | + | + | + | + | (+) | - | - | - | - | |
| <i>kerrii</i> King | ++ | + | + | + | (+) | (+) | - | - | - | - | |
| <i>Dryobalanops aromatica</i> Gaertn / | + | + | + | + | + | + | + | + | - | - | |
| <i>oblongifolia</i> Dyer | + | + | + | + | - | + | + | + | - | - | |
| <i>anisoptera</i> Lottl | + | + | + | + | - | + | + | + | - | (+) | greenish 0.80 |
| <i>Patula nitens</i> King | + | + | + | + | - | + | + | + | - | (+) | 1' → y 0.61 |
| <i>stephana</i> (King) V. Sl | + | + | + | + | - | + | + | + | - | (+) | dl → dull y 0.70 |
| <i>velutina</i> Dyer | + | + | + | + | - | + | + | + | - | - | gr 0.70 |
| <i>Uyapina borneana</i> | + | + | + | + | - | + | + | + | - | - | |

The data in Table 1 suggest that the genera can be arranged in groups, in the first instance according to the abundance and type of the leuco anthocyanins present. *Dipterocarpus* and *Dryobalanops*, abundant with consistent *L-D*, *Shorea* (and one *Vatica* sp.) less abundant, with both *L-D* and *L-Cy*, *Hopea*, *Balanocarpus*, *Anisoptera*, and two *Vatica* spp. with little or no *L-A*, and *Upuna* with none of the common phenolic constituents.

Dipterocarpus and *Dryobalanops* agree also in having consistent and often abundant myricetin, and no subsidiary constituents. In both *Shorea* and *Hopea* many of the species have a subsidiary constituent R_F 0.68–0.7 with intensely blue fluorescence, which may or may not be the same in all species. These two genera have also numerous other subsidiary constituents. *Hopea*, *Balanocarpus*, and one or two *Shorea* spp. also have caffeic acid, absent from the other genera. All the genera except *Anisoptera* and *Upuna* have ellagic acid, *Shorea foxworthyi* having in addition (probably) gallic acid.

Overall the grouping suggested is *Dipterocarpus* with *Dryobalanops*, *Shorea* with *Hopea* and *Balanocarpus*, *Vatica* rather closer to *Shorea* than to *Hopea*, *Anisoptera* and *Upuna* uncertain.

The groups of *Shorea* are not very distinct, neither yellow nor white meranti have much *L-A*, and *L-D* is absent from both sections, but species in both the balau and the red meranti groups have the same constitution. The nature of the pigments responsible for the colours of the sliced bark is unknown, it is not even known whether they are phenolic, so that there is no *prima facie* reason to expect that the phenolic constituents in the leaves would follow the proposed subdivision of the genus.

One further point is worth making. *Balanocarpus* Bedd. has become a repository for all wingless fruited dipterocarps. *B. heimu* should probably be included in *Hopea* on floral characters⁶ and wood characters⁷, and now we can reach the same conclusion from the chemistry. The suggested regrouping of other species is also supported by the present evidence.

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³ Bate-Smith, E. C. (In preparation).

⁴ Bate-Smith, E. C., *Chem. and Indust.*, 1457 (1954).

⁵ Symington, C. F., "Foresters' Manual of Dipterocarps", *Malay For. Rec.*, No. 10 (1941).

⁶ Desch, H. E., "Commercial Timbers of the Malay Peninsula. (1) The Genus *Shorea*", *Malay For. Rec.*, No. 12 (1936).

⁷ Desch, H. E., "Dipterocarp Timbers of the Malay Peninsula" *Malay For. Rec.*, No. 14 (1941).

PLANT-GROWTH SUBSTANCES AND THE COPPER CHELATION THEORY OF THEIR MODE OF ACTION

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FOLLOWING the observations that certain compounds possessing chelate groups can exhibit significant plant growth-regulating activity¹, several workers have been trying to demonstrate the converse, namely, that highly active plant-growth regulators can react with metal ions to form chelate complexes. The discovery by Cohen, Ginzburg and Heitner-Wirgun² that the ultra-violet absorption spectra of 3-indolylacetic acid and 1-naphthylacetic acid are profoundly altered in presence of cupric, but not calcium or magnesium ions, led them to postulate that the cupric ion reacted with the carboxyl group in these acids to form a copper complex which then formed a chelate by employing the aromatic ring as the second complexing group.

After repeating their experiments using solutions obtained by dissolving cupric nitrate trihydrate in 50 per cent aqueous ethanol, I observed that with 3-indolylacetic acid the optical density of each solution in the series measured at 360 m μ did not remain constant but tended to increase slowly (cf. ref. 3). Since with cupric nitrate and 1-naphthylacetic acid, measured at 330 m μ , the optical density of each solution remained constant for several minutes, this system was used for comparison with the cupric nitrate/1-naphthoic acid system measured at 348 m μ . It was found that the relationship between optical density and acid/copper ratio is similar for both 1-naphthylacetic acid (Fig. 1) and 1-naphthoic acid. Thus, the enhancement of ultra-violet absorption is not limited to the highly active 1-naphthylacetic acid but occurs also with the relatively inactive 1-naphthoic acid.

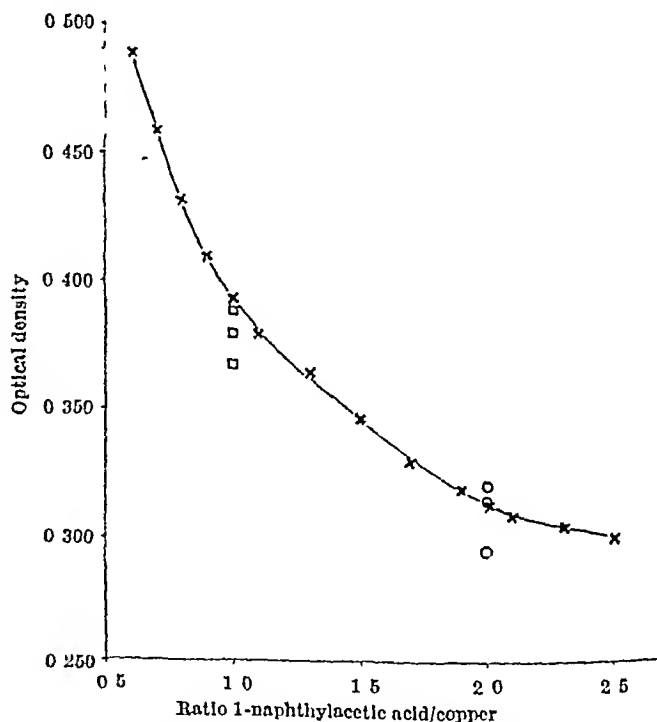


Fig. 1. Optical density of copper/1-naphthylacetic acid complex (330 m μ , 1 cm cells, pH ~ 3.0) in 50 per cent aqueous ethanol. x, Concentration of added cupric nitrate varied as shown with concentration of 1-naphthylacetic acid constant at 2×10^{-3} M; O, concentrations of added copper 1-naphthylacetate 10^{-3} M and nitric acid 2×10^{-3} M; □, concentrations of added copper 1-naphthylacetate 10^{-3} M, nitric acid 2×10^{-3} M and cupric nitrate 10^{-3} M.

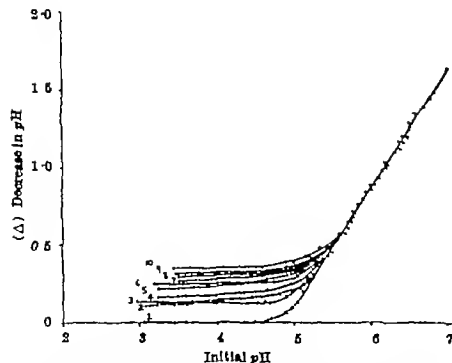
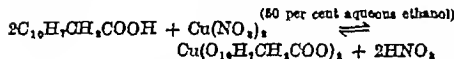


Fig. 2. The relationship between the initial pH of 50 per cent aqueous ethanol, containing the acid indicated, and the decrease in pH (Δ) on dissolving 4.83 mm. cupric nitrate trihydrate in 10 ml. Acids added to obtain initial pH: 1 nitric; 2 formic; 3 4-dichlorophenoxyacetic; 4 1 naphthyl; 5 succinic; 6 benzoic; 7 acetic; 8 1 naphthylacetic; 9 3-indolylacetic and 10 trimethylacetic acid

The general reaction in aqueous ethanol between cupric nitrate and 1 naphthylacetic acid can be written:



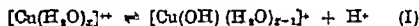
In writing this equation the various ionic species which may exist in solution have, for simplicity, not been characterized. For each 1 naphthylacetic acid/copper ratio the optical density of the solution at constant temperature should be independent of whether the equilibrium is attained by using reactants which give the forward reaction or reactants which give the reverse reaction. Accordingly, cupric 1 naphthylacetate was synthesized and used stoichiometrically with nitric acid in aqueous ethanol to give the reverse reaction and reconstitute the solution having a ratio 1 naphthylacetic acid/copper equal to 2.0. The optical density of this solution in which the reverse reaction had occurred was found to be identical with that of the solution containing the products of the forward reaction (Fig. 1). Furthermore, addition of cupric nitrate, sufficient to lower the 1 naphthylacetic acid/copper ratio to 1.0 in these reconstituted solutions, increased the optical density to the value found for this ratio when using the reactants of the forward reaction (see Fig. 1). Since the equilibrium may be reached from either side without adding a chelate group it is concluded that a reaction involving chelation is not required to account for the exaltation of ultra violet absorption given by cupric nitrate with 1 naphthylacetic acid.

By measuring the pH Cohen *et al.*⁸ also confirmed that cupric nitrate reacted differently from calcium and magnesium nitrates when added to solutions of 3-indolylacetic acid and 1 naphthylacetic acid in aqueous ethanol. Furthermore, they found that while the pH of these acids in solution was lowered due to release of hydrogen ions by complexing of the copper ion with the carboxyl group yet under the same conditions only slight complexing occurred with acetic acid or indole. The results were interpreted as evidence for the entire aromatic ring

functioning as a second complexing group thus resulting in chelate formation.

In a study using aqueous ethanol solutions of several closely related acids, comprising active and inactive growth regulators, it was found that in general the addition of cupric ions lowers the pH. Some of the results are shown in Fig. 2. The observed pH changes however, do not correlate with plant growth regulating activity, thus the aromatic carboxylic acids (for example, benzoic and 1 naphthoic), and the alkanecarboxylic acids (for example, formic, acetic and trimethylacetic), which are all inactive⁴ in the wheat cylinder elongation test exhibit an effect in presence of copper ions similar to that found with highly active⁴ 3-indolylacetic acid, 1 naphthylacetic acid and 2,4-dichlorophenoxyacetic acid. Furthermore, the results show no difference which would indicate the occurrence of chelation involving the aromatic ring (Fig. 2).

In the pH range studied two mechanisms of hydrogen ion formation are apparent. Mechanism I which operates over a pH region known to be of considerable physiological importance in plant cells, produces a large effect (Δ), which is the same for all the different compounds examined (Fig. 2). It is significant that at higher initial pH values, that is, when the concentration of carboxylic acid for adjusting the pH is decreasing, the effect (Δ) obtained by adding the copper salt is increasing linearly, and when no carboxylic acid is added to the aqueous ethanol solvent the effect (Δ) is the largest throughout the pH range investigated. The results lead to the conclusion that the effect (Δ) between pH 5.4 and 7 depends upon hydrolysis and they indicate that hydrogen ion formation occurs by a reaction of the following type



The cupric ion is represented here as described by Orgel, and the reaction written by analogy with his example for iron⁹. On the other hand, mechanism II appears limited to the pH region below about 5.4. The effect (Δ) is smaller, different for the different structures examined, and zero for nitric acid. There appears to be a correlation between the effect (Δ) and the pK value of each acid and further work on this aspect is proceeding. The results suggest that hydrogen ion formation by mechanism II depends upon salt (that is complex) formation, which

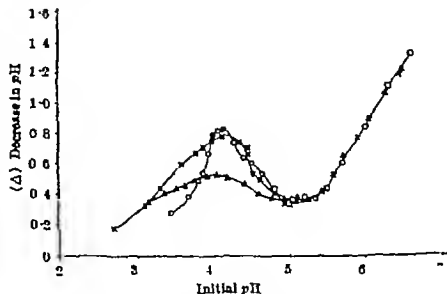


Fig. 3. The relationship between the initial pH of 50 per cent aqueous ethanol containing the acid indicated and the decrease in pH (Δ) on dissolving 4.83 mm. cupric nitrate trihydrate in 10 ml. Acids added to obtain initial pH: O aspartic; Δ glycolic and \times citric acid

O. sensibilis followed the application of the *Pteridium* factor with a delay of between 2½ and 3 days at all tested concentrations

The first-formed *Anemia* initials attained the four-cell stage, that is, the number of cells contained by mature antheridia, between 3½ and 4 days after the active substance was applied. No difference could be detected between the rates at which the first-formed antheridium initials attained the four-celled stage over the applied range of concentrations. On the other hand, an increase from 1/16 to ¼ full strength of the added *Anemia* medium increased the proportion of responding prothalli from about 15 to 100 per cent. If the *Anemia* factor was supplied to 5-day-old prothalli which comprised a maximum of 3 green vegetative cells, then between 3 and 3½ days elapsed before the first antheridium initials could be seen, that is, about 2 days more than in both the 12-day-old and the 18-day-old prothalli. It thus appears that the events leading to the appearance of antheridium initials proceed more slowly in very young prothalli. Alternatively, the very young prothalli may lack competence to respond to the active factor.

As indicated above, the *Pteridium* factor brings about antheridium formation in a large number of fern species. It should also be emphasized, though, that the minimally effective concentrations vary so widely that the prothalli of some species (for example, *Dennstaedtia punctilobula*) must be supplied with that factor at a concentration more than a hundred times higher than those of other species (for example, *Onoclea sensibilis*). The possibility must thus be considered that the induction of antheridia in *O. sensibilis* and in *A. phyllitides* is controlled by the same factor at different ranges of effective concentrations. *Pteridium* medium (active toward the prothalli of *O. sensibilis* to a dilution of 1:30,000) was inactive toward the prothalli of *A. phyllitides* at all concentrations which, with a dilution factor of 3, ranged from ¼ to 1/100,000 full strength. In turn, the prothalli of *O. sensibilis* were unresponsive toward *Anemia* medium (active toward the prothalli of *A. phyllitides* to a dilution of 1:300) at all dilutions which ranged again from ¼ to 1/100,000 full strength.

It is, therefore, difficult to avoid the conclusion that the induction of antheridia in *A. phyllitides* and in *O. sensibilis* is controlled by chemically distinct substances. This conclusion receives support from the demonstration that the antheridium-inducing activity of the *Anemia* medium is stable to boiling for 10 min. at pH 12, while the *Pteridium* factor was labile under those conditions*. The antheridium-inducing activity of the *Anemia* medium was further found to be stable to boiling for 10 min. at pH 2 and to autoclaving at pH 5.4, the pH of the culture medium, it was destroyed upon ashing and adsorbed on charcoal. The latter properties are similar to those of the *Pteridium* factor†.

The *Anemia* factor failed to promote antheridium formation in prothalli of *Osmunda claytonia* (checked 15 days after inoculation, 2 days prior to the onset of spontaneous antheridium formation), which were also unresponsive to the *Pteridium* factor. The prothalli of *Lygodium japonicum*, another species unresponsive toward the *Pteridium* factor, were shown to elaborate, and to secrete into the medium, a substance which greatly hastens the onset of the antheridial phase in this fern species which, like *A. phyllitides*, belongs to the family Schizaeaceae. Preliminary investigations indicate that this substance is chem-

ically distinct both from the *Pteridium* factor and from the *Anemia* factor.

It is apparent from these studies that antheridium formation is controlled by different substances in different groups of ferns. It should also be recalled that within the wide range of species responsive to the *Pteridium* factor, the minimally effective concentrations vary widely. Thus, the prothalli of *Dennstaedtia punctilobula* failed to respond unless they were supplied with the *Pteridium* factor at a concentration about 125 times higher than was necessary to induce antheridia in prothalli of *O. sensibilis*. In the prothalli of *Woodsia obtusa* the minimally effective concentration of the *Pteridium* factor exceeded that required for antheridium formation in the prothalli of *O. sensibilis* by a factor of about 25. The possibility must therefore be considered that the factors controlling antheridium formation in these species are actually different but structurally so closely related that the factor produced by *P. aquilinum* is capable of bringing about antheridium formation also in *Dennstaedtia punctilobula* and in *Woodsia obtusa* if it is supplied at a high enough concentration. Raper* also considers the possibility that hormonal specificities account for the failure to obtain oospores in some of the attempted inter-species and intergeneric crosses of water moulds.

The above results raise a question of biological specificity. The work of Kihnyver and Van Niel has directed attention to the similarity, even identity, of many basic biochemical patterns in taxonomically widely separated organisms. It is tempting to postulate that the metabolism associated with antheridium formation, an event that we conceive of mainly in morphological terms, is also similar in different fern species. The above results may be reconciled with such a postulate if we consider that the induction of an antheridium is likely to involve many reactions and compounds. Antheridium formation in *P. aquilinum* might thus be controlled by a different factor than in *A. phyllitides* because a different reaction became rate-limiting during evolution. Alternatively, we might be witness to evolution on a molecular level. On this assumption the inducing molecule has undergone a gradual structural modification probably concomitantly with changes in a receptor molecule. The isolation and characterization of the two substances should yield pertinent information. In the meantime, an attempt is being made to assay for similarity between the two factors based on the postulate that one factor might be a precursor of the other or that one factor might behave as a chemical analogue of the other and thus interfere with its synthesis or with the function it performs in the initiation of antheridia.

I am grateful to Dr. Armin C. Braun for the encouragement he has given this investigation and for a critical reading of the manuscript. I am also indebted to Drs. Ralph H. Wetmore and Max Ward for supplying plants and spores of *A. phyllitides*.

This investigation was supported in part by a National Science Foundation Research Grant (G-3225).

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FORTHCOMING EVENTS

(Meetings marked with an asterisk * are open to the public)

Monday November 2

INSTITUTION OF ELECTRICAL ENGINEERS ELECTRONICS AND COMMUNICATIONS SECTION (at Savoy Place London W.C.2) at 5.30 p.m.—Dr. A. J. Karbowiak "Some Comments on the Classification of Waveguide Modes" Mr. L. Levin "Some Comments on Quasi-Optical Methods at Millimetre Wave-lengths"

UNIVERSITY OF LONDON (at the School of Oriental and African Studies London W.G.1) at 5.30 p.m.—Prof. A. de Almeida (Lisbon) "Mucupes—a Native People from the Macaëdes Desert" (First of three lectures on The Non Nativ Peoples from Angola) Further lectures on November 3 and 5.)

SOCIETY OF CHEMICAL INDUSTRY LONDON SECTION (at 14 Belgrave Square London S.W.1) at 6.30 p.m.—Dr. Otto Horn "Chemical Research in Germany"

Tuesday, November 3

UNIVERSITY OF LONDON (in the Anatomy Theatre University College Gower Street London W.C.1) at 1.15 p.m.—Mr. N. J. H. Plomley "The Tasmanians: an Extinct Race?"

INSTITUTION OF ELECTRICAL ENGINEERS MEASUREMENT AND CONTROL SECTION (at Savoy Place London W.C.2) at 6.30 p.m.—Mr. P. Gleghorn "An Analogue Electronic Multiplier using Transistors as Square Wave Modulators"

UNIVERSITY OF LONDON (at Imperial College of Science and Technology London S.W.7) at 5.30 p.m.—Prof. S. G. Cherry "Telecommunication as Social Science" (Inaugural Lecture)

UNIVERSITY OF LONDON (at the London School of Hygiene and Tropical Medicine Keppel Street Gower Street London W.C.1) at 5.30 p.m.—Dr. J. M. Mitchell "The Life Cycle of Growing Cells" (Sixth of three lectures on The Scientific Basis of Medicine organized by the British Postgraduate Medical Federation) Further lectures on November 5 10 12 17 10 December 1 3 8 10)

PLASTICS INSTITUTE (at the Wellcome Building 123-125 Euston Road London N.W.1) at 6.30 p.m.—Dr. W. F. Watson "Recent Advances in Synthetic Rubbers"

SOCIETY OF CHEMICAL INDUSTRY PLASTICS AND POLYMER GROUP (at 14 Belgrave Square London S.W.1) at 6.30 p.m.—Dr. G. F. G. Harritt "Delrin Acetal Resin"

TEXTILE INSTITUTE (at the Chemical Society, Burlington House Piccadilly London W.1) at 6.30 p.m.—Mr. J. David "Modern Proofing"

Wednesday November 4

BRITISH INSTITUTION OF RADIO ENGINEERS (at the London School of Hygiene and Tropical Medicine Keppel Street Gower Street London W.C.1) at 3 p.m. and 6 p.m.—Half-day Symposium on Input/Output Devices

INSTITUTE OF PETROLEUM (at 61 New Cavendish Street London W.1) at 5.30 p.m.—Mr. W. 8 Ault "Oil and Transport"

ROYAL METEOROLOGICAL SOCIETY (at 40 Cromwell Road London S.W.7) at 5.30 p.m.—Mr. H. Charnock "Ocean Currents"

SOCIETY FOR ANALYTICAL CHEMISTRY (at the Chemical Society Burlington House Piccadilly London W.1) at 7 p.m.—Meeting for reading of Original Papers.

Thursday November 5

UNIVERSITY OF LONDON (at the Postgraduate Medical School of London Putney London S.W.15) at 1.15 p.m.—Dr. T. E. Ebert and Dr. H. H. Thompson "Biological Effects of Radiation—General Survey" (First of six lectures) Further lectures on November 12 19 26 December 3 and 10)

ROYAL SOCIETY (at Burlington House Piccadilly London W.1) at 4.30 p.m.—Prof. A. V. Hill F.R.S. and Mr. J. V. Howard "The Reversal of Chemical Reactions in Contracting Muscle During an Applied Stretch" Mr. J. W. Pringle and Dr. J. W. Pringle "The Physiology of Insect Fibillar Muscle 1 Anatomy and Innervation of the Basilar Muscle of Lamellicorn Beetles Mr. K. E. Machin and Dr. J. W. 8 Pringle, F.R.S. "The Physiology of Insect Fibillar Muscle 2 Mechanical Properties of a Beetle Flight Muscle"

UNIVERSITY OF LONDON (in the Physiology Theatre University College Gower Street London W.C.1) at 6.30 p.m.—Dr. E. T. C. Smith "The Synthesis of the Cytoplasmic Components of Animal Cells" (First of three lectures) Further lectures on November 12 and 19)

INSTITUTION OF ELECTRICAL ENGINEERS (at Savoy Place London W.C.2) at 5.30 p.m.—Mr. M. G. Crowley Kilving "The Application of Irradiation in Industry"

UNIVERSITY OF LONDON (at the London School of Hygiene and Tropical Medicine Keppel Street Gower Street London W.G.1) at 6.30 p.m.—Prof. G. U. Sneath "Genetic Analysis via Somatic Cells" (Seventh of fifteen lectures on The Scientific Basis of Medicine organized by the British Postgraduate Medical Federation) Further lectures on November 10 12 17 10 December 1 3 8 10)

SOCIETY OF CHEMICAL INDUSTRY MICROBIOLOGY GROUP (Joint meeting with the Agriculture Group at 14 Belgrave Square London, S.W.1) at 6.15 p.m.—Dr. M. E. Brown "Plant Roots and Soil Micro-organisms" Dr. R. M. Jackson "The Ecological Significance of the Rhizosphere"

Friday November 6

INSTITUTE OF PHYSICS (at 47 Belgrave Square London S.W.1) at 6 p.m.—Mr. R. D. Moore "The Role of Physics in the Investigation and Treatment of Heart Disease"

SOCIETY OF DYERS AND COLOURISTS (at the Royal Society Burlington House Piccadilly London W.1) at 6 p.m.—Mr. D. F. Anstead "The Use of Colour in Cosmetics"

SOCIETY OF CHEMICAL INDUSTRY FINE CHEMISTS GROUP (at 14 Belgrave Square London S.W.1) at 6.30 p.m.—Dr. H. G. L. Weddon "Electrolytic Methods in Preparative Organic Chemistry"

ROYAL INSTITUTION (at 21 Albemarle Street London W.1) at 6 p.m.—Prof. H. Bondi F.R.S. "What Goes On Inside the Stars"

Saturday November 7

LONDON COUNTY COUNCIL (at the Horniman Museum London Road Forest Hill London S.E.22) at 3.30 p.m.—Mr. B. D. Boycott: "Devilfish—Octopuses Squids and Cuttlefishes"

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned

DIRECTOR and ASSISTANT DIRECTOR of the British Institute of History and Archaeology in East Africa (Headquarters at Dar es Salaam and Kampala)—The Secretary The British Academy Burlington House Piccadilly London W.1 (November 10)

LECTURER (preferably with special experience in the field of organic chemistry) at Christchurch at Victoria University of Wellington, New Zealand—The Secretary Association of Universities of the British Commonwealth 30 Gordon Square London W.C.1 (New Zealand November 15)

IMPERIAL CHEMICAL INDUSTRIES FELLOW (preferably under 29 years of age) at Durham for research in Engineering Chemistry, Physics and allied subjects including the biological application of chemistry—The Registrar University Office 46 North Bailey Durham (November 16)

PLANT PHYSIOLOGIST (honours graduate in science or agricultural science (or equivalent) with some years relevant postgraduate research experience) at the Irrigation Research Station C.S.I.R.O. Griffith New South Wales Australia to investigate effect of water stress in plants in new laboratories containing controlled environment chambers—Chief Scientific Liaison Officer Australian Scientific Liaison Office Africa House Kingsway London W.C.2, quoting Appointment No. 600115 (November 20)

MOLLARD RESEARCH FELLOW (preferably with a Ph.D. degree or equivalent research experience) IN PHYSICS for research in various branches of solid state physics with particular reference to defects, semiconductors, or superconductivity—The Registrar University College of North Staffordshire (6 St. James Street Stoke-on-Trent 5) (November 30)

PRINCIPAL (with high academic qualifications wide experience in administration and conversant with developments in technological education)—The Clerk to the Governing Body Battersea College of Technology London S.W.11 (November 30)

SENIOR LECTURER IN PHYSICAL CHEMISTRY IN THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING—Prof. F. Bebb Professor of Physical Chemistry University of the Witwatersrand Milner Park, Johannesburg South Africa (November 30)

LECTURER IN THEORETICAL PHYSICS and a LECTURER IN PHYSICS—The Registrar (Room 22, O.R.B.) The University Reading (December 7)

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

Torrey Commission Bulletin No. 31 Code of Sample Plot Procedure by Dr. F. G. Hammett, G. M. L. Locke, J. N. R. Jeffers and J. C. Christie Pp. v+113. (London H.M. Stationery Office 1959) 15s net (1959)

Commonwealth Bureau of Helminthology Supplement to the Nematode Parasites of Plants Catalogue Under Their Hosts, 1955-1958. By Dr. J. Baill Guodry, Dr. Mary T. Franklin and David J. Hooper Pp. i+148. (London Royal Commonwealth Agricultural Bureau 1959) 7s 6d net (1959)

Chelsea College of Science and Technology Prospectus Session 1959-60 Pp. 35. (London Chelsea College of Science and Technology 1959) 1s net (1959)

Children in Britain—Their Problems and Education. Compiled by Mrs. W. A. Axford. (Books and Articles published in Great Britain from the 1914 Education Act to 1958) Pp. 63. (London Library Association, 1959) 4s net (1959)

Current Medical Research—a reprint of the articles in the Report of the Medical Research Council for the year 1957-1958. Pp. iii+46. (London H.M. Stationery Office, 1959) 3s 6d net (1959)

World Power Conference Annual Report 1958. Pp. 20. (London World Power Conference 1959) 4s net (1959)

Ministry of Agriculture Fisheries and Food. Fishery Investigations Series 2, Vol. 22, No. 7. The Spawning of the Haddock (*Pleuronectes platessa*) in the North Sea. By A. C. Simpson Pp. iii+114. (London H.M. Stationery Office 1959) 3s 6d net (1959)

Report of Her Majesty's Civil Service Commissioners for the period 1st April, 1958 to 31st March 1959 Pp. 25. (London H.M. Stationery Office 1959) 2s 6d net (1959)

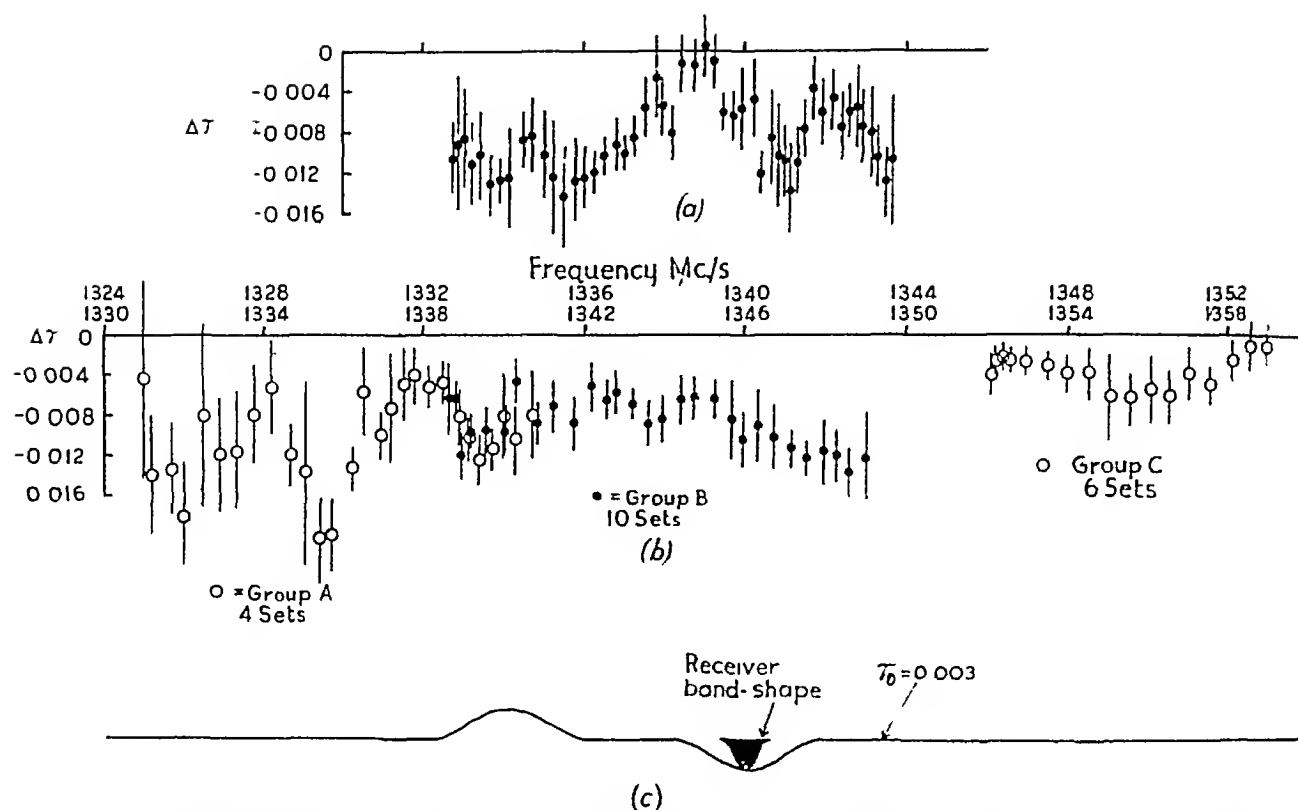


Fig. 1. Observed absorption spectrum of Cygnus A in the vicinity of 1340 Mc/s. The standard deviation of each point is shown by a vertical line. (a) Band-width = 100 kc/s. (b) Band-width = 700 kc/s. The full line plot (c) shows the shape that would be recorded for a Gaussian absorption spectrum with $\tau_0 = 0.003$.

profile in terms of optical depth was made by introducing a small square-wave signal into the intermediate frequency channel which produced a deflexion on both the switched and total-power recorders.

Frequency scans on local hydrogen at about 1,420 Mc/s showed the expected emission temperatures and in addition the absorption spectra in local hydrogen of Cassiopeia-A, Cygnus-A and Taurus-A were all in good agreement with the results given by Muller³.

The measurements were made in two groups using the receiver in different modes of operation to eliminate spurious effects so far as possible.

(a) February 14–23, 1959. Band-widths of 8 and 100 kc/s were used. The frequency range 1,330–1,355 Mc/s was investigated by scanning 4 Mc/s through the intermediate frequency bandpass by means of a variable-frequency second local oscillator. A series of first local oscillator frequencies was used to cover the frequency-range. The resultant spectrum of Cygnus-A showed no absorption feature down to a limit of peak optical depth $\tau_0 = 0.01$. This may be compared with a positive effect of $\tau_0 = 0.09$ indicated by the Lilley and McClain results.

(b) May 22–June 8, 1959. Band-widths of 100 and 700 kc/s were used and the stability of the receiver was improved. The frequency range 1,315–1,435 Mc/s was covered by setting the second local oscillator at a fixed frequency and tuning the first switched local oscillator over a range of 11 Mc/s about a series of fixed frequencies. These results obtained in the vicinity of 1,340 Mc/s are plotted in Fig. 1. They show $\Delta\tau$, the optical depth at the low frequency minus that at the high frequency, plotted against the frequency of the two switched receiving bands. Each point is the average of the corresponding points from a number of sets. Its standard deviation is represented by a vertical line. Fig. 1a gives the

results of the 100 kc/s switched receiver over a frequency range of 1,332–1,349 Mc/s. Fig. 1b gives the 700 kc/s band-width results in the range 1,325–1,359 Mc/s. These points are made up of three frequency groups each having the number of sets shown. The systematic shift of the points in these figures is due to some small but unresolved effect, this displacement amounts to 1 deg K on the switched records. Any absorption would appear on these plots in the form of a convolution of the true profile with two band-shapes of opposite sense spaced by 6 Mc/s. The response would be an upward excursion at 1,340 Mc/s on the high-frequency channel and a downward excursion at 1,340 Mc/s on the low-frequency channel. This is shown by the full-line in Fig. 1c in which the response is drawn for a Gaussian absorption profile with a width to half-intensity of 2 Mc/s (400 km/sec), $\tau_0 = 0.003$ and centre frequency 1,340 Mc/s. Both excursions must be present if any real absorption occurs. The 100 kc/s results show no absorption effect greater than $\tau_0 = 0.005$ and the 700 kc/s results point with certainty to an upper limit of $\tau_0 = 0.003$ and to a probable limit of perhaps half this value.

Thus the present results do not confirm the Lilley and McClain observations. The radio-frequency confirmation of the distance of Cygnus-A no longer holds and moreover, the measurements provide no check that the radio and optical cosmological red shift velocities are the same.

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Jodrell Bank Experimental Station,
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Sept. 14

¹ Lilley, A. E., and McClain, D. I., *Astrophys. J.*, **123**, 172 (1956).
² Baade, W., and Minkowski, R., *Astrophys. J.*, **119**, 200 (1954).
³ Muller, O. A., *Paris Symposium on Radio Astronomy*, edit. Bracewell, R. N. (Stanford University Press, 1959).

Association of Radio Outbursts with Solar Flares

SEVERAL authors have paid attention to the association of radio outbursts with solar flares, for example Dodson¹ and Loughhead, Roberts and McCabe². Outstanding flare events are very commonly accompanied by a radio event at decimeter and/or metro wave-lengths but only a minor fraction of the less important flares produce a distinctive radio event.

Since the beginning of the International Geophysical Year the flare patrol coverage has been very nearly complete whereas for radio frequencies 200 and 545 Mc/s complete radio information is available from the observatory Nera (Holland) and associated observing stations at Paramaribo (Surinam) and Hollandia (New Guinea). At frequencies near 3000 Mc/s nearly complete coverage is accomplished by the observatories at Ottawa, Tokyo, Berlin and Nera.

The great amount of information now available enables a detailed investigation into the relationship between solar flares and associated radio events.

In order to verify whether the association of outbursts with flares of a special type or belonging to a particular sequence is above or below normal we derived mean frequencies of occurrences of 'radio flares'. These figures were obtained by carefully comparing our records with the list of flares compiled by the Meudon Observatory for the *Quarterly Bulletin on Solar Activity*. As in many cases there is a close correspondence in time between the starting times of flare and outburst, we allowed no time differences exceeding 10 min. between the two events unless there were indications that there still existed a physical relationship (for example, if both flare and outburst were very outstanding).

In treating the data covering the period July 1957–December 1958 we arrived at the relative frequencies listed in Table 1.

Table 1. RELATIVE FREQUENCIES OF OUTBURST ASSOCIATED FLARES

| Optical importance | Associated outburst at | | | Associated outburst at any frequency | |
|--------------------|------------------------|----------|-----------|--------------------------------------|---------------------------|
| | 200 Mc/s | 545 Mc/s | 3000 Mc/s | All flares | Thinly established flares |
| 1 | 0 | 8 | 12 | 10 | 27 |
| 2 | 21 | 21 | 37 | 46 | 60 |
| 3 | 70 | 83 | 97 | 97 | 97 |

The last column of Table 1 gives percentages of association for those flares that have been observed by at least two observatories. For these 'thinly established' flares the percentages of association is greater than for the flares in general. From this fact we conclude that a number of those flares that have been reported by only one observatory apparently had not very outspoken flare characteristics and should be considered as somewhat doubtful cases.

It has appeared that certain sequences of flares, originating in very much the same heliographic position are distinctive for an abnormally great or for a very low production of outbursts or for a special type of associated radio events. In such cases one might speak of a 'radio family' of flares. We just mention two of the most clear-cut cases of distinctive flare sequences that occurred during recent years.

(a) On September 10, 17 and 18, 1957, a region of great flare activity was situated close to the centre

meridian, at 22° N. 17 flares in this region were associated with sudden ionospheric disturbances. Of these flares only two produced a radio response at 3000 Mc/s or lower frequencies. No outbursts were associated with the flares that did not produce a sudden ionospheric disturbance. This production of outbursts is much less than expected as we found that in general more than half of the flares associated with sudden ionospheric disturbances give rise to a radio event. Therefore this flare sequence was remarkable for an outstanding lack of radio responses.

(b) A rather great flare activity was displayed during the period December 10–13, 1958, by the region that passed the central meridian on December 11 at latitude 2° S. All but one of the 14 flares of importance 2 produced outbursts, most of which occurred at all three frequencies 200, 545 and 3000 Mc/s. Among the 18 flares of importance 1 there were 8 radio flares whereas also 6 sub flares had a radio response. So the production of outbursts was greater than normal. The distinctive characteristic of the sequence is the fact that almost all outbursts at 545 Mc/s reached exceptionally great intensities.

During the International Geophysical Year and afterwards many flares were observed by two or more observatories. For a number of them there is very good agreement as to the starting times reported by various observers. It seems likely that these are flares which flashed up suddenly leaving little doubt about the exact time of commencement. On the other hand, observatories might very well report different starting times for flares which come into existence more gradually. The flares for which the starting times given by different observers are nearly the same (differing only by 1 min. or so) often reach their maximum development shortly after their beginning (47 min. on the average). This corroborates their impulsive character.

From the Meudon lists of flares covering the period July 1, 1957–December 31, 1958 we selected the 'impulsive flares of importance 1'. A greater than normal percentage of these flares was accompanied by radio events (Table 2).

Table 2. FREQUENCIES OF OUTBURST ASSOCIATION FOR FLARES OF IMPORTANCE 1

| | No. | Percentage of outburst association (per cent) |
|---------------------------|------|---|
| All flares | 6061 | 18.6 |
| Thinly established flares | 211 | 26.5 |
| Impulsive flares | 475 | 35.7 |
| Non-impulsive flares | 1706 | 21.6 |

This circumstance seems to give at least partly an answer to the question why certain flares cause an outburst whereas others do not. It is that the impulsiveness might have a bearing on it. No difference though, was found between the frequencies of outburst association for impulsive and non-impulsive flares of importance 2 or 3.

The enhanced outburst association for impulsive flares of importance 1 might also be tied up with the problem of distinguishing which is a flare and which is not. As a matter of fact there exists a continuous transition between the bright plage regions in which the brightness is gradually changing and the clearly defined flares that flash up suddenly. Various observatories certainly apply different criteria as to when a particular brightening should be considered as a flare.

The working group on flare classification of Commission 11 of the International Astronomical Union considered the suddenness of commencement as one of

the main criteria for distinguishing flares³. We now see that the radio evidence lends support to this point of view

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- ¹ Dodson Prince, H. W., *Proc. Inst. Radio Eng.*, **46**, 149 (1958)
² Loughhead, R. I., Roberts, J. A., and McCabe, M. K., *Austr. J. Phys.*
10, 483 (1957)
³ *Trans. Int. Astr. Union IX*, 146 (1955)

Distribution of Flares on the Solar Disk Associated with Noise

THE association of solar noise bursts at 48 Mc/s and solar flares has been examined for the periods June 20–July 31, 1957, September 1–October 1, 1957, and June 1–July 31, 1958. The noise burst data were obtained from the Resolute auroral radar film records. Resolute was the northern station (75° N, 95° W) of the National Research Council's International Geophysical Year Auroral Radar Chain¹. For the purpose of this analysis, bursts are defined as solar radio noise events with durations of the order of 30 seconds or less (probably due to spectral type III bursts). Association with a particular flare was assumed probable if the burst occurred during an interval of 2 minutes preceding, to 3 minutes following the flare commencement. This is a more stringent requirement than that usually used^{2,3}. During the periods listed above, a total of 535 such events were recorded with 12 per cent of the noise-producing flares occurring within $\pm 5^\circ$ of the central meridian, while for the same periods 8 per cent of all flares occurred in the same interval.

Hev and Hughes have found an east-west asymmetry for the period 1947–1950 where both the number and intensity of flares associated with noise at 73 Mc/s were greater in the eastern half of the solar disk². They also observed a reduction in the number of such flares near the central meridian. The data summarized in Fig. 1 indicate a definite peak in

flares associated with noise near the central meridian. Of a total of 3,671 flares considered in the analysis, 54.5 per cent occurred east of the central meridian, while only 47.4 per cent occurred east of the central meridian. The dip in the curves at 10° W will require the analysis of more data before its validity can be established, but it does appear to be common to the data for each of the 3 periods so far analysed.

The north-south distribution for the same periods was examined for both total number of flares and flares associated with noise. The great preponderance of flares in the northern hemisphere shown in Fig. 1 was unexpected. Newton and Milsom have observed a shift in the 'spottedness' of the northern and southern hemispheres from cycle to cycle over many sunspot cycles¹. Their results indicate that the present cycle has a definite increase in spot activity in the northern hemisphere. An increase in flares associated with noise in the northern solar hemisphere has also been observed in Japan⁴.

The results presented here indicate that the present conditions in the solar corona favour the emission of radio noise at very high frequencies from flares occurring in the north-west quadrant of the solar disk.

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¹ McNamara, A. G., *Can. Electronics Eng.*, **1**, 26 (1957)

² Hev, J. S., and Hughes, V. A., *M. N. Roy. Soc.*, **115**, 697 (1955)

³ Warwick, C. S., *Astrophys. J.*, **120**, 277 (1951)

⁴ Newton, H. W., and Milsom, A. S., *M. N. Roy. Soc.*, **115**, 303 (1955)

⁵ Shino, K. (private communication)

Observations of 'Whistlers' and Very Low Frequency Phenomena at Godhavn, Greenland

As part of the research programme for the International Geophysical Year, recording of very low-frequency phenomena was initiated at Godhavn, Greenland, on July 19, 1957. The geomagnetic co-ordinates for Godhavn are 79.8° N, 32.5° E. The station is situated 950 km south-east of the geomagnetic pole and approximately 1800 km north-east of the dip-pole.

A little more than one year's recordings of whistlers have now been sealed and analysed. These cover the period from July 19, 1957, to the end of July, 1958. On July 21, 1957, the first possible whistler was heard but it was too faint to analyse. Whistlers have also been recorded on October 10 and 11, November 26, December 12 and 21, 1957, and on January 11, 1958. Maximum activity was observed on October 11, when 7 consecutive hourly recordings contained whistlers at a rate of up to 30 per two minutes. The total number of whistlers observed during one year is nearly 125, of which about 50 have been analysed.

It is difficult to find the whistlers by listening directly to the record, mainly because of lack of low frequencies in the whistlers, but the interpretation is facilitated by listening to the tape at half speed. This

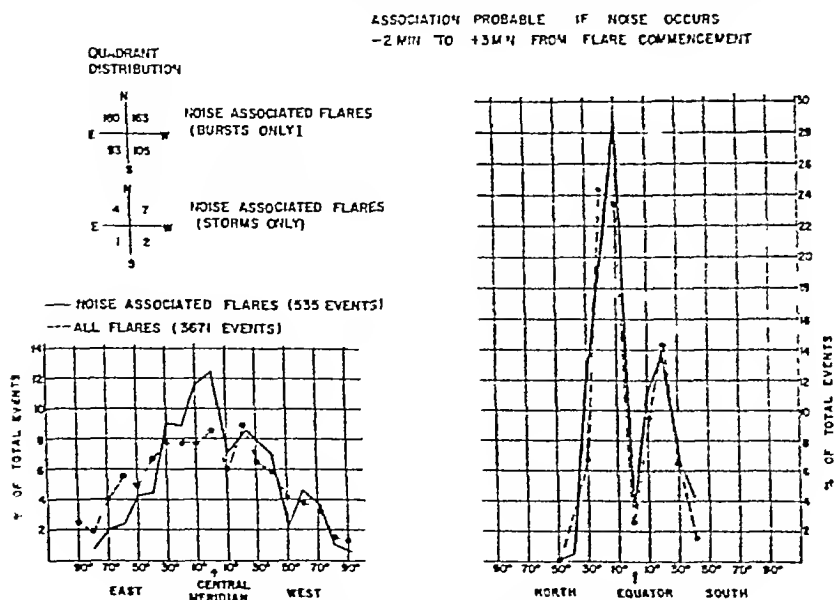


Fig. 1. Distribution of noise associated flares for periods June 20–July 31, 1957, September 1–October 31, 1957 and June 1–July 31, 1958. Noise data from Resolute 48 Mc/s auroral radar records.

is time-consuming, and therefore, for the time being we only listen at half speed to tapes when we suspect there is some whistler activity.

The recordings were made with a tape speed of 7.5 in./sec and the corresponding upper frequency limit is 16 kc/s.

As a result of the analysis it has been found that the Godhavn whistlers as compared to whistlers from lower latitudes all show a lack of low frequencies, and that the whistlers observed during October have nose frequencies of at least 15 to 16 kc/s.

The observed minimum frequencies are distributed as shown in Fig. 1. No frequency components have

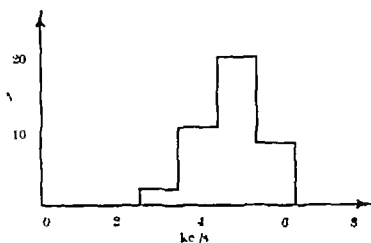


Fig. 1. Distribution of minimum frequencies of whistlers observed in Godhavn.

been detected in the ranges 0.6-1.5 or 1.6-2.5 kc/s, and the most common minimum frequencies lie in the 4.6-5.5 kc/s range.

We have computed some dispersions for the whistlers observed on October 11 to about 55-60 S^{1/2}. It is not possible to determine other dispersions because the rest of the whistlers are too indefinite but we judge that they are of about the same magnitude.

The geomagnetic activity at the times of whistler occurrence was moderate and the ionosphere only slightly disturbed.

The high nose frequency of about 16 kc/s seems to indicate that the Godhavn whistlers penetrate the ionosphere at a point south of Godhavn. According to the accepted theory, the nose frequency is proportional to the minimum value of the gyro frequency f_{\min} along the path. If we take this ratio as 0.4 we find $f_{\min} = 16/0.4 = 40$ kc/s which corresponds to a geomagnetic latitude of 53°. If the Godhavn whistlers have penetrated the ionosphere at this latitude they have been propagated about 3000 km along the earth below the ionosphere. This aspect was discussed with American colleagues during a recent visit to the United States.

The missing low frequency components in the Godhavn whistlers seem to indicate a wave guide type of propagation along the Earth from the point of penetration to the observation point^{1,2}. During the penetration of the ionosphere the whistler is guided along a magnetic field line which is parallel to the inclination and accordingly rather steep. The circularly polarized down-coming wave can be resolved into linearly polarized TE and TM waves with a cut-off frequency of about 1750 c/s for the dominant modes. The attenuation of the TM wave is rather high for all frequencies while it decreases exponentially with increasing frequency for the TE wave. Accordingly one would expect to receive the TE mode.

Support for the wave guide theory may be derived from the fact reported by Rivault⁴ that most whistlers have frequencies descending to about 1.75 kc/s.

Lower end frequencies were observed only in exceptional cases.

A proof of the supposed penetration through the ionosphere at about 53° N geomagnetic latitude could be obtained if whistlers were heard nearly simultaneously at stations situated south of Godhavn. Such a proof has not been obtained because several of the higher latitude stations of the American Whistler East Chain were inoperative at the times when whistlers were heard at Godhavn. The only possibilities for comparison hitherto has been with Hanover, New Hampshire, for the observations in October, 1957, and for some of the observations in December 1957. No whistlers were heard in Hanover at these times, and this seems to contradict our theory. When more observations are available we plan to compare data with other stations.

Whistler observations in the antarctic have been reported by Martin⁵. During the observation period April 1-15, 1958, whistlers were heard consistently but no dawn chorus was observed. These frequencies of appearance are the opposite of those observed at Godhavn.

As a result of the analysis of the first year's observations we have found that 'twos' are not heard during the polar day but they begin to appear as soon as the sun is below the horizon during part of the night. The highest activity is observed in the months of August and September.

Chorus and hiss are most often heard between 10 and 12 local mean time when chorus is observed in about 18 per cent and chorus plus hiss in about 22 per cent of the recordings. The maximum magnetic activity occurs at the same time of the day⁶. There is a seasonal variation in the relative frequency of chorus and hiss with a lower activity during and around the polar night.

Our analysis has shown that the observed chorus is normally in a lower frequency range than further south. Except for a very few observations the frequency range has been 500-1000 c/s. The range from 1000 to 1200 c/s is heavily disturbed by harmonics of the power frequency and the high pass filter applied gives a sharp cut-off at 500 c/s. However, we are trying to improve our observations of the chorus and hiss phenomena.

If the wave guide model proposed above applies chorus in the observed frequency range at high latitudes should be a rather local phenomenon because of high attenuation below the cut-off frequency.

The research reported here has been sponsored by the Geophysics Research Directorate of the U.S. Air Force Cambridge Research Center, Air Research and Development Command through the European Office under contract AF 61 (514) 1300 and by the Danish Science Foundation and the Danish Research Foundation for Technical Sciences.

FIGURE UNSTRUCTURED

Royal Technical University of Denmark
Copenhagen
July 6

- ¹ Chapman, E. W., and Mariani, R. C. V. *Nature* 177, 920 (1956).
- ² Wall, J. H. *Proc. Inst. Elec. Eng.* 45, 760 (1957); 45, 768 (1957).
- ³ Ramo, S., and Whittaker, J. R. *Fields and Waves in Modern Radio*, p. 315 ff. (Wiley, New York, 1953).
- ⁴ Rivault, R. *Laboratoire National de Radioélectrique Note Préliminaire* No. 131 (Feb. 1958).
- ⁵ Martin, L. H. *Nature* 181, 1706 (1958).
- ⁶ Jensen, K. J. *Institut for Radiofysik danske Kommunikationstegninger* etc. No. 23 (1958).

A New Microwave Harmonic Generator*

If my estimate¹ of up to 10^7 amp/cm² for the emission current density of free cathode 'spots' on a clean mercury surface is accepted, the mercury arc may be regarded as an indestructible point-contact rectifier with interesting microwave properties. At high rates of growth of current (that is, in excess of 6×10^7 amp/sec) the cathode emission appears to be unable to follow the rising current by its normal method of increasing size¹ and presumably (at microwave frequencies) must either change its emission density or become unstable, or both. In either case a 'non-linear' current-voltage relationship is still to be expected.

Instability of short mercury arcs at microwave frequencies has already been reported², and following a suggestion by Prof B Bleaney, this communication describes the use of such arcs for the purpose of harmonic generation from a relatively high-powered microwave input.

Fig 1 shows in diagrammatic form the essentials of the harmonic generator. Microwave power at 2.5 Gc/s (from a continuous-wave magnetron of up to 100 watts output) is used to maintain a very short mercury arc between a mercury pool 'cathode' and tungsten wire 'anode'. The harmonics generated are collected by the smaller wave guide shown, coupling to which is assisted by the adjustable tuning plunger placed inside the discharge tube. The tube is filled with argon to a pressure of at least one atmosphere, an even higher pressure being desirable. By using such a gas pressure it is possible to maintain a great density of ionization in the 'positive column' plasma of the arc, so that harmonics generated in the very small region of cathode-fall can be communicated to the anode wire. By tilting the discharge tube the arc may be adjusted to minimum length, the shortest possible arc being the most efficient.

With an estimated input power of a few watts at 2.5 Gc/s, an output in excess of one milliwatt was obtained at 10 Gc/s, also a strong signal at 30 Gc/s was detected by a spectrum analyser placed close to the arc tube. The anode wire for these experiments was 0.5 mm in diameter and length of arc was about 0.1 mm. An ammeter connected from anode to cathode indicated a rectified current of 100-600 m amp, the electrons flowing from the mercury to the tungsten wire 'anode'.

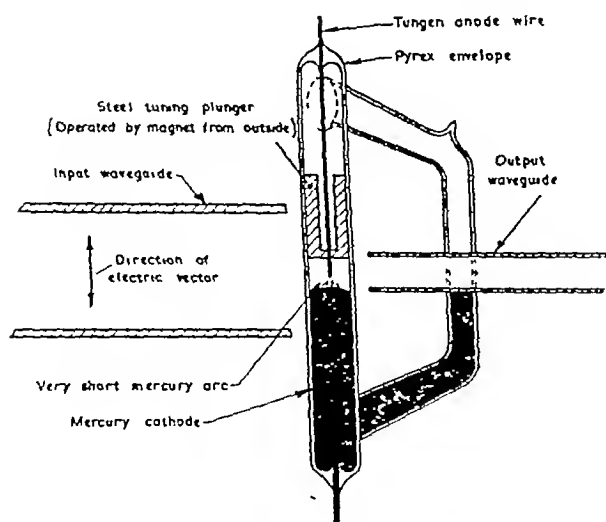


Fig 1 Arc harmonic generator

If a 4-8 volt battery is connected externally so as to assist this electron flow, the microwave driving power may be reduced. If, in addition, the anode wire is made thin enough (for example, 0.1 mm. diameter) to become red hot under the action of the discharge, a very short arc indeed may be obtained in the dimple formed by insertion of the anode below the normal free mercury surface, a cushion of mercury vapour preventing all but occasional short-circuiting of the arc. This 'dimple arc' mode of operation can be the most efficient of all, but care has to be taken to avoid melting the rather fine anode wire necessary for low shunt capacity.

For the input frequency described, the quality and efficiency of the arc harmonic generator seem entirely comparable with the 'non-linear' semi-conducting crystal type, but the arc has one considerable additional virtue: there is no upper limit to the input power that can be used, for the arc cathode spot cannot be damaged. Work is continuing with the view of extending the use of the generator into the millimetre-wave region.

This work has been carried out as part of the research programme of the National Physical Laboratory and is published by permission of the Director of the Laboratory.

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*Patent Application No. 30205/59

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A Spectrum of Turbulence at Very High Reynolds Number

THE downstream component of the turbulent velocity has been recorded in a sea-water channel with a Reynolds number, based on the depth, of 4×10^7 . The measurements were made near the southern end of Discovery Passage ($50^\circ 00' N$, $125^\circ 12' 5' W$) with a tidal current of 100 cm/sec flowing northward at the point of observation. At this point the channel is about one mile wide and the water has been flowing with a depth of about sixty metres for a little over a mile, having entered the passage from the wide and deep basin of Georgia Strait.

The turbulent velocity was measured with a hot film anemometer, the form of the probe being a platinum film of thickness 4×10^{-6} cm, plated around the tip of a glass cone which pointed into the stream. The maximum dimension of the film is about 1 mm and it has a resistance of five ohms. An a-c bridge was used with a carrier frequency of 7.5 kc/s. The probe was mounted on the nose of a heavy body towed at a depth of 25 feet from the stern of a ship steaming against the current so as to maintain a fixed position.

A thirty-minute sample of the turbulence signal has been analysed with narrow band filters. Fig 1 shows the high frequency end of the energy spectrum and the dissipation spectrum, each multiplied by the wave number k so that the area under the curves represents the energy and dissipation on the semi-logarithmic plot. Fig 2 is a logarithmic plot of the energy spectrum.

The points at the extreme values of k are not very reliable. For $k < 0.02$ cm⁻¹, the motion of the towed

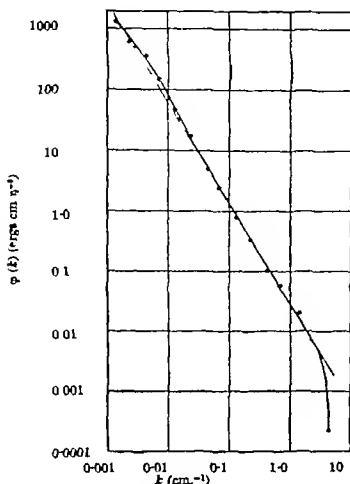
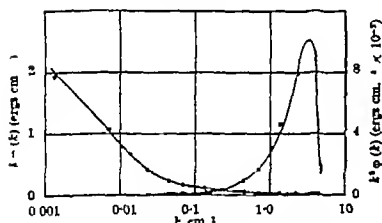


Fig 1

Fig 2 —●— refers to $k^2 \varphi(k)$ —×— refers to $1 - \epsilon$

body makes a contribution to the reading of the hot film. A crude accelerometer showed that the spectrum of the longitudinal motion of the body extends up to values of k in the neighbourhood of 0.02, and this is believed to be the reason that the curve in Fig 2 lies above the $k^{-5/3}$ line over this region. The main cause of this is orator motion of the ship. Variations in engine speed cause pitching and surging while the large-scale turbulence produces transverse movements of the stern requiring continual helm adjustments to maintain course. In addition towed body motions are excited directly by turbulence too small to affect the ship. The natural period of the towed body and its towing wire, acting as a pendulum, is in this range of k . Unfortunately, we do not have sufficient information about the motion of the towed body to attempt a correction. For values of $k > 1 \text{ cm}^{-1}$ the electronic noise level becomes an appreciable part of the signal. Here we have made a correction to the data but the points are not as reliable as those for $0.02 < k < 1$.

The two spectra in Fig 1 are well separated on the wave number axis and it seems likely that an inertial sub range exists. The straight line in Fig 2 has a slope of $-5/3$ and fits the data reasonably well over a very extensive range of k in the region between the peaks of Fig 1. This cannot, however, be taken as verification of the $k^{-5/3}$ relation predicted for the inertial sub range by the Kolmogoroff theory¹ because it has not been demonstrated that local isotropy exists. The spectra obtained by Laufer² in fully developed

pipe flow ($R = 2.5 \times 10^4$), indicated that the turbulence was anisotropic at high wave numbers and Kraichnan³ has shown that, although the spectrum of the downstream component follows a $k^{-5/3}$ law, the one dimensional spectrum of the total energy is proportional to $k^{-3/2}$.

The total dissipation can be obtained by integrating the dissipation curve of Fig 1. Using the isotropic relation

$$\epsilon = 15\nu \int k \cdot \varphi(k) dk$$

we obtain $\epsilon = 2.5 \times 10^{-3} \text{ ergs cm}^{-3} \text{ sec}^{-1}$. The area of the curve is open to question because it depends upon two points which contain a large correction for noise but this figure can be confirmed by estimating ϵ in less direct ways. We may assume the spectrum function predicted for the inertial sub range by the Kolmogoroff theory

$$\varphi(k) = \lambda \rho^{1/3} \epsilon^{2/3} k^{-5/3}$$

We find λ , from the spectrum measured by Laufer for which ϵ was determined fairly accurately, to be 0.25 and using $\varphi(1) = 2.75 \times 10^{-7}$ from the present spectrum, $\epsilon = 3.7 \times 10^{-3} \text{ ergs cm}^{-3} \text{ sec}^{-1}$. That these figures are of a reasonable order of magnitude can be seen without reference to the spectrum from the relation $\epsilon = \tau dU/dy$. By comparison with other channel flows, we may expect that typical values of the shear stress and velocity gradient are given by $\tau \approx 10^{-3} U_0^2$ and $dU/dy \approx 0.2 U_0/d$, where d is the depth of the water. This leads to $\epsilon = 3 \times 10^{-3} \text{ ergs cm}^{-3} \text{ sec}^{-1}$.

The value of λ at which the peak of the dissipation curve occurs, λ_m , may be compared with λ , the characteristic wave number of the dissipation range, defined by $\lambda_c = (\epsilon/\nu^3)^{1/4}$. It is a result of the Kolmogoroff theory (but not of Kraichnan's theory) that λ_c/λ_m is an absolute constant and Table 1 shows the

| Type of Flow | Table 1 | | Ref |
|-------------------|--------------------|-----------------------|-----|
| | Reynolds No | λ_c/λ_m | |
| Discovery Passage | 4000×10^4 | 5.4 | 5 |
| Grid turbulence | 1 | 0.5 | 6 |
| Boundary layer | 25 | 15.2 | 7 |
| Pipe | 25 | 15.2 | 7 |
| Channel | 3 | 12.1 | 7 |

value obtained from the present experiment compared with other measurements of dissipation spectra.

When the experimental difficulties are taken into account the first three, or the last two values of λ_c/λ_m can be considered to be consistent with the idea of a universal constant but the two measurements reported by Laufer appear to differ significantly from the others.

We cannot obtain the total turbulent energy directly because a large proportion of it is associated with scales of motion comparable to the dimensions of the ship and is therefore not measurable even with a hot film fixed rigidly to the ship. From visual observation of the water surface and ship motion, however, we estimate the integral scale of the turbulence L , to be about 60 m. Using the isotropic turbulence relation $\epsilon = 3\rho(u^2)^{3/2}/2L$ and taking $\epsilon = 3 \times 10^{-3}$ we have $u^2 \approx 20 \text{ cm}^2 \text{ sec}^{-2}$. This value, which is not particularly sensitive to errors in the estimate of either ϵ or L , corresponds to about 4.5 per cent turbulence which is reasonable for such a channel. It should be noted that the measured portion of the energy spectrum contributes only about 1/5 of this value of u^2 which further strengthens our opinion that the portion of the spectrum $k > 0.02 \text{ cm}^{-1}$ cannot contribute signif-

cantly to the Reynolds stress, and so should be within an equilibrium range if Kolmogoroff's assumptions are valid

We propose to make a more extensive series of spectrum measurements with an improved noise level. This will be done in the northern end of Discovery Passage, where the water flows for five miles through a deeper channel after passing through the constriction at Seymour Narrows at a Reynolds number of over 10^8 on a strong tide

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Evidence for Distinct Sectors in Polymer Single Crystals

It was reported earlier that long-chain polymers could form single crystals in which the molecules have a regularly folded configuration^{1,2}. Polyethylene in particular can have a paraffin-like crystal habit consisting of thin lozenge-shaped layers with each segment of the folded molecular chain normal, or

approximately normal, to the plane of these layers. It was suggested³ that the molecules might fold in the plane of the growing faces, which are of the {110} type in the purely lozenge shaped crystals. This implies that in the four different quadrants the chains are folded along four different $\langle 110 \rangle$ directions, and hence that the apparent single crystal consists in fact of four structurally distinct sectors in twin relation. So far as we know, this situation is unprecedented in crystalline substances.

Some evidence for the existence of distinct quadrants has already been reported^{3,4}. Thus surface corrugations were noticed which divide the crystal into four parts. Further deductions from interference effects in electron micrographs (Bragg fringes, moiré patterns) revealed that adjacent quadrants of the crystals satisfied different conditions of diffraction. We add here that current work has confirmed these deductions through direct observations of the electron diffraction patterns given by individual crystal sectors. These showed that different quadrants added different reflexions to the diffraction pattern given by the crystal as a whole. This situation would arise if the crystal layers were dished pyramids buckled along the two lozenge diagonals, or if the lattice were sheared differently in the different quadrants or possibly if both effects existed together. The dished pyramidal configuration is suggested by a number of observations. The most consistently recurring one is that of a triangular central fold along the short lozenge diagonal (Fig. 1). The crystal is three layers thick along this thickening. It is readily seen that this would be the result if a hollow pyramid collapsed. The uncollapsed pyramid, however, has never been observed, though crystals with the triangular fold have been seen in suspension. There is no apparent reason why the pyramidally dished crystal should collapse except in contact with a flat substrate, and it is possible that the fold, with the same resultant geometry, is produced by a progressive shear transformation within the crystal, without actual realization of the intermediate dished pyramid. Either picture leads one to look for some splitting of diffraction spots, though of different magnitude according to the details of the mechanism. Such splittings, of various magnitudes, have been observed, and are the subject of current work. We first saw such a splitting in an electron diffraction picture communicated to us privately by S. Mitsuhashi.

The various observations indicating distinct sectors, sheared and/or hollow pyramidal crystals are related. If the folds in one sector are along one kind of $\langle 110 \rangle$ direction only, the structure will have a lower symmetry than it would have without the fold, and the lattice will no longer be orthorhombic as in the ideal polythene structure. The obliquity introduced in this way would be identical in magnitude but opposed in sign in quadrants which grew at different {110} faces. The diagonal containing the fold would be either shorter or longer within the sheared cell. In the first case the crystal consisting of four different non-orthorhombic quadrants in twin relation, would be automatically a dished pyramid. In the latter case it would be a flat lozenge with edge dislocations in it, probably in rows along the lozenge diagonals. In either way the obliquity would depend on the relative abundance of the folds, and thus on the length of fold. Consequently the uniformity of the lattice would require a uniform length of fold throughout the crystal. In this way the observed uniformity of the length of fold, perhaps the most puzzling property of

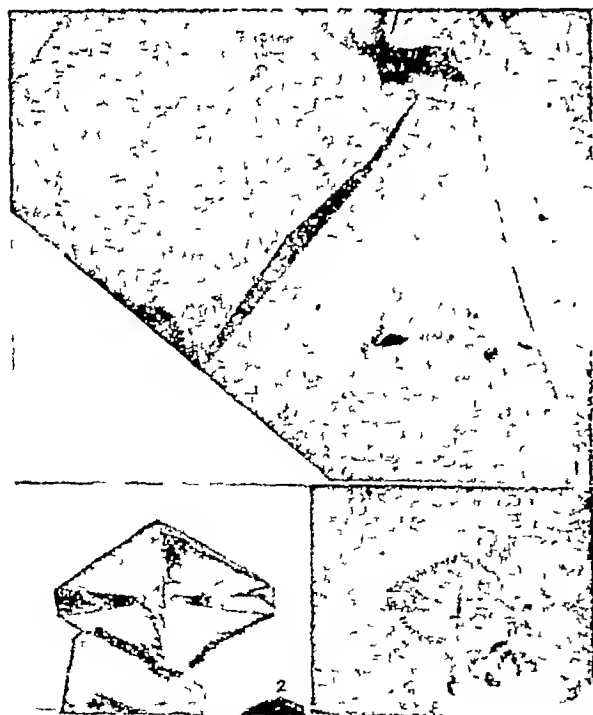


Fig. 1 Polyethylene crystal grown from xylene at 00° C. Electron-micrograph, $\times 2,500$

Fig. 2 Polyethylene crystal grown from xylene at 90° C. showing sector through extinction effects. Electron-micrograph, $\times 1,500$

Fig. 3 Polyethylene crystal grown from xylene at 90° C., after thermal treatment (see text). Photomicrograph, phase contrast $\times 750$

these crystals, would be accounted for

In Fig 1 the crystal is a truncated lozenge, showing also $\{100\}$ faces in addition to the $\{110\}$. In this case we expect six distinct sectors, four with folds along $\{110\}$ and two along $\{100\}$ planes. The existence of the first four has already been demonstrated. That of the additional two is revealed by electron micrographs like Fig 2 where such sectors appear in Bragg contrast because they satisfy different reflexion conditions from the rest of the crystal. Sometimes a surface corrugation can also be seen bounding such sectors.

As stated earlier, the sectors bounded by $\{110\}$ faces are in twin relation, that is the lattices also including the fold along $\{110\}$ planes, are identical but in different orientation. However, the remaining two sectors with folds along $\{100\}$ planes would represent a different lattice. This is strikingly brought out by the following experiment. The crystals, sedimented on a slide were heated to about $128-130^\circ\text{C}$. When examined after cooling they appeared as in Fig 3. It is seen that the sectors in question are now distinct, thus they must have melted (or become otherwise transformed) at a lower temperature than the rest of the crystal. This difference in thermal stability is in agreement with the postulate of a different lattice.

We conclude that the existence of distinct sectors within the same crystal is definitely established in agreement with the predictions based on the folded molecular configuration in polymer crystals.

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Deviation of Zone Lenses Produced by Polarization

Zone lenses are systems of alternate opaque or phase retarding rings which are usually made in one of the following ways: (a) by describing larger circles on cardboard and photographically reproducing them, (b) by photographing Newton fringes occurring between a slightly convex lens and an optical flat, or (c) following Wood¹ but cutting out narrow ring circles on a previously coated surface by means of a turntable or lathe. The least distance (d) resolved by a zone lens is given by:

$$d = 1.22\lambda B \quad (1)$$

where λ is the wave-length and B the focal length/diameter. Since the focal length is proportional to the square of the radius of the innermost zone², small zone lenses will have higher resolving power. Thus the originals made are usually further reduced photographically in one or two subsequent steps.

Another way of producing zone lenses is based on the birefringent properties of certain crystals such as basal sections of calcite or sodium nitrate. The crystal is sandwiched between two Polaroid films (C in Fig 1). A is a monochromatic light source, B is an aspherical collecting lens, D a collimator, E a photographic objective (Tessar) of 50 mm focal length, and F is the image plane. Photographs were taken on Kodak type 649 high resolution film; they were developed in D 11' to a high gamma and some of

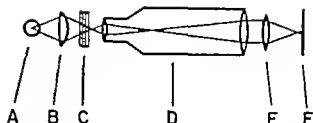


Fig 1 Polarization arrangement for producing zone lens-like concentric fringes

them further cleared in Farmer's reducer. In this way, zone lenses not larger than about 1 to 2.4 mm in diameter were produced in one single step.

Zone lenses of this type were then scanned by means of a densitometer comparator. The upper graph in Fig 2 shows the radii of an experimental zone lens,

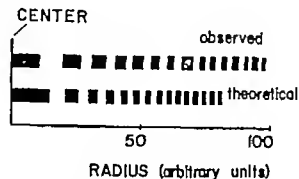


Fig 2 Radii of an experimental zone lens obtained by birefringence and compared with the theoretical figures.

scanned from centre to periphery in different directions. Generally, the radii, r_m , of the rings in a zone lens are proportional to the square roots of the natural numbers

$$r_m = r_1 \sqrt{m}, \quad m = 1, 2, 3, \quad (2)$$

where r_1 is the radius of the central zone. This relation is shown in the lower graph in Fig 2. Evidently, equation (2) does not rigorously describe the properties of zone lenses obtained by polarization for the individual zones decrease slightly slower in radius, toward the periphery, than required by theory.

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ELECTRONICS

Use of the Silicon Resistor in the d.c. Stabilization of Transistor Circuits

It is well known that changes in the d.c. characteristics of transistor amplifiers with temperature are particularly severe and tend to limit the range over which these devices can operate. The d.c. parameters, the changes of which are of interest are the collector-emitter leakage current (I_{co}), the d.c. current gain (α) and the base-emitter input impedance. This last producing a change in the base-emitter voltage. Up to the present stabilization has either been by minimizing these effects by suitable circuit design or by the use of thermistors and non-linear elements in some cases of circuit. These have the disadvantage in some cases of higher power consumption, and thus loss of the in-

herent high efficiency of the transistor amplifier, and limited range of stability

We have been using experimental samples of silicon resistors, supplied by Standard Telephones and Cables Ltd, Footscray, which have a high positive resistance temperature coefficient of about 0.7 per cent per degree. It would appear that the silicon is doped to such an extent that it is in the saturation region at room temperature, thus giving the positive coefficient.

We have achieved remarkable results, using these devices, for the stabilization of grounded emitter small signal stages. Some of the characteristics are shown in Fig 1.

Curve 1 shows the variation of collector current with no emitter resistor. The changes are very large indeed. Curve 2 shows the effect of inserting a carbon resistor in the emitter circuit. The improvement is quite

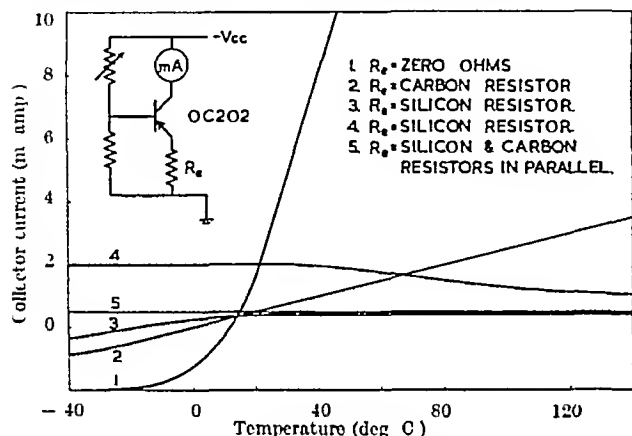


Fig 1 d.c. Stabilization of silicon transistor

impressive, but there is still a 4:1 change in collector current over the full range. Curves 3 and 4 show the effect of placing a silicon resistor of the same value as the carbon resistor in the emitter circuit at different collector currents. The stability at either high or low temperatures is very good. Curve 5 shows the result obtained when a carbon resistor of predetermined value is connected in parallel with a silicon resistor.

A stability factor (defined as the ratio of collector current at 25°C to collector current at T° C) of 1 is indicated over the whole temperature range of -50°C to +150°C. We believe this result is far better than any achieved by other methods.

The advantages of this method are as follows: no elaborate compensating network required, simplicity of design, stabilization over the whole temperature-range.

The use of silicon resistors has been applied to power transistors dissipating several watts, and it has been found that under certain conditions, using the silicon resistor in the base circuit, results giving a stability factor of 1 may also be obtained. These results agree very well with those predicted by theory and when the work is finished, a full account will be published elsewhere.

We wish to thank Messrs Standard Telephones and Cables, for their help in supplying the silicon used for the experiments.

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ENGINEERING

Blunt-Nosed Bodies in a High-Temperature Gas Jet

RECENTLY, the heating of nose cones on re entry vehicles has become a challenging technical problem. To provide thermal protection of an object in the core of the nose cone for short duration, two major kinds of shielding materials may be used, namely, metals and plastics. The former is favourable for a heat sink while the latter is favourable for ablation cooling. To demonstrate these features, some simple experiments were performed using a variety of these common materials. The materials were machined into $\frac{1}{8}$ -in. diameter hemispheres. A thermocouple (Fig 1A) was attached to the centre of the base of the hemispherical sample (B) next to a boron nitride insulator (C). The whole assembly was mounted on an arm (D) and swung into a jet of argon $\frac{1}{8}$ in. in diameter emitted from a plasma generator (E). The velocity of the jet impinging on the testing sample was subsonic. The temperature of the jet, T_f , as estimated from ref 1, was approximately 15,500° R. The measured temperature of the thermocouple, T_0 , increased with time, t , and was recorded on a Sanborn strip-chart recorder. Figs 2 and 3 show these results respectively for metal and plastic samples. For convenience, both T_0 and the non-dimensional temperature, $\theta_0 = (T_f - T_0)/(T_f - T_i)$, are used for the ordinate and t is chosen for the

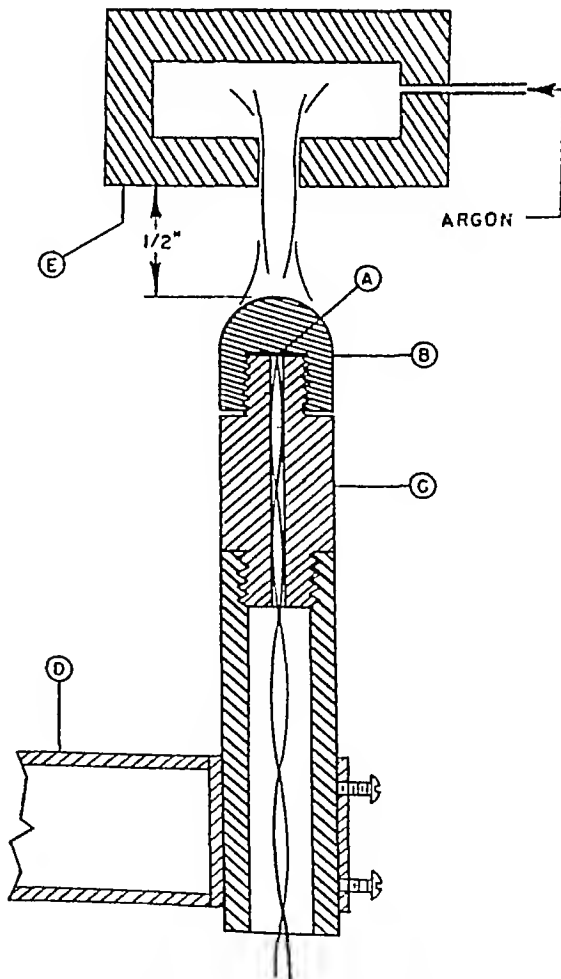


Fig 1 Schematic diagram of plasma jet and sample in operation

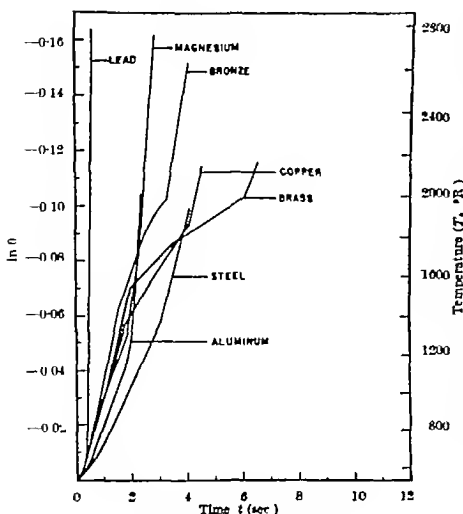


Fig 2. Measured thermocouple temperature T_m of metal samples with time, t
($0_0 = T_0 - T_0 / T_0 - T_1$)

abscissa in the figures (here T_1 is the room temperature)

A few interesting features in Figs 2 and 3 were observed

(1) For all the metals, four distinct periods can be seen (a) *Initial Stage* $\log_1 0_0$ versus t is curved upward for each metal. This trend may be explained by basic heat transfer theory, but the discussion is too lengthy to include here (b) *First Intermediate Stage* $\log_1 0_0$ versus t is practically linear. This will be discussed later (c) *Second Intermediate Stage* Copper and its alloys such as brass and bronze, distinguished themselves by a pronounced decrease in slope of

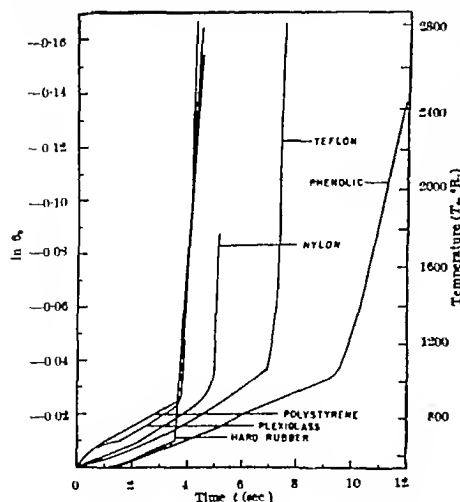


Fig 3. Measured thermocouple temperature (T_m) of plastic samples with time (t)

$\log_1 0_0$ versus t . This is probably due to evaporation of the base metal, copper (d) *Final Stage* All metals turn to a high and practically straight slope of $\log_1 0_0$ versus t . This is probably due to reduction of sample wall thickness through ablation

(2) For the majority of the tested plastic materials $\log_1 0_0$ started to drop linearly with time until T_0 reached 800° R or more. One exception was hard rubber which rose in temperature sharply at 680° R. From photographic evidence the rubber was apparently melted and vaporized and blown away by the jet. Consequently the thermocouple became closer to the jet and the temperature rose sharply. This also happened to the other plastics tested at temperatures higher than 800° R.

(3) Tests of the transparent plastics (Plexiglass and polystyrene) showed an initial sharp rise in temperature. This effect was probably due to direct thermal radiation absorbed by the thermocouple from the brilliant light of the plasma jet of argon. Later the blurring surfaces of these samples reduced such radiation appreciably and $\log_1 0_0$ became nearly linear.

(4) The phenolic laminate shows exceptionally good thermal insulation.

At present, no theory is known with which to analyze the transient temperature under the unusual conditions of these experiments; however, it may be worth while to attempt some simple correlation of the testing results with existing theory. For the case of a sphere surrounded by an atmosphere at high temperature T_0 , a well known formula is available to relate the measured time to the temperature T_0 at its centre. That is, $\log_1 0_0 = A r_1^3 / V N_{Fo} N_{Bi}$. Here A and V are respectively the surface area and volume of the sphere. N_{Bi} is the so-called Biot number and is equal to $h r_1 / k$, where k is the thermal conductivity of the sphere and h is the heat transfer coefficient from the fluid to the solid surface. N_{Fo} is the so-called Fourier number, defined by $N_{Fo} = \alpha t / r_1^2$, where α is the thermal diffusivity of the sphere and r_1 is the sphere radius. Within the limits of $N_{Fo} < 0.2$ and $N_{Bi} > 10^{-3}$, $\log_1 0_0$ is approximately linearly related with N_{Fo} , as indicated by the formula. Roughly, at the initial stage of the tests (Figs 2 and 3), $\log_1 0_0$ is fairly linear with time although many of the sample materials are beyond the above limits. This means that the heat transfer coefficient h is fairly constant at least within the initial period. Therefore h is calculated for these materials from the above formula using the classical data on α and k . These are presented in Table 1, which shows that h for the metals (except magnesium and lead) is about ten times or more than that of the plastics. It is believed that the low values of h for plastics is due to heat absorbed in surface melting.

Table 1. THERMAL PROPERTIES OF MATERIALS

| Material | α ft ² /hr | k BTU/hr ft. F | h BTU/hr ft ² F |
|-----------------|---------------------------------|---------------------|---------------------------------|
| Metals | | | |
| Brass | 0.667 | 32 | 30.6 |
| Steel | 0.57 | 31 | 29.2 |
| Lead | 0.924 | 20 | 18 |
| Brass | 1.2 | 62 | 49.0 |
| Magnesium | 1.655 | 43.5 | 17.8 |
| Aluminum | 2.22 | 82.3 | 22.1 |
| Copper | 4.39 | 123 | 42.0 |
| Plastics | | | |
| Phenolic | 0.00534 | 0.169 | 3.30 |
| Plexiglass | 0.00183 | 0.123 | 2.67 |
| Nylon | 0.00178 | 0.123 | 2.64 |
| Polystyrene | 0.0063 | 0.124 | 3.14 |
| Teflon | 0.00115 | 0.145 | 2.45 |
| Hard Rubber | 0.00242 | 0.14 | 3.05 |

The following potential sources of inaccuracy have not been evaluated

(1) Deviation of the direction of the jet caused 15 per cent scatter in initial rise in temperature. Typical tests, used in Figs 2 and 3, were chosen to be those with the maximum initial rise in temperature.

(2) The hemispheres were impinged by the jet stream with non-uniform temperature and velocity.

(3) Hemisphere bases were not perfectly insulated against heat loss.

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CHEMISTRY

Estimation of the Interchange Energy for Binary Systems from Mutual Solubility Data

If the theory of strictly regular solutions developed by Guggenheim¹ is applied to ordinary binary systems and compared with experiment in order to evaluate the interchange energy the results are not good, since very few systems satisfy all the conditions for forming regular mixtures, in which the molecules are assumed to be sufficiently alike in size and shape to be interchangeable on a lattice or quasi-lattice. A few examples have been shown for this comparison. It is desirable that more comparisons with many experimental results are made in order to verify the validity of the theory and to extend their application to the field of the chemical engineering design.

Cox and Herington² have shown that straight-line relationships between the functions $(T - T_c)^{1/2}$ and $\log\{(1 - x')/x'\}$ and between the functions $(T - T_c)^{1/2}$ and $\log\{(1 - x'')/x''\}$ hold for temperatures T within 30° of a critical solution temperature T_c , where $1 - x'$ and $1 - x''$ are the mole fractions of component 1 in the two co-existing liquid phases, and x' and x'' are the corresponding mole fractions of component 2 of a binary liquid mixtures. The following equation is immediately derived from their relationships

$$\log\{(1 - x')/x'\} = m \log\{(1 - x'')/x''\} + K \quad (1)$$

where m and K are constants. At the critical solution temperature the two co-existing phases become identical, having the composition $x' = x'' = x_c$. Equation (1) may be transformed into

$$\frac{1 - x'}{x'} \frac{x_c}{1 - x_c} = \left(\frac{1 - x''}{x''} \frac{x_c}{1 - x_c} \right)^m \quad (2)$$

It is possible that the solubility curve for a binary liquid system can be represented symmetrically with respect to the composition by plotting properly selected units. For example, if the quantities ϕ and ξ are defined by

$$\phi' = \frac{x'/x_c}{x'/x_c + (1 - x')/(1 - x_c)} \quad (3)$$

$$\phi'' = \frac{(x''/x_c)^{-m}}{(x''/x_c)^{-m} + (1 - x'')/(1 - x_c)^{-m}}$$

$$\xi' = \frac{x'/x_c}{x'/x_c + (x''/x_c)^m} \quad (4)$$

$$\xi'' = \frac{(1 - x_c)/(1 - x')}{(1 - x_c)/(1 - x') + (1 - x_c)/(1 - x'')^m}$$

then the resulting solubility curve will be symmetrical with respect to ϕ or ξ , since $\phi' + \phi'' = 1$, and $\xi' + \xi'' = 1$. The former fractions (equation 3), which are the variations of volume fractions, are more convenient since they are simpler. Therefore, when the compositions are plotted in terms of such ϕ fractions, in which the concentrations of component 1 in one phase are multiplied by $x_c/(1 - x_c)$ and the sum of concentrations after the change of units is brought back to unity, the solubility curve of the system will be symmetrical with respect to ϕ as for regular binary mixtures. The mole fraction of component 2 at the critical composition, x_c , and the empirical constant m may be estimated from the mutual solubility data determined at two temperatures by equation 1.

If it is assumed that each component forms clusters consisting of each pure component in its liquid phase, the number of moles being $(1 - x')x_c$ and $x'(1 - x_c)$ respectively, and that the two kinds of clusters are stable and sufficiently alike in size and shape to satisfy all the conditions for forming strictly regular solutions on mixing, the interchange energy w between two kinds of clusters may be obtained from the theory of regular solutions, as well as the cases where $x_c = 1/2$ corresponding to the strictly regular mixtures. For example, in the first approximation which has been treated according to the quasi-chemical equilibrium conditions, w is given by

$$\exp(w/zkT) = \eta = \frac{1 - r}{r^{1/2} - r^{(1-1)/2}} \quad (5)$$

where z is the co-ordination number and k is Boltzmann's constant. By the definition of equation 3 the molecular ratio, r , becomes

$$r = \frac{1 - \phi}{\phi} = \frac{1 - x'}{x'} \frac{x_c}{1 - x_c} \quad (6)$$

Several values evaluated from the mutual solubility data by equations 5 and 6 assuming $z = 4$ are shown in Table 1.

Table 1

| Component | | T_c | T | η | Ref |
|--------------|--------------------|---------|---------|--------|-----|
| 1 | 2 | (deg C) | (deg C) | | |
| n Butane | Perfluoro-n butane | -41.0 | -57.2 | 2.2358 | 3 |
| | | | -43.2 | 2.0192 | |
| | | | -41.0 | 2.0000 | |
| Cyclohexane | Aniline | 29.422 | 23.817 | 2.0215 | 4 |
| | | | 29.392 | 2.0017 | |
| Ethylbenzene | Ammonia | 10.7 | -15.5 | 2.3035 | 5 |
| | | | 9.0 | 2.0372 | |
| | | | 10.7 | 2.0000 | |
| Water | Phenol | 65.85 | 20 | 2.2903 | 6 |
| | | | 35 | 2.1516 | |
| | | | 65.85 | 2.0000 | |

Thus it should be possible to predict the solubility relationships of the system from mutual solubility data, determined at more than one temperature, when the dependence of the interchange energy upon temperature is known.

It seems that this method, in which the theory of regular solutions is applied to the behaviour of solutions represented symmetrically by the change of

units, assuming the formation of stable 'clusters' consisting of each pure component in its liquid phase will be applicable in the field of the chemical engineering calculations. For example, for the correlation and prediction of the data for liquid liquid equilibria and vapour liquid equilibria.

The detailed paper referring to the dependency of the interchange energy upon temperature and the applications of this method in chemical engineering calculations will be published in the *Bulletin of the Chemical Society of Japan*.

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Some Activation Analyses of Six Trace Elements in Marine Biological Ashes

SYSTEMATIC knowledge of the abundance of trace elements in marine organisms is far from complete. Most currently accepted values have been determined by spectroscopy or flame photometry but for a number of elements these methods leave much to be desired. The method of activation analysis not only increases the sensitivity for many trace elements¹ but also eliminates the necessity for running blank analyses on the reagents since small amounts of impurities contained in the reagents will not be measured.

Activation analyses have been carried out for vanadium, arsenic, molybdenum, tungsten, rhodium and gold in several different types of marine ashes using the Ford Nuclear Reactor of the University of Michigan and associated facilities of the Michigan Memorial Phoenix Project.²

The ash samples were prepared by igniting dried marine organisms in a quartz crucible at a temperature below 550° C. (There admittedly is a possibility of losing some part of the desired elements in this step.) About 500 mgm of ash were used for each analysis except for vanadium and molybdenum, where 50–100 mgm and 200–250 mgm of the ash were used respectively.

Samples were irradiated in the reactor for periods of 10 minutes to 15 hours the length of irradiation depending on the isotope to be measured. When short lived radio isotopes were to be measured the sample was analysed immediately, otherwise it was set aside for a while to cool to reduce the radiation encountered in the processing. A chemical separation of the element in question was then performed and the purified radio isotopes measured by a 3 in. x 3 in. NaI(Tl) γ ray scintillation detector coupled with a 100 channel pulse height analyser with dual memories.

Nuclear properties^{3,4} of the isotopes measured, irradiation conditions, separation methods, and experimental sensitivities obtained are summarized in Table 1. The sensitivities listed are probably good to within a factor of 2 and are given only as an indication of the approximate limitations of the specific methods used. This is not to imply that higher sensitivities are not possible with additional improvements in the method.

The abundance of the elements in the ashes is given in Table 2. The overall errors accompanying these

Table 1. PERTINENT INFORMATION FOR THE ACTIVATION ANALYSES

| Element | V | As | Mo | W | Rh | Au |
|--|--|---|---|--|---|---|
| Atomic number | 23 | 33 | 42 | 74 | 75 | 79 |
| Isotope (parent) | ⁵¹ V | ⁷⁵ As | ⁹³ Mo | ¹⁸⁷ W | ¹⁰³ Rh | ¹⁹⁷ Au |
| Abundance (per cent, ref. 3) | 99.75 | 100 | 9.6 | 28.4 | 37.07 | 100 |
| Thermal neutron cross-section (barns ref. 4) | 4.5 | 4.2 | 0.2 | 31 | 100 | 160 |
| Daughter | ⁵¹ V | ⁷⁵ As | ¹⁰³ Mo | ¹⁸⁷ W | ¹⁰³ Rh | ¹⁹⁷ Au |
| Half-life of daughter (ref. 5) | 3.8 min. | 26.8 hr. | 14.0 min. | 24.0 hr. | 3.7 days | 2.7 days |
| γ-energy for γ-ray spectroscopy (MeV ref. 3) | 1.44 | 0.56 | 0.57 | 0.02 | 0.137 | 0.412 |
| Irradiation period | 10 min | 9 hr. | 15 min | 0.3 hr. | 11.5 hr. | 14.1 hr. |
| Average neutron flux (n/cm ² /sec) | 0 x 10 ¹⁴ | 7 x 10 ¹⁴ | 0.4 x 10 ¹⁴ | 1.5 x 10 ¹⁴ | 3.5 x 10 ¹⁴ | 2.5 x 10 ¹⁴ |
| Radiochemical separation | euphron-chloroform | co-precip. with phosphomolybdate | (C ₂ H ₅) ₂ AsCl chloroform | (C ₂ H ₅) ₂ AsCl ethyl acetate | (C ₂ H ₅) ₂ AsCl chloroform | ethyl acetate |
| Approximate sensitivity (gm normalized to flux of 1 x 10 ¹⁴ n/cm ² /sec) | 2 x 10 ⁻¹¹ (10 min. irradi.) | 5 x 10 ⁻¹¹ (10 hr. irradi.) | 5 x 10 ⁻¹¹ (15 min. irradi.) | 3 x 10 ⁻⁹ (10 hr. irradi.) | 1 x 10 ⁻⁹ (10 hr. irradi.) | 5 x 10 ⁻¹⁰ (10 hr. irradi.) |

* The computation of sensitivity includes the cooling period of one half life for long lived isotopes of arsenic, tungsten, rhodium and gold.
† This value was estimated on the basis of counting with a gamma scintillation well.

Table 2. ABUNDANCE OF TRACE ELEMENTS IN MARINE BIOLOGICAL ASH (gm./gm. ash)

| Sample | V | As | Mo | W | Rh | Au |
|--|-------------------------|------------------------|------------------------|--------------------------|------------------------|------------------------|
| <i>Ulva</i> sp. (seaweed) Collected at Enoshima Sagami Bay Japan, in May, 1956 | 5.9 x 10 ⁻⁸ | 5.4 x 10 ⁻⁸ | * | 1.3 x 10 ⁻⁷ | 3 x 10 ⁻⁸ | 9.3 x 10 ⁻⁸ |
| <i>Ulva</i> sp. (seaweed) Collected at Urayasu, Tokyo Bay Japan in May 1956 | 1.33 x 10 ⁻⁸ | — | — | 1.8 x 10 ⁻⁷ | 4.6 x 10 ⁻⁸ | 1.5 x 10 ⁻⁸ |
| <i>Porphyra</i> sp. (seaweed) Collected at Chiba, Tokyo Bay Japan, in January, 1957 | 2.62 x 10 ⁻⁸ | — | 1.7 x 10 ⁻⁸ | — | — | — |
| <i>Fucus japonicus</i> (Little Neck Clam) (soft parts) Collected on the shore of Japan Islands in 1958 | 1.0 x 10 ⁻⁸ | < 5 x 10 ⁻⁸ | — | 4.6 x 10 ⁻⁸ | 6.4 x 10 ⁻⁸ | 7.0 x 10 ⁻⁸ |
| <i>Pandanus</i> sp. (Prawn) (soft parts) Collected in the vicinity of Japan Islands in 1958 | 1.1 x 10 ⁻⁸ | 8.3 x 10 ⁻⁸ | — | < 5 x 10 ⁻⁸ | < 5 x 10 ⁻⁸ | 4.6 x 10 ⁻⁸ |
| <i>Penaeus japonicus</i> (Blackened) (meat) Collected in the vicinity of Japan Islands in 1955 | * | 3.4 x 10 ⁻⁷ | — | < 1.4 x 10 ⁻⁸ | < 8 x 10 ⁻⁸ | 2.6 x 10 ⁻⁸ |

* Below detection limits.

values should rarely exceed ± 30 per cent. The numbers in Table 2 suggest a general tendency towards decreasing abundance the higher the trophic level.

A detailed description and discussion of these experiments will be presented elsewhere.

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Preparation of Crystalline *trans-trans* Methyl Linoleate Hydroperoxide

A METHOD has been worked out for the continuous separation of the hydroperoxide of oxidizing methyl linoleate, the oxidation level of the latter being maintained at about 2 per cent. The product obtained has been purified and ultimately crystallized.

Methyl linoleate, prepared by debromination of tetrabromostearic acid, was oxidized in solution in petroleum ether (b.p. 60–80° C) with oxygen gas, the resulting peroxide being continuously extracted from solution by finely dispersed 85 per cent aqueous methanol saturated with petroleum ether. In this way the peroxide value of the oxidizing methyl linoleate was kept within the range 55–70 (ml. 0.002 *N* sodium thiosulphate per gm), and the tendency for the reaction to proceed beyond the hydroperoxide stage was reduced to a minimum.

The methanol solution obtained usually contained equal weights of hydroperoxide and unchanged ester, which were then separated by partition between 85 per cent aqueous methanol and petroleum ether (b.p. 60–80° C). The product finally obtained from the combined methanol fractions was a pale yellow oil with a peroxide value of 3,400 as determined iodometrically, which is known to give higher values than theoretical, and an *E* (1 per cent, 1 cm) of 810 at 231.5 mμ in ethanol ($\epsilon = 26,400$).

An infra-red spectrum of the product showed a strong band at 2.92 μ (the hydroperoxide group)¹, a strong maximum at 10.10 μ and a weaker one at 10.52 μ, together with indications of the presence of a carbonyl group, in addition to the ester. The material thus appeared to be a mixture of *cis* and *trans* conjugated diene hydroperoxides contaminated with a small quantity of decomposition products.

The hydroperoxide was purified further by two crystallizations from petroleum ether (b.p. 40–60° C) at –35° and a further two from ethanol at –76° to yield a compound with an *E* (1 per cent, 1 cm) of 890 at 231.5 mμ ($\epsilon = 29,000$). Further crystallization from ethanol produced no change in the extinction coefficient at 231.5 mμ. The infra-red spectrum showed that carbonyl decomposition products had been removed by crystallization. In addition although there was strong absorption at 10.11 μ there was no band at 10.52 μ, which indicates that the product was pure conjugated *trans-trans*-methyl linoleate hydroperoxide.

Experiments verifying the predominance of the 9- and 13-hydroperoxides in the product² are at present being concluded and will soon be published together with details of the experiments outlined in this communication.

The work described in this paper was carried out as part of the programme of the Department of Scientific and Industrial Research.

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BIOCHEMISTRY

A Concave Concentration Gradient of Methanol in Chloroform Employed in Elution of Lipids from Silicic Acid

IN several laboratories, where whole lipid extracts are chromatographed on silicic acid in chloroform-methanol, experience has suggested the need for continuous concave gradient elution. Devices are described in the literature for producing concave gradients of solutes in aqueous solution, but they are unsuitable for chloroform-methanol mixtures: they fail for liquids of unequal density, waste eluent, or are not easily constructed without rubber joints, greased stopcocks, etc. Hitherto, therefore, discontinuous gradients or continuous linear or convex gradients have been used for elution of lipids.

Fig. 1 shows a simple and reliable apparatus, possessing none of the above disadvantages, which

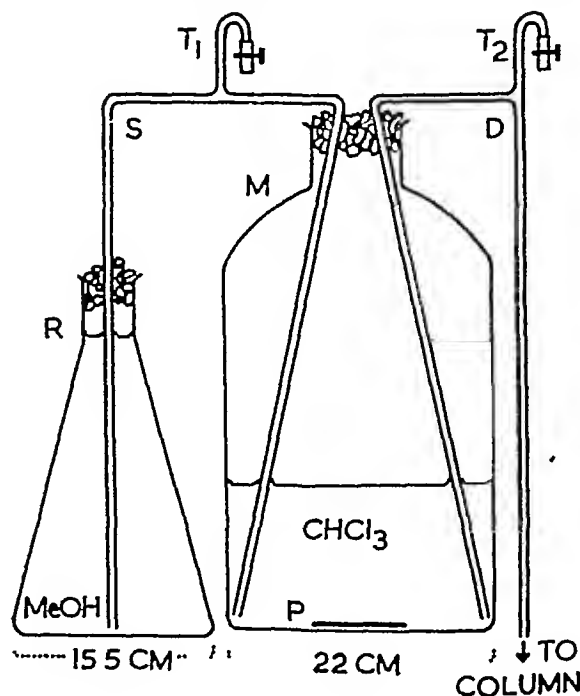


Fig. 1. Apparatus for producing a concave concentration gradient of methanol in chloroform.

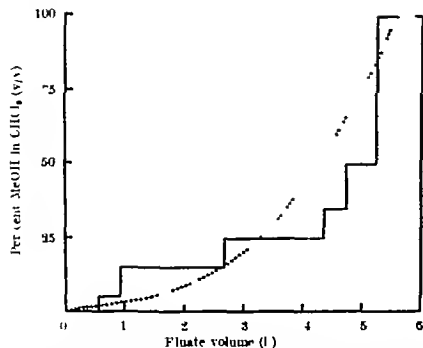


Fig. 1. Concentration gradient (dotted line) produced in the apparatus illustrated in Fig. 1; also (solid line), discontinuous gradient for purposes of comparison.

produces the gradient shown in Fig. 2. The reservoir (*R*) is a 2 l conical flask filled with methanol and the mixing chamber (*M*) a 10 l aspirator bottle its lower opening stoppered with polyethylene containing chloroform (400 l). The siphon (*S*) and delivery tubes (*D*) have internal diameter 2.5 mm. Side tubes (*T₁*, *T₂*) closed by screw clips on plastic tubing facilitate filling *S* and *D* and removing gas which sometimes accumulates. *R* and *M* are closed by cotton wool bungs. The contents of *M* are stirred magnetically by means of a steel plate (*P*). The height of *R* is adjusted initially to produce a steady flow of methanol.

The value of continuous concave gradient elution was proved, for blood lipid, by comparison with discontinuous gradient elution with a chosen sequence of eluents. The total volumes of chloroform and methanol used in each experiment were the same. Elution curves (Fig. 3) as anticipated, showed that the continuous gradient gives sharper peaks and less tailing and avoids spurious peaks produced by abrupt changes of eluent. Chemical examination of fractions, particularly after hydrolysis, showed further that the continuous gradient improves resolution of the numerous constituent lipids.

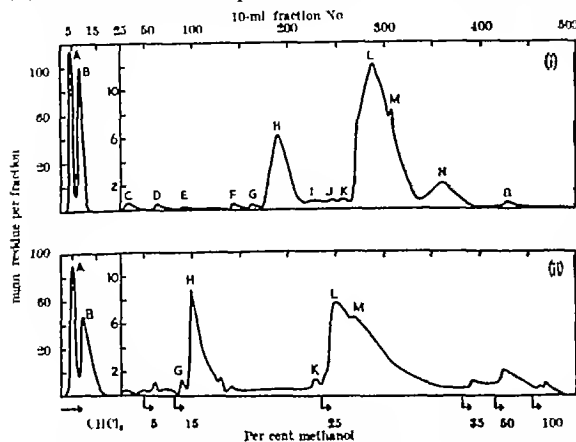


Fig. 3. Elution curves of equal quantities of lipid (1.25 gm) from alkali acid columns (0.0 gm.) using the continuous (i) and discontinuous (ii) gradients illustrated in Fig. 2.

Requiring little attention during running of the column, this apparatus realizes the usual practical advantage of continuous over discontinuous gradient elution. It can be widely employed in chromatography, using different liquids and vessels of different dimensions. A basically similar apparatus has been employed to produce a linear pH gradient in aqueous solution¹. The lipid used in these experiments was extracted in one batch from fresh horse blood at -15°C and washed three times by the Folch procedure². Some constituents were as follows: bile pigments (Fig. 3 peaks C–G), cholesterol (*B*), cholesterol ester (*A*), lipid bound amino acids (C–O), monol phospholipid (*L*), phosphatidolcholine (*L*, *M*), phosphatidolethanolamine (*H*), phosphatidylcholine (*L*, *M*), phosphatidylethanolamine (*H*), phosphatidylserine (*H*), phosphatidylserine salt (*H*)³ (*L*–*L*), sphingomyelin (*N*), and triglyceride (*A*).

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Presence of Behenic Acid in Sphingomyelin from Horse Spinal Cord

It is known that sphingomyelin from various animal tissues contains lignoceric, nervonic, stearic and palmitic acids as the component fatty acids. We have found a considerable amount of behenic acid together with nervonic, stearic and palmitic acid in sphingomyelin which was prepared from horse spinal cord. Corebrosides from spleen of Gaucher's disease was reported to have behenic acid as a constituent by Klenk¹ and Rosenberg *et al.*², and sphingomyelin from brain to have a very small amount of the acid by Rennkamp³. The present study describes the presence of behenic acid as the essential constituent in sphingomyelin from normal animal tissue.

Crude sphingomyelin isolated from horse spinal cord was carefully purified by treatment with dilute alkali⁴ and by column chromatography through alumina⁵. The purified sphingomyelin was several times recrystallized from ethyl acetate. Thus 3 kgm of fresh tissue yielded about 15 gm of snow white crystals of sphingomyelin, which melted at $197\text{--}198^{\circ}\text{C}$ and was practically pure, it was quite uncontaminated with glycerophospholipide and cerebroside. Analysis: $\text{P}, 3.05$, $\text{N}, 3.40$, $\text{P:N} = 1.2$, glycerol, 0, galactose, 0 $[\alpha]_{\text{D}}^{20} = +5.20^{\circ}$.

A sample of pure sphingomyelin (0.0 gm) was refluxed with 10 per cent sulphuric acid in methanol for

8 hours After cooling, three fractions of methyl esters of fatty acids were taken from the reaction mixture Petroleum-ether soluble material was extracted from the filtrate of the mixture (fraction 1, 0.5 gm) The precipitate consisted of a smaller amount of yellow oily material (fraction 2, 0.7 gm) and a larger amount of white rustling material (fraction 3, 1.4 gm) Each fraction was saponified with 0.5 *N* potassium hydroxide in methanol, and the salt of fatty acid was shaken with 2 *N* sulphuric acid in ether Each of the free fatty acids was repeatedly recrystallized from ethanol before investigation of its chemical properties

Fatty acid from fraction 1 melted at 39–40°C, the iodine number, the analytical data and the molecular weight by titration were in good agreement with those of nervonic acid Fatty acid from fraction 2 melted at 54–55°C, the analytical data, the neutralization equivalent and the behaviour on paper chromatogram indicated a mixture of stearic and palmitic acids

Fatty acid from fraction 3 could not be identified from the elementary analysis However, the melting point of the material and its methyl ester, 79–80°C and 52.5–53.5°C respectively, suggested behenic acid The neutralization equivalent and paper chromatography supported this Furthermore, the infra-red spectra of this material and its barium salt were almost identical with those of C_{22} series Especially in the spectrum of the salt, eleven bands were distinctly recognized between wave-lengths 7.43 and 8.47 μ , which is characteristic for the salt of a C_{22} acid according to Meiklejohn *et al.* These results show that the fatty acid from fraction 3 is behenic acid

Details of the study will be published elsewhere⁷ We thank Mr J. A. Rothfus for the infra-red spectra

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Secondary Structure of Ribonucleic Acid in Solution

It has been shown previously that ribonucleic acid behaves as a coiled single-stranded^{1,2} molecule in solution The results presented here indicate that an organized secondary structure which might involve intra-molecular bonds may be present

The intrinsic viscosity of *E. coli*³ and rat liver⁴ ribonucleic acid varies markedly with the concentration of added salt, there being a ten-fold drop over a narrow range of ionic strengths, in contrast with the behaviour of other polyelectrolytes (see Table 1) The abruptness of the fall in viscosity (which is indicative of a phase transition) shows that the change from an extended to a contracted conformation, on increasing the ionic strength, is also

abrupt The concentration of added salt required to bring about such contraction was found to increase with temperature

Table 1 DEPENDENCE OF THE VISCOSITY OF *E. coli* RIBONUCLEIC ACID (RNA) AND SODIUM POLYMETHACRYLATE (Na-PMA) ON THE CONCENTRATION OF ADDED SALT

| Concentration of sodium chloride (M) | | Temperature (deg. C) | Limiting viscosity numbers (ml./gm.) $\times 10^{-2}$ | | | | | | | | | |
|--------------------------------------|----|----------------------|---|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|
| | | | 0.1 $\times 10^{-1}$ | 5 $\times 10^{-2}$ | 1 $\times 10^{-1}$ | 5 $\times 10^{-2}$ | 1 $\times 10^{-2}$ | 1 $\times 10^{-3}$ | 1 $\times 10^{-4}$ | 1 $\times 10^{-5}$ | 1 $\times 10^{-6}$ | 1 $\times 10^{-7}$ |
| Na-PMA (ref. 4) | 2 | 25 | 3.5 | 2.5 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 0.75 |
| RNA | 10 | 0.4 | — | — | 1.0 | 0.60 | 0.20 | 0.03 | 0.03 | — | — | — |
| RNA | 10 | 25 | 2.8 | 2.4 | 1.9 | 1.20 | 0.33 | 0.10 | 0.03 | — | — | — |
| RNA | 10 | 35.5 | — | — | 1.9 | 1.35 | 0.54 | 0.29 | 0.03 | — | — | — |

This change in configuration was also found in the sedimentation behaviour of *E. coli* ribonucleic acid in very dilute solutions (0.005 per cent) The sedimentation pattern always showed two peaks of about equal magnitude, having sedimentation constants of 16.5 and 23.7, at high ionic strengths, and 12.9 and 18.1 in solutions of sodium chloride of 0.001 *M* and less The decrease of the sedimentation constants of both components on lowering the ionic strength is in accord with the viscosity data

Further evidence for configurational changes within the contracted structure has been obtained from potentiometric titration studies of *E. coli* and rat liver ribonucleic acid at various temperatures, the results of which are summarized in Table 2

Table 2 THE ANOMALOUS TITRATION OF *E. coli* RIBONUCLEIC ACID AS SHOWN BY THE DIFFERENCE IN ACID (OR ALKALI) BOUND AT A GIVEN pH OF FORWARD AND BACK TITRATION

| pH | 3.0 | 3.4 | 4.0 | 4.6 | 5.0 | 6.0 | 8.0 | 10.0 | 11.0 | 12.0 |
|-----------------------------------|--|------|------|------|------|------|------|------|------|------|
| Temperature of titration (deg. C) | Difference in the equivalents of acid (or alkali) bound per tetramole of ribonucleic acid phosphorus | | | | | | | | | |
| 0.4 | 0.05 | 0.20 | 0.21 | 0.20 | 0.13 | 0.08 | 0.00 | 0.10 | 0.13 | 0.25 |
| 25 | 0.00 | 0.00 | 0.12 | 0.12 | 0.11 | 0.06 | 0.00 | 0.03 | — | — |
| 38.5 | 0.00 | 0.00 | 0.10 | 0.10 | 0.10 | 0.05 | 0.00 | — | — | — |
| 38.5* | 0.00 | 0.00 | 0.00 | 0.00 | 0.06 | 0.00 | 0.00 | — | — | — |
| 0.4† | 0.06 | 0.14 | 0.16 | 0.18 | 0.12 | 0.10 | 0.00 | 0.04 | — | — |

* Second titration cycle at 38.5°C

† Titration at 0.4°C of sample previously titrated at 38.5°C

‡ Because of the large apparent heat of ionization of the 6-keto groups the data obtained in alkaline solutions cannot be adequately presented in this table

At 25°C a small difference between the forward and the back curves was found on titration from neutrality to the extremes of pH and back, as has previously been reported^{2,5,6} The difference between the two curves was considerably enhanced at 0.4°C These same differences were again found on a second titration cycle, the original forward and back titration curves were reproduced This hysteresis is accounted for by the spontaneous formation of an ordered structure in neutral salt solution, as suggested by the viscosity data, and its breakdown on titration to acidic and alkaline pH's At 38.5°C a single curve was followed on all occasions after the first treatment with acid, but hysteresis was again found on subsequent titration at 0.4°C (Table 2) These results indicate that upon titration at 38.5°C, the transition to a more random form was irreversible, but upon cooling to 0.4°C, the ordered configuration was reformed The presence of hysteresis in both the acidic and alkaline pH regions shows that ionization of both 6-keto and 6-amino groups may modify the structure Acid and alkali appear to bring about the

same configurational change since after titration with acid at 38 °C both the 6 keto and 6 amino groups ionize without hysteresis

These results show that ribonucleic acid in solution may be present in one of at least two configurations depending on ionic strength, pH, and temperature. The transition from one configuration to another may be impeded as shown by the hysteresis in the titration cycle. These observations could be accounted for if rotations about the linkages of the sugar phosphate backbone were sterically hindered. It is possible that one configuration may be stabilized by sequences of intra molecular bonds although the sedimentation velocity and intrinsic viscosity of *E. coli* (and also tobacco mosaic virus ribonucleic acid) are consistent with a randomly coiled configuration. Further experiments are required to elucidate the configurations indicated above and to determine the extent to which they may reflect the *in vivo* structure⁴ found for ribonucleic acid in nucleoproteins.

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Glyceric Acid in Broad Bean (*Vicia faba* L.)

In recent years there have been one or two reports of the occurrence of free glyceric acid in higher plants. Balansard¹ identified the acid as the diuretic principle in the pods of broad bean (*Vicia faba* L.) but gave no indication of the amount present other than could be inferred from the diuretic effect. Isherwood, Chen and Mapson² isolated D-glyceric acid from cross seedlings; they found that it was present in amounts ranging from 5 to 50 m equiv/kgm of fresh weight in seedlings cultured for 5 days at 20 °C in the dark on 0.04 M sodium bicarbonate solution. Palmer³ isolated D-glyceric acid from tobacco leaves (*Nicotiana tabacum* var. Connecticut) grown in the shade and estimated the quantity present to be of the order of 5–15 m equiv/kgm (fresh weight).

We have recently determined the levels of D-glyceric acid in leaves and other parts of broad bean plants grown under various conditions and the results (Table 1) show that it is one of the major organic acids accumulated by the plant.

Table 1 PRINCIPAL ORGANIC ACIDS IN *Vicia faba* L.
(m.equiv./kgm. fresh weight)

| Sample | Description | Origin | Maleic | Citric | Glyceric |
|--------|----------------|---------------|--------|--------|----------|
| 1a | leaves | Field | 6.6 | 2.4 | 29.7 |
| b | stems | Field | 13.7 | 15.6 | 53.4 |
| 2a | leaves | Water culture | 12.8 | 48.0 | 25.5 |
| b | stems | Water culture | 31.4 | 27.6 | 24.0 |
| 3a | roots | Pot grown | 1.3 | 0.45 | 1.10 |
| 1 | leaves (young) | " | 10.8 | 36.7 | 44.9 |
| c | leaves (old) | " | 8.5 | 73.5 | 21.4 |
| d | stems | " | 15.7 | 19.7 | 51.7 |
| e | flowers | " | 16.4 | 3.7 | 6.6 |
| f | Pods | " | | | |

The acids were extracted from the plant tissue and determined by titration after separation by partition chromatography on a column of silica gel according to methods already described⁴. Recovery of glyceric acid under those conditions is practically quantitative. It is however poorly separated from shikimic acid. The two acids are however readily separated by paper chromatography⁵ and distinguished by the charac-teristic colour reaction⁶ given with sodium nitroprusside and piperazine after oxidation with periodate. No shikimic acid could be detected in these extracts.

The identity of the D-glyceric acid was established by isolation as the crystalline calcium salt after being separated from other acids by partition chromatography on silica gel followed by ion-exchange chromatography on Dowex 1⁷ (acetate form)⁸. The calcium salt had $[\alpha]_D^{25} + 12.8^\circ$ (c, 4 water) and its infrared spectrum was identical with that of an authentic sample of calcium D-glycerate prepared by resolution⁷ of DL-glyceric acid obtained by the oxidation of glycerol⁸.

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Partial Identification of Lysins and Agglutinins in Lymphomatous Mouse Tissue

LYSINS and agglutinins have been extracted from normal mouse tissue from mammary carcinomas of female C3H mice, and recently from human leukemic cells¹, and from the lymphomatous glands of AKR mice². The lytic materials have been tentatively termed soap like and 'lysolecithin like' supposedly bound to proteins³, but in reality the nature of both the lysins and the proteins is still unknown. This communication is concerned with the last point.

The methods of 'pre incubation' and of extraction with organic solvents have been largely abandoned because they probably involve the splitting of complexes. Instead lymphomatous tissue is removed from the AKR mouse placed in saline in the proportion of 1 gm of tissue to 3 ml of saline, and immediately homogenized for 5 minutes in a 'VirTu' homogenizer at 23 000 r.p.m. Gross particles are immediately removed by slow centrifugation. Examination of the supernatant fluid with phase contrast shows innumerable myelin forms and tiny fragments. The supernatant fluid of the homogenate after the throwing down of the gross particles, is diluted in powers of 2 with Michaelis buffer at pH 8.5. Washed mouse or human red cells are added and both inhibitors (in the less diluted homogenates) and lysins are observed within 3 hours at 37 °C.

Identification of the lysins. The homogenate after the removal of the gross particles is placed on a strip of fat free filter paper so that it spreads over about 1 cm. The paper is dried at 50 °C; saturated rhodamine B in benzene and 1 per cent uranyl acetate are added to the paper (a) in the region to

which the homogenate was applied, and (b) in regions to which it was not applied. Immediate examination of the paper with ultra-violet light shows that the region to which the homogenate was added gives a green fluorescence, whereas the other regions do not fluoresce. The fluorescence is specific for the presence of fatty acids, which at pH 8.5 are almost certainly soaps, in the homogenate⁶. The lytic activity of the homogenate is about the same as that of 0.05 M sodium palmitate at 37°C at pH 8.5. In these concentrations sodium palmitate gives a yellow fluorescence with rhodamine B and uranyl acetate and ultra-violet light, but a green fluorescence when mixed with 0.2 per cent of albumin before treatment with the reagents. The fat-free paper strips must be manipulated with scissors and forceps which have been washed with ether and dried, they must never be touched by hand.

Extraction of soaps from paper. The fluorescent region and the non-fluorescent regions of the paper strip are cut out and separately extracted in small crucibles with hot ethanol. The strips are removed after an hour and the solvent is dried off with a fan, 0.5 ml of Michaelis buffer at pH 8.5 is added to each crucible, the contents of which are transferred, with stirring, to small haemolysis tubes. To each of these is added 0.1 ml of a washed human red cell suspension (0.2 ml finally suspended in 10 ml of saline). Ethanol extraction of the region of the paper to which the homogenate has been added gives complete lysis in 1 hour or less, while extracts of the areas of the paper to which the homogenate was not added are non-lytic. Warm ether and hot benzene are not as effective in extracting the lytic material as is hot ethanol.

Estimation of protein and soaps in the homogenate. These can be estimated by a micro modification of the method of Folin and Denis⁶. To 1 ml of the homogenate is added 4 ml of water, and 1 ml of this diluted homogenate is placed with a tuberculin syringe in each of two conical centrifuge tubes of about 1.5 ml capacity and of known weight. To each is added 0.1 ml of 5 per cent acetic acid. The tubes are placed in boiling water for 15 minutes. They are then centrifuged and the coagulated material (protein plus lipid) is thrown down. The supernatant fluid is removed and the precipitate is stirred up with 1 ml of hot 0.5 per cent acetic acid. The tubes are again centrifuged and the supernatant fluids are removed. To the precipitate in one of the tubes is added 1 ml of hot 50 per cent ethanol, to the precipitate in the other tube is added 1 ml of water. After 15 minutes, the two tubes are centrifuged, the supernatant fluids are removed, and the tubes are placed for 2 hours in an air bath at 110°C, they are then cooled in a desiccator and weighed. This method shows that the homogenates usually contain between 2 and 7 gm per cent of protein and between 2 and 7 gm per cent of a material which is soluble in hot ethanol. The amount of lipid removed from the homogenate by hot ethanol is only a little smaller than the amount removed by a mixture of 1 part of methanol and 4 parts of methylal. The proteins can also be eluted at 37°C from fat-free paper with Michaelis buffer at pH 8.5. The principal protein eluted resembles a serum albumin, little or no precipitation being obtained except with saturated ammonium sulphate. It is a tissue protein, however, and not a serum protein. The homogenate is best made in saline and not in buffer.

Electrophoretic patterns. Using the Antweiler micro-Tiselius apparatus these can be obtained from homogenate or from the material which is soluble in hot ethanol.

The electrophoretic pattern of the whole homogenate consists of two spikes which are so closely associated that they cannot be satisfactorily separated at pH 8.5. The more rapidly moving component is so closely associated with the less rapidly moving component that, when the area under its spike is compared with the area under a 2 per cent serum albumin spike, it has a specific refractive increment, very difficult to measure, of less than 0.0010, as compared with 0.0018 for the albumin. This more rapidly moving component seems to be a protein, strongly interacting with the more slowly moving component, which seems to be a soap soluble in hot 50 per cent ethanol. If the protein component plus the soap are dialysed, the result is the double spiked complex, but if the soap is extracted from the homogenate with hot 50 per cent ethanol and dialysed, it passes across the dialysing membrane and gives virtually no electrophoretic pattern at all. Apparently protein must have interacted with it, thus preventing it from diffusing away through the dialysing membrane.

Two curious points remain. If the homogenate is made in saline instead of in Michaelis buffer, the two components of the electrophoresis pattern appear more clearly, and if the homogenate is eluted from fat-free filter paper, the two components appear more clearly still. At present, we have no explanation for this.

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An Antimetabolic Action of Vitamin K

In recent studies *in vivo* and *in vitro*, we have shown that the K vitamins (K₁, K₂, phylloquinone, menadiol and 'Synkavit') inhibit the synthesis of nicotinic acid at the stage 3-hydroxyanthranilic acid → quinolinic acid. We suggested that the mechanism of inhibition is competition between vitamin K and 3-hydroxyanthranilic acid, that is, the K vitamins exert an antimetabolic action on the substrate of the reaction catalysed by 3-hydroxyanthranilic acid oxidase. On the basis of this hypothesis, investigations were undertaken to determine if the inhibition of 3-hydroxyanthranilic acid oxidase produced *in vivo* by administration of menadiol or 'Synkavit' could be reversed by subsequent administration of 3-hydroxyanthranilic acid. The results of these experiments demonstrated the capacity of 3-hydroxyanthranilic acid to overcome the inhibitory effect of vitamin K.

Tryptophan, as a precursor of 3-hydroxyanthranilic acid, was also effective in restoring, *in vivo*, the 3-hydroxyanthranilic acid oxidase activity inhibited by the K vitamins. But a proof of the competition between vitamin K and 3-hydroxyanthranilic acid could be supplied by demonstrating the phenomenon of mutual antagonism between 3-hydroxyanthranilic acid and vitamin K. Therefore, now

experiments were carried out to test whether the concentration of menadione in the urine of rats was higher after administration of menadione (or 'Synkavit') plus 3 hydroxyanthranilic acid than after administration of menadione (or 'Synkavit') alone.

The method of Richert² was employed for determining the quantity of menadione in the urine. The analysis was carried out on urine collected for 48 hours after treatment of the rat with vitamin K alone or in combination with 3 hydroxyanthranilic acid.

The averages of the results obtained are as in Table 1.

| Table 1. MENADIONE IN URINE OF RATS | |
|--|---------------------------------|
| Treatment | Menadione in urine (μ gm.) |
| 20 mgm. menadione | 1240 |
| + 20 mgm. 3 hydroxyanthranilic acid | 1090 |
| 20 mgm. 'Synkavit' | 1070 |
| 20 mgm. 'Synkavit' + 20 mgm. 3 hydroxyanthranilic acid | 1450 |
| 10 mgm. 'Synkavit' | 377 |
| 10 mgm. 'Synkavit' + 20 mgm. 3-hydroxyanthranilic acid | 879 |

The results of these experiments demonstrate a marked increase in the excretion of menadione under the influence of 3 hydroxyanthranilic acid and therefore no evidence for the existence of an anti-metabolic action of vitamin K on 3 hydroxyanthranilic acid.

The results of Evans³ agree with our work: he noticed symptoms of nicotinic acid deficiency in a large number of patients treated with 'Synkavit' (10 mgm. per day).

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ANIMAL PHYSIOLOGY

Absorption of Magnesium in the Large Intestine of the Calf

THERE appears to be little evidence concerning the site of magnesium absorption from the alimentary tract with levels of magnesium likely to be found under normal conditions. Stewart and Moodie¹ found magnesium absorption to occur in almost the whole tract from the rumen to the caecum in sheep but enormous amounts of magnesium salts were introduced to demonstrate this (I found little or no absorption from the rumen of milk fed calves with low levels of magnesium²). They concluded that the small intestine was probably the principal site of absorption. The following results were obtained while attempting to gain information on the reasons for the decrease in magnesium absorption previously observed during the first month or so of a calf's life^{2, 3}.

A number of male calves were provided at a few days old with fistulae in the small intestine close to the junction with the caecum. The fistulae were formed either by a simple cannulation or by severing the intestine inserting a cannula into each side and then joining these canulae outside the animal with flexible tubing (re-entrant cannulation). The calves which appeared otherwise to be quite normal

satisfactorily retained the simple and re-entrant cannula for up to 12 and 7 weeks respectively. The calves were fed twice daily (8 a.m. and 5 p.m.) with 2.20 l of whole milk containing 2.5 gm. polyethylene glycol (molecular weight 4000) as a marker. Previous experiments have shown that polyethylene glycol is recovered to an extent of about 80-90 per cent after passing through the alimentary tract of a milk fed calf⁴. Collections of small intestine effluent were made from the cannulae from time to time. Polyethylene glycol was determined by a previously described method⁵ and magnesium essentially by a method described previously for faeces⁶. In the calves with a re-entrant cannulation complete collections from the efferent cannulae were made over periods of 24 hr. In the calves with a simple cannula it was possible only to collect small samples as they appeared at uncontrollable and irregular intervals after feeding. However experiments with two calves with re-entrant cannulae showed that samples taken between 2 hr and 6 hr after the morning feed contained about 70-85 per cent of the residue from that feed and, presumably owing to the smaller proportion of endogenous effluent present, possessed magnesium/polyethylene glycol ratios rather lower than for the small intestine effluent as a whole. Values for 20 small samples taken at various times between 2 and 6 hr after the morning feed were 6-30 per cent (mean 16 per cent) lower than for the corresponding 24 hr collections. Magnesium⁶ and polyethylene glycol⁵ were determined in faeces samples as described previously. The magnesium/polyethylene glycol ratio in the diet did not vary by more than ± 5 per cent over periods of say one week and it was found that over such periods this ratio was also reasonably uniform in successive faeces samples. Standard errors for individual samples in a number of groups of 3 or 4 successive faeces samples from 3 calves were ± 15 , 10, 24, 10 and 17 per cent respectively. The results given in Table 1 are for faeces samples obtained within 2 days of the corresponding collections from the small intestine.

For each calf in the youngest group the magnesium/polyethylene glycol ratio in the small intestine effluent was much higher than that in the faeces (Table 1). The differences were too great to be accounted for by errors resulting from faeces variations. Moreover the ratios in the small intestine effluent from the calves with simple cannulae were probably minimum values (see above). It is unlikely that there was any appreciable destruction of polyethylene glycol in the large intestine⁷, but even if this did occur the main argument would not be affected and in fact it would lead to an under-estimation of magnesium

TABLE 1

| Age (weeks) | Calf | Magnesium/polyethylene glycol ratio | | | |
|-------------|------|-------------------------------------|--------------------------|-------------------|-------------------|
| | | Milk | Small intestine effluent | Faeces | |
| 2-4 | 1B | 0.118 \pm 0.001 | 0.043 \pm 0.007 | 0.016 \pm 0.002 | 0.014 \pm 0.000 |
| | 3B | 0.119 \pm 0.001 | 0.040 \pm 0.020 | 0.035 | 0.035 |
| | 14B | 0.114 \pm 0.001 | 0.065 | 0.035 | 0.035 |
| | 15B | 0.099 \pm 0.001 | 0.082 \pm 0.014 | 0.035 \pm 0.004 | 0.035 \pm 0.004 |
| | 9C | 0.106 \pm 0.001 | 0.070 \pm 0.009 | 0.033 \pm 0.006 | 0.033 \pm 0.006 |
| 5-9 | 10C | 0.103 \pm 0.001 | 0.093 \pm 0.003 | 0.039 \pm 0.004 | 0.039 \pm 0.004 |
| | 14D | 0.100 \pm 0.002 | 0.079 \pm 0.001 | 0.005 \pm 0.001 | 0.005 \pm 0.001 |
| | 15B | 0.107 \pm 0.000 | 0.095 \pm 0.004 | 0.009 \pm 0.002 | 0.009 \pm 0.002 |
| 11-12 | 9C | 0.096 | 0.080 | 0.081 | 0.081 |
| | 14B | 0.100 \pm 0.001 | 0.079 \pm 0.013 | 0.097 | 0.097 |
| | 15B | 0.110 | 0.091 | 0.096 | 0.096 |

Results shown with standard errors represent mean values for two determinations. Results for the small intestine effluent from calves 9C and 10C were for 24 hr collections (these results for the other calves were for small samples taken 2-6 hr after the morning feed).

absorption in the large intestine. It seems therefore that in these calves, as a minimum estimate, about 40-70 per cent of the magnesium escaping absorption in the small intestine was absorbed in the large intestine (about 25-40 per cent of the dietary magnesium).

In the older age groups a different situation existed. The magnesium/polyethylene glycol ratio in the faeces increased with age to such an extent as to indicate a decrease in overall magnesium utilization comparable to that shown previously by balance experiments^{3,4}. Although net absorption in the small intestine may have fallen to some extent with age (this could be at least partly explained by there being a relatively greater amount of endogenous magnesium for the older and bigger calves) it appears that the factor mainly responsible was a decrease in the absorptive function of the large intestine. Exact interpretation is difficult since most of the results for the older calves were obtained on small samples from simple canulae but it seems probable that these calves did not absorb any appreciable amount of magnesium in the large intestine.

These results also suggest that the increase in endogenous faecal magnesium on a unit body weight basis previously observed as calves get older⁵ may be due to the failure of re-absorption in the large intestine.

I am greatly indebted to Dr A. T. Cowie who inserted the canulae for these experiments. I also wish to thank Mr H. S. Hallett, Miss P. Lewis and Mrs O. M. Campbell for technical assistance.

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An Attenuated Strain of Canine Distemper Virus in Tissue Culture

CANINE distemper virus was cultivated in dog kidney tissue culture with a clear cytopathogenic effect¹ and the 56th passage of the virus was tested in ferrets. Each of four non-immune ferrets were inoculated intraperitoneally with 1 ml of tissue culture fluid ($10^{5.5}$ TCID₅₀). Three non-immune ferrets were kept in the same laboratory as control animals and a further two in a neighbouring room in order to test for possible air-borne contamination from the inoculated animals. During an observation period of 25 days no animal showed any signs of disease. Blood was drawn from all the animals before the experiment and 17 days after inoculation. Tissue culture neutralization tests were performed with the sera, inactivated for half an hour at 56°C, against 300 TCID₅₀ of canine distemper virus after incubation at room temperature for one hour. The 50 per cent neutralizing titre of sera from inoculated animals was more than 10^{-2} (final dilution of serum) on day 17, while neutralizing antibodies were not found, either in the pre-inoculation sera or in the sera from the control animals on day 17.

On day 25 all the animals (from now on placed in the same laboratory) were challenged with Green's distemperoid virus (75 mgm of freeze-dried ferret spleen). All the control animals developed clinically typical distemper after a uniform incubation time of 7 days, and were dead or killed with pronounced

symptoms of distemper 11 days after challenge. The four animals inoculated with tissue culture virus showed no symptoms during an observation period of 3 weeks.

Apparently, during 56 passages in dog kidney tissue culture the virus becomes attenuated with a loss of pathogenicity for ferrets but it still retains a satisfactory antigenic capacity.

Tests in dogs are in progress and a complete report will be published elsewhere.

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Physiological Activity in Extracts of *Albizia* Species

INFORMATION was first received from Prof C. Rendle-Short of the Department of Obstetrics and Gynaecology of this Medical School, that pregnant African women frequently take native medicines at or near term, even when in hospital, in an attempt to accelerate birth. It was thought likely that the excessively high incidence of uterine rupture occurring locally¹, might be due in part to powerful uterine spasmogens in these medicines, and some of the plants were obtained from African herbalists and identified.

Cold aqueous extracts of the dried bark of *Albizia gummifera* (Gmel.) C. A. Smith and *Albizia grandibracteata* (Taub.) and *Albizia chinensis* (Osbeck) Merrill were found *in vitro* to produce powerful contractions in strips from the gravid uteri of mice, rats, guinea-pigs, sheep, cows and humans. The mouse and rat uteri were less sensitive than those of the other animals, and non-gravid uteri were responsive but much less sensitive. Marked effects were produced by a concentration of the extracts in the isolated organ bath of the order of 100-500 µgm/ml, expressed as dry bark weight/bath volume.

The responses still occurred unchanged in the presence of sufficient atropine and antihistamines to abolish the responses to acetyl choline and histamine, and the extracts did not affect guinea-pig duodenum or ileum *in vitro*, nor did they affect the rectus muscle of the local toad, *Bufo regularis* (Var).

For further study, inert residues were removed by preliminary extraction of the bark with neutral low-boiling hydrocarbons, extracts then obtained with aqueous lower alcohols were found to contain most of the active material.

A further inactive fraction was removed either by precipitation from aqueous solutions by basic lead acetate, or by a method devised by Drs S. Wilkinson and H. T. Openshaw of the Wellcome Research Laboratories, Beckenham, England, involving dialysis and freeze-drying. The yield varied from 10 to 45 mgm/gm of dry bark.

The activity was completely destroyed on mild acid hydrolysis, and prolonged boiling or prolonged standing, especially in sunlight, caused a steady decline of potency. The active material was not taken up by chloroform from neutral, acid or alkaline solution. The tentative conclusion that it was glycosidal and probably saponin in character, is supported by the work of Drs Wilkinson and Openshaw. Saponins have been found in plants of the genus *Albizia* by other workers².

The extracts were administered intravenously to guinea pigs, rabbits, cats, and monkeys (*Macaca fascicularis*) under nembutal, urethane or chloralose anaesthesia. A small transient fall in blood pressure proportional to the dose always occurred and some times obnoxious in respiration were observed. The gravid and non-gravid female monkeys showed powerful prolonged uterine contractions recorded by means of a guard ring tocodynamometer externally or using a catheter and pressure transducer system.²

Some of the smaller animals also showed increased uterine activity on intravenous administration of the extracts.

Conscious, intact mice, rats, rabbits and guinea pigs were given intraperitoneal intravenous or gastric tube doses of solutions of the drug. No abortions and few deaths occurred in mice even with large doses in rats, rabbits, and guinea pigs however doses by any route could induce partial or complete abortion in gravid animals at any stage of gestation although doses by gastric tube needed to be much larger for the same effects. Toxic effects appear at higher doses although examination of these animals showed no obvious pathological changes in any tissues and the only fairly general symptoms were anorexia and a somewhat inflamed intestine diarrhoea was sometimes present, but microscopic examination failed to show abnormality in any organs. Control animals given very large doses of ergometrine were unaffected.

All extracts were tested in aqueous solution controlled for pH and temperature and containing appropriate ions in solution.

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Differential Analysis of the Effects of Phenothiazine-Tranquillizers on Emotional and Motor Behaviour in Experimental Animals

A RECENT communication¹ pointed out that chlorpromazine simultaneously reduces emotional defecation and ambulation in rats to the same degree. Ryall therefore concluded that the main behavioural effect of this drug in animal experiments is one of sedation and that the reduction in fear motivated behaviour observed in animal experiments is secondary to the sedative action.

In the study of a series of phenothiazine derivatives in which similar methods were employed, we obtained results which show that Ryall's conclusion is not generally applicable. In our experiments rats were trained to avoid an electric shock when an acoustic signal (conditioned stimulus) was given, by climbing a vertical pole in the centre of the cage.²⁻⁴ A correct conditioned avoidance response was obtained in 98 per cent of the tests. During the experiment the rats also exhibited a high degree of behavioural tension. One main symptom of this behavioural state is an increased defecation rate (emotional defecation). Quantitatively 8-9 faecal pellets are excreted within a 10 minute

period during which 10 successive conditioned escape responses are elicited. To analyse the action of each drug, the motor and defecational behaviour of rats treated subcutaneously two hours before the test was compared with that of control animals. At least three different dosages of the drug producing minimal or pronounced inhibitory effects were given to groups of 8 rats. The doses inhibiting the conditioned avoidance response in 50 per cent of the tests and the doses reducing the number of excreted faecal pellets by 50 per cent (ED₅₀) were calculated.

The locomotor activity of mice was determined using a modification⁵ of Dew's method.⁶ Two mice were placed together in a cage measuring 20 x 30 cm. A beam of light was projected from the front of the cage to the back where it was reflected to the front of the cage. Owing to the unfamiliar environment a period of curiosity induced excitation lasting 20 minutes was first observed. This period of increased ambulation was recorded in control animals and in mice treated one hour before with various subcutaneous doses of the drugs. Groups of 16 animals were used per dose. From these data the ED₅₀ that is the dose of the drug decreasing the spontaneous motor activity by 50 per cent was calculated.

Table 1. EFFECT OF PHENOTHIAZINES ON MOTOR AND EMOTIONAL BEHAVIOUR.

| | Inhibition of conditioned escape response in rats ED ₅₀ (mgm./kgm. s.c.) | Inhibition of emotional defecation in rats ED ₅₀ (mgm./kgm. s.c.) | Inhibition of motor activity in mice ED ₅₀ (mgm./kgm. s.c.) |
|------------------|---|--|--|
| Perphenazine | 0.11 | 0.4 | 0.22 |
| Prochlorperazine | 0.5 | 0.6 | 1.0 |
| Chlorpromazine | 1.5 | 1 | 1.9 |
| Thioridazine | 2.6 | 2.6 | 7.2 |

* s.c. = subcutaneous

The results are summarized in Table 1. Chlorpromazine inhibited, to about the same degree emotional defecation and the conditioned avoidance response of rats as well as locomotor activity of mice. These data are in perfect agreement with Ryall's¹ results. Prochlorperazine was 2-3 times more potent than chlorpromazine in all tests, but exhibited qualitatively the same activity pattern. Perphenazine—the most active drug studied—inhibited conditioned escape response and locomotor activity to a greater extent than the emotional defecation. (Species differences in these tests can be excluded since the relative sedative potencies of these drugs is similar in rats and mice).⁷ Since all three drugs reduce emotional defecation only in doses slightly higher than those which cause sedation, it could be concluded that the inhibition of the emotional behaviour is secondary to the sedation.

However, results obtained with another phenothiazine compound thioridazine⁸, do not justify such a conclusion. As shown in Table 1 thioridazine is much more effective in inhibiting emotional defecation than in inhibiting the conditioned escape response or the motor activity of mice. Even in high doses (10 mgm./kgm.) thioridazine does not interfere with the normal defecation rate in rats, have any notable anticholinergic effect *in vitro*, or inhibit normal intestinal activity as measured in the charcoal meal test. The inhibitory effect of thioridazine on emotional defecation can therefore not be attributed to a peripheral anticholinergic or spasmolytic effect.

We must therefore conclude that a certain type of phenothiazine derivatives selectively depresses the emotional defecation and has relatively little effect on

motor performance (thioridazine), while others inhibit both functions equally (chlorpromazine, prochlorperazine) and yet others (perphenazine) predominantly reduce the conditioned avoidance response and the motor activity. It seems therefore that the sedative and anti-emotive effects of these drugs are independent of each other.

Further experiments with the above-mentioned drugs (to be published) revealed a striking parallelism between their inhibitory potency on the conditioned escape response and their cataleptic activity in rats. Previous studies¹⁰ and recent findings^{6, 11} have also stressed the parallelism between the cataleptic effect of these compounds in animals and the incidence of extrapyramidal side-effects in man. The depressant effect of these drugs on conditioned and motor performance of experimental animals is apparently not directly related to their therapeutic tranquillizing effect, but rather to the manifest depression, apathy or extrapyramidal symptoms. The inhibitory effect on emotional behaviour, on the other hand, seems rather to be related to their therapeutic activity.

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PATHOLOGY

An Attempt to Produce Malignant Change with Deoxyribonucleic Acid from Rat Sarcoma and Hepatoma

BENOIT, Leroy, Vendrely and Vendrely^{1, 2, 3, 4} have described changes in the pigmentation of the Pekin duckling after injection of deoxyribonucleic acid from the Khaki-Campbell drake, which they interpreted as a somatic mutation. Perry and Walker⁵ and Bearn and Kirby⁶ have repeated similar work in the rat and failed to produce any change. Hewer and Meek⁷ injected young mice with deoxyribonucleic acid from herring sperm, and within 23 days produced death from malignant disease of the intestine. Leuchtenberger, Leuchtenberger and Uyeki⁸ produced cytological changes in the livers of mice by intraperitoneal injection of deoxyribonucleic acid prepared from breast cancers of *C₃H* mice. This work has now been repeated in the rat using deoxyribonucleic acid prepared from rat sarcoma and rat hepatoma.

The deoxyribonucleic acid used in these experiments was prepared from rat hepatoma and rat sarcoma by the method described by Kirby^{9, 10, 11}. The final product was precipitated and dried and then made into a highly viscous suspension by adding 0.9 per cent saline. 56.8 mgm of rat sarcoma deoxyri-

bonucleic acid were injected in equal amounts into 18 newly born Wistar rats subcutaneously and intraperitoneally within 3 hr of birth. Abdominal distension was caused with each injection, but no mortality resulted. 57.3 mgm of hepatoma deoxyribonucleic acid were injected into 8 newly born rats in the same way. Each rat received either 3 mgm of sarcoma or 7 mgm of hepatoma deoxyribonucleic acid.

All animals survived and were weaned at 3 weeks. They grew normally from then on, and at nine months are all well. No tumours are present.

These results show, at present, a failure to produce malignant change using deoxyribonucleic acid from the rat sarcoma and hepatoma.

Deoxyribonucleic acid is now of very considerable interest in view of the transformations produced in viruses by Avery, Macleod and McCarthy¹² and the somatic mutations produced in ducks by Benoit, Leroy, Vendrely and Vendrely^{1, 2, 3, 4}. As a working hypothesis it is widely accepted that deoxyribonucleic acid is the primary genetic material¹³. In these transformation experiments the molecules of deoxyribonucleic acid become incorporated into the host and so produce a change in the virus or cell type from then on. The cancer cell may be considered as a mutant cell which proceeds to grow as a result of this mutation in an abnormal manner. On this theory it should be possible to produce malignant changes in normal cells using deoxyribonucleic acid from cancer cells. One obstacle is to effect the incorporation of the deoxyribonucleic acid from malignant cells into the normal cell. It is believed that many workers are proceeding along these lines of research at the present time and, therefore, it is of importance to report methods that have failed to produce positive results.

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Differentiation Between a Growth-Promoting Factor and a Tumour-Susceptibility Factor in Eggs

SZEPFENWOL¹ reported that feeding a diet composed mainly of cooked eggs to mice resulted in a significant increase in the number of animals spontaneously developing tumours. Denton² found that feeding egg yolk increased the growth of chicks. Recently Hradec³ presented evidence, based on fractionation studies, which indicated the identity of the tumour susceptibility-enhancing and the growth-promoting factors.

The study presented in this report was undertaken to determine by feeding experiment whether or not these factors were identical.

In order to measure susceptibility to tumour a lymphoid tumour transplant RPL 12 was used. It should be noted that none of the tumours found by Szepienwol¹ was of this type however, preliminary experiments indicated that feeding cooked eggs to chicks increased the susceptibility to this transplant.

Forty White Plymouth Rock chicks were fed each experimental diet from the day of hatching. At six days of age the chicks were inoculated in the right pectoral muscle with a saline suspension of tumour cells containing the equivalent of 10 mgm of tumour cells. The suspension was prepared as described previously.⁴ After inoculation the experiment was continued for four weeks. At this time mortality had ceased and tumours could not be palpated among the survivors.

At two weeks of age, before any mortality had occurred, the chicks were weighed. The results of this weighing are presented in Table 2. The data on weights were analysed for significance by the *t* test that for mortality by the χ^2 test.

The eggs were prepared by autoclaving fresh eggs for twenty minutes at fifteen pounds' pressure. The shells were removed, the eggs ground and air dried at about 53° C. After drying a portion of the eggs were extracted continuously for 36 hours with 95 per cent ethyl alcohol. This procedure was designed to extract the growth promoting factor. After extraction, the residue was air dried at room temperature, reground and added to the feed at a level equivalent to that of the whole egg. The solvent was removed from the extract by distillation and it was also added to the feed at equivalent whole-egg levels. In this study the eggs replaced corn meal.

Table 1 lists the ingredients of the diet used. The results of the study are presented in Table 2.

Table 1 COMPOSITION OF THE DIETAL DIET

| | Per cent |
|---|-----------|
| Soybean oil meal (solvent) | 50.0 |
| Ground yellow corn | 60.85 |
| Defluorinated rock phosphate | 5.0 |
| Salt | 0.5 |
| Alfalfa meal | 0.7 |
| Vitamin mixture | 0.2 |
| Choline chloride | 0.15 |
| Min. SO ₂ , R ₂ O | 10 mgm. |
| * Suppl. per lb. of diet | |
| Thiamine | 0.0 mgm. |
| Riboflavin | 1.6 mgm. |
| Niacin | 8.0 mgm. |
| Pantothenic acid | 8.0 mgm. |
| Folic acid | 0.45 mgm. |
| Biotin | 45 mgm. |
| Pyridoxine | 1.6 mgm. |
| Choline | 700 mgm. |
| Vitamin B ₁₂ | 8 mgm. |
| Vitamin A | 1000 I.U. |
| Vitamin D | 180 I.U. |
| Meadskoe | 10 mgm. |
| Alpha Tocopherol Acetate | 10 mgm. |

Table 2 EFFECT OF EGGS ON WEIGHT GAINS AND MORTALITY TO RPL 12

| | Wt. Gain per cent of control | Mortality (per cent) |
|---|------------------------------------|-------------------------|
| Control | 138.9† | 45.4 |
| 25 per cent dried eggs | 138.9† | 45.4 |
| Extracted eggs equivalent to 25 per cent | 104.4 | 73.9 |
| Alcohol extract of eggs equivalent to 25 per cent | 118.5† | 35.1 |

* Significantly greater ($P \leq 0.05$) than control
† Significantly greater ($P \leq 0.01$) than control

The alcohol extract contained the growth factor but not the tumour-enhancing factor. These findings

clearly show that the two factors as measured in this experiment are not identical.

These results apparently conflict with the conclusions of Hradec.³ It is possible that the tumour enhancing factor for rats studied by Hradec and that for chicks as measured in this experiment are different entities. Support for this view lies in the fact that the rat tumour enhancing factor is destroyed at 90° C while the cooked eggs were still active. Furthermore the rat tumour enhancing factor is soluble in common fat solvents³ while the chick factor is not soluble in 95 per cent ethyl alcohol.

We wish to express our appreciation to Myrl K. Warren for her technical assistance in this study.

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PLANT PHYSIOLOGY

Occurrence of 3-Indolylacetic and 3-Indolecarboxylic Acids in Tomato Crown—Gall Tissue Extracts

A NUMBER of publications¹ report high auxin activity in extracts of tumour tissue initiated by the crown gall organism, *Agrobacterium tumefaciens*, and indirect evidence indicates a high rate of auxin metabolism in this tissue.² Suggestions have been made that 3-indolylacetic acid is involved although this has not been proved. There is evidence that auxin activity occurs at the same or a similar R_f as 3-indolylacetic acid on one-dimensional chromatograms and other investigations indicate that 3-indolylacetic acid or an auxin with same R_f is present in extracts of aseptically cultured gall tissue of tobacco and sunflower.³ We have carried out single and two-dimensional paper chromatography with the acid fraction from other extracts of large quantities of tomato crown gall tissue grown on the stems of whole plants to determine whether 3-indolylacetic acid is in fact present.

Gall tissue obtained by inoculating tomato plants with *Ag. tumefaciens*, was harvested after 6–8 weeks stored at -10°C until required then macerated under peroxide free ether at about 0°C , and kept for 24 hr at -10°C in darkness. Normal stem tissue from plants of the same age and wounded in the same manner as that bearing the galls, was extracted for comparison. On allowing the extracted frozen tissue to thaw an aqueous liquid separated out. This was brought to pH 2 and extracted with ether. This extract being combined with that from the tissue. Aqueous compounds were removed from the combined ether extracts by shaking three times with 5 per cent aqueous sodium bicarbonate. After acidification to pH 2, this was re-extracted with peroxide free ether to remove organic acids. Preliminary experiments showed that 10 μgm 3-indolylacetic acid added to 100 gm of ether tissue before maceration could be recovered almost quantitatively by the above extraction procedure.

Activity in the wheat cylinder test was obtained on chromatograms of gall extract equivalent to 250 gm

fresh weight of tissue. Not less than 650 gm was required, however, for positive chromogenic reactions. To enable the extract from this amount of material to be loaded on the papers, a second extraction with 0.1 per cent aqueous sodium bicarbonate was necessary, to separate pigments from the acids present in the extracts.

Extracts from some 1,000 gm of both gall and stem tissue were submitted to two-dimensional ascending chromatography, the first solvent being isopropanol/ammonia (specific gravity 0.880)/water in the ratio 80:5:15 v/v, and the second either *n*-butanol/pyridine/water in equal volumes, or *n*-butanol/acetic acid/water in the ratio 12:3:5 v/v.

Treatment of developed chromatograms with Ehrlich or Salkowski reagents established that 3-indolylacetic acid, added to similar amounts of stem or gall tissue extracts, ran as a discrete spot with a low R_F (0.36–0.41 in isopropanol/ammonia/water instead of 0.48) in the first direction, but with the correct R_F in the second direction (R_F in *n*-butanol/pyridine/water, 0.66, R_F in *n*-butanol/acetic acid/water, 0.89). Thus, separation from other components was achieved in the first solvent and the retarding effect of impurities with the second solvent was negligible.

Chromatograms of gall extract, equivalent to 1,000 gm tissue, showed typical chromogenic reactions for 3-indolylacetic acid at the same R_F values as the tissue extract plus 3-indolylacetic acid marker, and identical gall chromatograms showed high activity in both the wheat cylinder and pea segment tests⁴ in the 3-indolylacetic region. There was no evidence of a chromogenic pattern which might suggest the presence of 3-indolylpyruvic acid⁵, although a pink spot was observed on the chromatograms, which was later shown to be due to 3-indolecarboxylic acid, with R_F 0.31 in isopropanol/ammonia/water, 0.77 in *n*-butanol/pyridine/water, and 0.88 in *n*-butanol/acetic acid/water. The pink spot obtained on treatment with both Ehrlich and Salkowski reagents showed a characteristic dull red fluorescence in ultra-violet light.

There was no region of auxin activity on the corresponding two-way chromatogram from stem tissue, but 3-indolecarboxylic acid was again found to be present. Chromatograms sprayed with Salkowski reagent showed no colours other than the pink one due to 3-indolecarboxylic acid, but with Ehrlich reagent, a blue spot was obtained which, however, disappeared within 24 hr of spraying the paper. Although the position of this spot (R_F 0.38 in isopropanol/ammonia/water, 0.64 in *n*-butanol/pyridine/water and 0.89 in *n*-butanol/acetic acid/water) corresponded closely with that of 3-indolylacetic acid, the complete absence of auxin activity in this region of the chromatogram, the negative Salkowski test and the transient nature of the blue colour obtained with Ehrlich reagent, all indicate that the compound is quite different from 3-indolylacetic acid. It would therefore appear that the ether extract of mature tomato stem tissue contains a compound inactive as an auxin but which behaves on chromatograms very similarly to 3-indolylacetic acid. In this connection it is of interest to note that some sugars⁶ and other substances, probably leucoanthocyanins⁷, have been shown to give chromogenic reactions similar to those of 3-indolylacetic acid on paper chromatograms. It is clear, therefore, that claims for the identification of 3-indolylacetic acid in tissue extracts, based on chromogenic reactions without supporting biological evidence, should be accepted with reserve.

The present experiments have shown that whereas free 3-indolylacetic acid is not detectable in extracts of up to 1 kgm of healthy mature tomato stems, it is present in those of crown-gall tissue. In our work, however, large amounts of this tissue were used and only small amounts of free 3-indolylacetic acid were detected. This result is perhaps not surprising, for whilst auxin is likely to be synthesized rapidly in actively growing galls, it is equally likely to be rapidly utilized in the growth reaction. Furthermore other non-acidic growth-substances may be present which contribute with 3-indolylacetic acid to the overall growth of crown-gall.

Full experimental details of this work will be published elsewhere.

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Joint Action of Gibberellic Acid and Coumarin in Germination

THE stimulatory effect of gibberellic acid on germination has been recently observed¹⁻³ and the possible modes by which this is brought to pass have been discussed by Brian⁴. Coumarin is well known as a germination inhibitor^{5,6} and is also known to induce light sensitivity in certain seeds not normally requiring light for their germination⁷. It seemed of interest therefore to determine whether gibberellic acid, like light, could reverse inhibition in coumarin treated seeds. Lettuce seeds, variety Grand Rapids, were allowed to germinate for 48 hr at 25°C in the dark in water, or solutions of coumarin, gibberellic acid (sodium salt), or mixtures of the two. The results are shown in Table 1.

Table 1 COMBINED ACTION OF GIBBERELIC ACID AND COUMARIN ON GERMINATION OF LETTUCE SEEDS (RESULTS ARE GIVEN AS PER CENT GERMINATION)

| Gibberellic acid concentration (M) | Coumarin concentration (M) | | | |
|-------------------------------------|----------------------------|------------------|------------------------|------------------------|
| | 0 | 10 ⁻⁴ | 3.3 × 10 ⁻⁴ | 6.6 × 10 ⁻⁴ |
| 0 | 74 | 13.5 | 2 | 0 |
| 0.95 × 10 ⁻⁴ (33 p.p.m.) | 97.5 | 32 | 1.5 | 0 |
| 1.9 × 10 ⁻⁴ | 100 | 45 | 8.5 | 0.7 |
| 3.8 × 10 ⁻⁴ | 100 | 95 | 21 | 10 |

It can be seen that gibberellic acid does in fact reverse the inhibition of germination by coumarin, the extent of reversal being a function of the concentration of both the substances. It is important to note however that the concentrations of gibberellic acid required to cause this reversal are rather higher than those at which this substance is active in other ways, for example, germination stimulation or growth^{2,3,8}.

However, coumarin and gibberellic acids are active at about the same external molar concentrations. Although gibberellic acid reversed the inhibition of germination it did not appear to reverse the effect of coumarin inhibition of growth. This was shown by allowing seeds to germinate either in solutions of coumarin ($1.7 \times 10^{-4} M$) or in the same solution of coumarin with the addition of $3.8 \times 10^{-4} M$ gibberellic acid. The seeds were given a light stimulus after 2 hr and then replaced in the dark in order to produce 100 per cent germination so that effects on growth would not be obscured by effects on germination. Measurements of length of roots and hypocotyls of the 48 hr seedlings showed that gibberellic acid in the dark had no detectable effect on the growth inhibition induced by coumarin in either case. This is of interest because gibberellic acid is known to cause marked elongation in hypocotyls of lettuce seedlings⁹.

Coumarin is known to affect both germination and growth¹⁰. Gibberellic acid is capable of reversing its action in germination, but apparently not in growth, in a way somewhat similar to that of red light. This provides support of the view of Brian⁴ on the mode of action of gibberellic acid and its relation to the light effect. It is also consistent with the hypothesis that coumarin inhibits germination through its action on the production or metabolism of growth substances, which may be gibberellin like. This view however leaves unexplained the blocking by coumarin of growth processes, or the failure of gibberellic acid to reverse it. It will be of interest to study the inter actions of these two substances in other tissues known to respond to them.

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BIOLOGY

Eels in Southern Africa

FIELD work carried out in South Africa and extended into Southern Rhodesia has enabled me to link the study of the biology of the fresh water eels with work carried out by Frost in Kenya¹, and on material from Northern Rhodesia². A more detailed report is in preparation but the following may be of interest to other workers.

Five species are represented: the two predominant African eels *Anguilla nebulosa labiata* Peters, and *A. mossambica* Peters, the widely distributed *A. marmorata* Quoy and Gaimard and *A. bicolor bicolor* McColland, and the rare *A. obscura* Günther. Eiders of the two predominant eels reach the mainland during the period January-February, those of *A. n. labiata* 54-58 mm in length, and those of *A. mossambica*

45-55 mm. The main body of eiders of the former species reaches the coast between Kenya and a point 21°S, and those of *A. mossambica* from 21°S to a point 32°S. Outside these southerly limits eiders of either species become rare. In those rivers flowing into the Indian Ocean within these eider zones we find that it is the adult of the predominant species of eider that is furthest inland, and that has reached the highest altitudes. For example from Kenya to the Inyanga Mountains of north eastern Southern Rhodesia it is *A. n. labiata* that is found in the high land trout streams, south of this and through the Transvaal to Natal it is *A. mossambica*. The dispersal of these two species over a river system appears to be governed by the size of the eel renouling the river mouth, and not by water temperature or any particular environment. The ability of these small creatures to carry out amazing migrations is shown by the number of eels found above waterfalls some over 300 ft in height but it is evident that once they have reached a critical length they are unable to negotiate these obstacles. Young eels 80-100 mm in length of the species *A. mossambica* have been found inland at a height of 4 600 ft and 475 miles along the river from the sea, some have even negotiated the Vaal Limpopo River watershed and have entered the Orange River system which flows into the Atlantic Ocean.

Frost³ has also reported eiders of the species *A. bicolor bicolor* from the coast of Tanganyika but their southerly limit is not known. It is, however significant that small eels of this species were collected in Southern Rhodesia 100 miles away from the sea by river, an unusual distance inland for this short flannel eel to be found.

Whilst *A. n. labiata* and *A. mossambica* are the predominant eels in the areas specified, their distribution beyond these limits is considerably particularly towards the south. This additional dispersal is due to the migrations of young eels or post-eiders and the number involved decreases with distance from the river zone. For example south of latitude 32°S eiders of *A. mossambica* are rare and eiders of other species have not been found. The rivers of the south-eastern and southern Cape Colony are populated by secondary migrations of post-eiders 90-130 mm in length all *A. mossambica* accompanied by young eels 140-250 mm in length, of the same species as well as *A. marmorata*, *A. n. labiata* and *A. b. bicolor*. These migrations are carried out with the same enthusiasm and determination as shown by migrating eiders but it is only the smaller eels that are able to negotiate man made obstacles such as the walls of large dams. Specimens taken during these migrations either coming from, or near the sea, lack the full pigment of young eels taken further inland, and appear to have been at sea for a long period. It is fairly obvious that their route was not a direct one and some of the answer may lie in the complex sea currents of this area. That considerable wandering around in the sea takes place after metamorphosis is shown by the fact that young eels as well as adults of the species *A. marmorata*, *A. n. labiata* and *A. b. bicolor* have been found as far west round the south Cape coast as Kynsna, all some 2 000 miles from their known eider zones. Even more astounding are the records of *A. anguilla* from Kenya⁴ which must have reached there via the Suez Canal, and *A. obscura* from the Buffalo River⁵ near East London.

By comparing vortical counts and the sizes of eiders of the eels of the Indian Ocean there is no

indication, except in the case of *A. n. labiata*, that distances involved in distribution are associated with a prolonged larval life, secondary migrations earned out by post-elvers could account for the extraordinary distances covered. The elvers of the closely related *A. nebulosa nebulosa* McClelland and *A. nebulosa labiata* Peters, separated by vertebral counts, are similar in size, but it is possible that the examination of more material may show that, as suggested by Tucker in the case of *A. anguilla*⁶, the increase in vertebral count is associated with a prolonged larval life, and that the east African mottled eels, which are quite distinct from *A. marmorata*, are indeed the Indian eel *A. nebulosa* and originate from the same breeding ground.

Mature female eels of the species *A. marmorata*, *A. n. labiata*, *A. mossambica* and *A. b. bicolor* have been found near the sea, as well as males of just one species *A. mossambica*, in South African rivers. These have all been taken during the period November–March. Like the European eel these have had the characteristic dark dorsal surface, silvery belly, much enlarged gonads, large eyes and pointed snout, but all have been feeding on fishes and crustacea, and there has been no sign of degeneration of the gut. It is noteworthy that in South Africa the migrations of mature eels to the sea, and those of olvers and post olvers from the sea, take place during the summer months with maximum activity during January and February, but, being dependent upon good rains and substantial river flow, these migrations are erratic.

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June 26

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A Free-Floating Marine Red Alga

On April 14, 1959, during a research trip along the coast of Victoria, Australia, the beach at Bridgewater Bay, near Portland, was observed from a distance to show a deep red band at about high-water mark, and the sea to be similarly coloured close inshore. The band on the beach was up to 25 ft broad and several hundred yards long, and consisted of enormous numbers of deep red algal balls, each about 1 cm in diameter. The mass of balls was generally 1–2 in deep, but in places reached 10 in. Amongst rocks at the end of the beach the balls were piled up 2–3 ft high, and large rock pools were completely filled with them. Other algae were virtually absent from this drift, but further eastwards along the beach fairly rich drift of other algae occurred. In no case were the red algal balls found attached to any other algae or marine angiosperm.

From the top of nearby cliffs, numerous red streaks were seen extending 200–300 yards out to sea beyond the immediate beach waves, these streaks were probably several yards across, with clear water between them and were orientated perpendicular to the beach. They were present throughout the morning of observation.

The alga concerned appears to be a species of *Antithammon* which was growing actively as a free floating form offshore from the beach, with some being continually washed up on the beach. The absence of any plants attached to other algae, and the structure of the balls described below, precludes the possibility that they had been detached in enormous numbers from some sublittoral substratum or host. The balls can be described as of the 'æga gropilous' form, and of one hundred balls examined, 96 were tetrasporangial and 4 were apparently sterile. No sexual plants were seen.

The base of the plants consists of an axial cell, in general with no evidence of any attaching organs. In about 25 per cent of the plants, however, 2 to a few multicellular rhizoidal filaments had developed from the end cell, but these showed no signs of having been attached to anything. The oldest parts of the thallus were situated near the centre of the balls. Multiplication apparently occurred by fragmentation of the thallus, and axial cells from which branches had broken were frequently observed. In a few cases dead cells occurred in lower parts of the thallus, but fragmentation usually appeared to take place between two adjacent cells.

The thallus is dichotomously branched, with verticils of short pointed laterals at the upper end of each cell. The cells are 1–2 times as long as broad, varying from about 60 μ diameter near the apices to 180–250 μ in the oldest parts. The short laterals occur in verticils of 4 except immediately above a branch axil, where the inner lateral is usually absent, in the latter case the outer lateral is usually larger than the other two. The laterals are not placed in line with those of adjacent cells. The laterals are up to 80 μ long, 25–35 μ broad at the base, consisting of 3–5 cells, unbranched, tapering sharply to a blunt point, and often bearing hairs on a short stalk cell, most commonly on the upper side of the basal cell. The thallus is not mucilaginous. Epiphytic growth of diatoms, other microscopic algae and protozoans was considerable.

The tetrasporangia are sessile on the upper side of the basal cell of short laterals, 45–60 μ in diameter, and are cruciately divided, though often appearing tetrahedral when mature, the division, however, appeared to be successive in all cases, with the second and third divisions almost simultaneous and at right angles to each other. Sporangia are not frequent on most plants, and in some cases only one or two per plant were found.

The alga was maintained in culture for 2–3 weeks, but soon became overgrown with the numerous epiphytes originally present. Further development of the short laterals into longer shoots, themselves with very short laterals, was observed.

In the absence of sexual material the genus cannot be determined with certainty, though it is certainly close to *Antithammon*, and it appears to be distinct from any previously described Australian species. Revisional studies at present under way on Australian *Crouaniera* will include this alga.

The water in which this alga was growing is open-ocean water, within a wide bay, and is not subject to any pollution or dilution. The salinity is approximately 36 per mille and the sea temperature about 16°C.

As far as we can ascertain, this is a unique case of a free-floating member of the Rhodophyta in open water. The following additional information on its occurrence before and after our observations are from

Mr O Beaugliolo, a local algal collector. Local residents had observed a 'red beach' for a few days before April 14, but not on any previous occasion within recent years. On April 15, a very high tide almost completely removed the beach drift, but great masses were visible out to sea, somewhat east of the original streaks. The floating masses, with some beach drift, were present on April 18 (forming a line about 20 yards wide and a mile or more long) but had disappeared at Mr Beaugliolo's next visit on April 26, and have not been observed since. On April 18 large breakers just off a reef were coloured red by the algae, which always appeared to maintain its position offshore. No trace of this alga was seen in nearby bays during the period of observations.

This occurrence is apparently more in the nature of a bloom¹ during especially suitable conditions though its development under the normally fairly rough conditions of Bridgewater Bay is remarkable. On April 14 waves near the beach were about a foot high and similar conditions had prevailed since a storm 8-10 days earlier.

The most striking free floating marine alga is the *Sargassum* of the Sargasso Sea¹. Loose lying forms of other marine alga are known from the Baltic¹ and such forms of Puccin in salt marshes are well known. Moore², has recorded loose lying forms of *Macrocystis pyrifera* and *Hormosira banksii* in New Zealand. These loose lying forms all appear to be confined to calm, shallow bays with illution a prominent feature in the Baltic and in most cases the alga concerned lie on the bottom. Such cases seem to be distinct from the *Antithamnion* reported here. Also these loose lying forms are invariably sterile while nearly all of the *Antithamnion* plants were tetrasporangial.

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Feeding of a Ctenophore, *Bolinopsis infundibulum* (O F Müller)

Bolinopsis infundibulum a lobate ctenophore is known to occur from the arctic to the Mediterranean in European waters, and from the arctic to the Gulf of Maine in North American waters¹⁻³. Full taxonomic details are given by Chun¹ and Krumbach².

On May 15 and 16, 1959 immense numbers of this ctenophore occurred in Port Erin Bay, and up to 1½ miles seawards where they were taken by tow nets in the shallow waters of the Bay their distribution appeared to be fairly uniform from the surface to the sea bed. The next two days witnessed a rapid fall in numbers and the organisms had practically disappeared by the eighteenth morning after this date few were observed in the area. The ctenophores appeared during a warm spell, when the waters were fairly calm. They disappeared when a cold east wind sprang up, and the seas became choppy. Previous records attest to the presence of this species during the months of May and June in Manx waters⁴.

The size range taken in the Bay during present observations was 3 mm to more than 40 mm in length (the longer axis of the body was measured). The samples (40-80 specimens) were carefully transferred

to a large aquarium, and their feeding habits observed.

The ctenophores fed voraciously on the smaller copepods, *Podon*, *Eurytemora* and nauplii offered to them. They appeared unable to capture decapod larvae and the large copepod *Calanus*. They progressed through the water with their large paired peristomial (or oral) lobes expanded like trawl-doors, and these were observed to come together occasionally to enclose a quantity of water containing food-organisms. The food organisms were then propelled, by the strong beating of the stout flagella on the auricles, towards the oral tentacles surrounding the ocelli like mouth. The oral tentacles are heavily armoured with colloblasts (or lasso-cells) which have the effect of immobilizing the prey so that they helplessly and passively pass into the stomodaeum in a sheet of mucus motivated by the oral cilia.

One specimen 23 mm long was thus observed to capture 18 small copepods (*Parudocalanus elongatus*, *Acartia clausi* and *Temora longicornis*), 11 *Podon intermedius* and 4 *Eurytemora nordmanni*. Its stomodaeum was only about a quarter full with this meal. This specimen was transferred to a bowl devoid of food organisms and the food organisms it contained were observed to be digested in about an hour (58 minutes) after ingestion. The end products of digestion were found streaming away from the stomodaeum via the four large inter radial canals into the gastro vascular network. Indigestible particles were voided through small apertures of the gastrovascular canals, as has been described for ctenophores in general by Hyman⁵.

The samples kept in the aquarium did not survive for more than 4 days even though they were fed on fresh plankton.

My thanks are due to Dr D I Williamson for his help and to Mr J S Colman for his criticism and interest in these observations.

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ENTOMOLOGY

Stomoxys Control in Uganda, East Africa

SINCE 1956, field research on the bionomics of *Stomoxys* has been in progress in the north of the Mengo District of Buganda Province, Uganda. The experimental area lies in an irregular tract of country of approximately 200 square miles and includes territory ranging from wet seasonal swamps at an altitude of 4 000 ft above sea level to wind-swept hills up to 6 000 ft.

The *Stomoxys* population supports an approximate species density of (per cent) *S. calcitrans* 60, *S. nigra* 30, *S. omega* 10.

For simplicity in collecting field data the area was split into six sections. This report deals with an area of approximately 50 square miles (8 miles × 6 miles) of low lying open acacia woodland. During the dry season this area dries out completely but in the rainy

season becomes water-logged and partially flooded. It is sparsely populated by a few Bahuma settlements, whose sole interest, like those of the Karamojong in north-east Uganda and the Masai in Tanganyika, lies in the rearing of cattle. The Bahuma are a nomadic race and take no interest in agricultural pursuits. This disinclination to practice agriculture is mainly responsible for the non-existence of *Stomoxys* breeding places in this particular Bahuma area, inasmuch as bananas, which are universally grown by the Baganda, are not to be found in Bahuma settlements. One of the main requirements of *Stomoxys* breeding sites during the dry season is the shade afforded by banana trees, coupled with the accumulation of rotting banana leaves, on the surface of the ground. During the dry season, I have found heavy breeding occurring in and around cattle bomas outside the Bahuma area, in rotted banana leaves mixed with animal faeces and urine. In the absence of urine and sufficient shade to keep the substrate moist, no *Stomoxys* breeding was found.

During the dry season, September to March, adults of *Stomoxys calcitrans* and *Stomoxys nigra* are present in large numbers in this Bahuma area, despite the fact that no breeding places were detected.

Typical Bahuma bomas consist of dry-cut acacia thorn palisades, with no significant shade. Every day the interiors of these open bomas are swept clear of animal droppings and the manure stacked in irregular heaps outside the bomas. (From personal experience, manure heaps (consisting only of manure with no decaying vegetable matter) have proved unsuitable as breeding places for *Stomoxys*.)

A search for breeding places during the dry season proved negative, for everywhere the soil, both in the forest and bomas, was rock-hard and dry—conditions unsuitable for *Stomoxys* breeding. It was difficult, therefore, to reconcile such a heavy and continuous population of *Stomoxys* in an area completely devoid of breeding places.

A heavy breeding place of *S. calcitrans* and *S. nigra* existed adjacent to the swamp area. This consisted of a well-shaded cattle boma, from which the manure was seldom removed, but was allowed, together with dead leaves and cattle urine, to decompose, thus producing an ideal breeding site. The cattle from this boma were grazed during the week throughout the length and breadth of the 50 square miles of swamp area in which no breeding places had been found. It was noticed that adult *Stomoxys* were present in large numbers, resting at dawn on vegetation surrounding the boma, and that when the cattle left the boma en route for the forest grazing area, the flies disappeared.

The adult population in this boma was destroyed by attacks on the adult fly, using 4 per cent chlordane miscible oil sprayed upon foliage surrounding the boma. Over a period of 3 months two such applications were made, the second application was considered essential as a result of a freak rainstorm which produced 3 inches of rainfall in a period of a few hours, six weeks after the initial spraying. One month after the initial spraying, no breeding was found inside the boma and no adults were seen resting on the boma vegetation at dawn. Within less than 3 months, the *Stomoxys* population over an area of 50 square miles had been reduced by 99 per cent. During the 3 months under consideration, the *Stomoxys* population in the other four sections of the experimental area remained at a high and constant level.

Further and more detailed experiments are now being planned to substantiate the above results.

It would therefore appear that, in this particular case, *Stomoxys* does not breed in numerous small breeding sites scattered over a wide area, but is confined to only a few sites, where intense breeding occurs. In my opinion, breeding places of *Stomoxys* are very select, very few and far between, and easily identifiable under local African cattle farming conditions.

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Age Determination in *Mansonioides* Mosquitoes

OBSERVATIONS by Bertram and Samawickrama¹ have shown that it is possible to determine the number of times that *Mansonioides* mosquitoes have laid eggs by examination of the ovaries for corpora lutea, a technique developed by Russian workers using *Anopheles maculipennis*². Knowing this, and the time taken from feeding to maturation of eggs it has been suggested that a precise estimate of the age of individual mosquitoes should be possible. Examination of the ovaries of laboratory-bred *M. uniformis* which had laid one to four times confirmed that, with practice, it was possible to count the number of corpora lutea and the technique was then tried with wild *M. longipalpis*, *M. annulata* and *M. uniformis*. The first two species are typically swamp-forest mosquitoes and the major vectors of filariasis due to *Wuchereria malayi* in several parts of Malaya, while *M. uniformis* breeds mainly in open swamps and is also a vector.

Mosquitoes were caught unfed as they attempted to bite in the early evening and the ovaries of practically all were early stage II when examined the following morning. With these mosquitoes it was a simple matter to identify nulliparous specimens, and relatively simple to identify specimens which had laid once only, but in specimens which had laid more than once it was difficult to separate the ovarioles properly to show the maximum number of corpora lutea. There was considerable variation in the amount of pigmented material in the corpora lutea, both between mosquitoes of the same category and between ovarioles in the same ovary. However a much more serious problem in age estimation has arisen with the finding that some *M. longipalpis* mosquitoes carrying infective stage filarial larvae, had laid only one batch of eggs. Both *Wuchereria* and *Dirofilaria* infections develop in *M. longipalpis* and the minimum incubation period from ingestion of microfilariae to the appearance of infective larvae is 10 days. A total of 22 *M. longipalpis* with infective larvae have now been examined, one had laid three times, 12 had laid twice and 9 had laid once only. Thus over 40 per cent of these mosquitoes, known to have lived for at least 10 days since feeding on an infected man or animal, had laid only one batch of eggs. Although *Mansonioides* mosquitoes require 3–4 days for eggs to mature, eggs almost invariably develop after the first blood-meal so the explanation that two blood meals were required to complete the first gonotrophic cycle, as is apparently the case with *A. gambiae*³, seems unlikely. Most of the mosquitoes were caught in swamp-forest at least a mile from the nearest known breeding place and three miles from the nearest houses. Some time must therefore have been

spent in travelling to and from oviposition sites and, unless suitable wild animals hosts were readily available a considerable time may have been spent in search of blood meals. These two time factors have been given little attention in the calculation of mosquito survival. They may be of little significance in species living and breeding in close proximity to man such as *A. gambiae* and *A. fuscus* which Davidson⁴ assumed to feed every second or third day depending on whether the gonotrophic cycle occupied 2 or 3 days. On the other hand they are clearly important in species which occur in very large numbers in places where sources of blood appear to be scarce and which may have to travel considerable distances from their breeding sites in search of a blood meal. Preliminary results of age grading *Mansonioides* mosquitoes (Table 1) indicate that nearly half the *M. longipalpis* mosquitoes caught in forest are nulliparous and few have laid more than once. An even larger proportion of *M. uniformis* caught near houses a short distance from their breeding sites are nulliparous but comparatively more go on to lay 2 or 3 batches of eggs. Haddow⁵ has suggested that 'in the vicinity of a tropical swamp the numbers may be so overwhelming that it seems quite inconceivable that more than quite a small proportion can ever obtain a blood meal. This is an exaggerated version of the *Mansonioides* mosquito population in swamp forest in Malaya but under such circumstances determination of the actual age in days of individual mosquitoes becomes an impossibility.

Table 1. NUMBERS OF EGG LAYING CYCLES COMPLETED BY WILD POPULATIONS OF *Mansonioides* MOSQUITOES IN MALAYA

| Species | | Number of egg laying | | | |
|-----------------------|----------|----------------------|-----|----|----|
| | | 0 | 1 | 2 | 3+ |
| <i>M. longipalpis</i> | Number | 167 | 148 | 32 | 0 |
| | Per cent | 47 | 42 | 0 | 2 |
| <i>M. uniformis</i> | Number | 178 | 86 | 37 | 10 |
| | Per cent | 57 | 27 | 12 | 4 |

Another method of age-estimation has been suggested by Gillett⁶ who found that young *M. africana* mosquitoes were infected with parasite larval haemaphysid mites more often than old mosquitoes. Examination of Malayan *Mansonioides* mosquitoes shows that mites occur on *M. longipalpis*, *M. annulata* and *M. uniformis* but that only *M. uniformis* is heavily infested (Table 2). This limits the value of the method for Malayan conditions but examination of the ovaries of infested mosquitoes indicates that practically all are nulliparous only 3/94 *M. uniformis* and 2/40 *M. longipalpis* had laid eggs and only one filarial infection has been recorded in a mosquito carrying mites (Table 2). The mites apparently remain attached to the mosquito until it returns to water for egg laying. Thirty two mite infested *M. uniformis* were confined over *Pistia* plants for egg laying one evening and when examined the following morning 13 were still infested but the total number of mites on the mosquitoes was reduced from 93 to 24 and many mites were found quiescent among

Table 2. INFESTATION OF *Mansonioides* MOSQUITOES WITH LARVAL HAEMAPHYSID MITES AND FILARIAL INFECTION RATES IN MITE INFESTED AND UNINFESTED MOSQUITOES

| Species of mosquito | Numbers | | Filarial infection rate | |
|-----------------------|----------|----------|-------------------------|-----------------------|
| | Examined | Infested | Infested mosquitoes | Uninfested mosquitoes |
| <i>M. longipalpis</i> | 2210 | 13 | 0.7 | 1.0 |
| <i>M. annulata</i> | 625 | 3 | 0.0 | 1.1 |
| <i>M. uniformis</i> | 1085 | 475 | 0.0 | 1.3 |

the *Pistia* rootlets. Presumably under natural conditions very few mites remain attached after the first egg laying and the presence of mites can be regarded as a reliable indication that the mosquito is young and probably nulliparous.

A further qualitative character noticed first by Crosskey⁷ with *Simulium damnosum* which distinguishes old mosquitoes, is the condition of the Malpighian tubules. In nulliparous mosquitoes the tubules are always dark and opaque but in old mosquitoes they become cleared and transparent. Not all mosquitoes which have laid once or even twice show significant differences from nulliparous specimens but any mosquito in which the tubules have become transparent is almost certain to have laid at least two batches of eggs.

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BACTERIOLOGY

Taxonomic position of *Arthrobacter*

It has long been recognized that a considerable number of different types of Gram positive non sporing bacilli of irregular morphology occur in soil and their relationship to the *Corynebacteria* has been much discussed. One solution to the problem has been to widen the scope of *Corynebacterium* to include all such bacilli, but it is now generally felt¹ that this would place together in one genus very dissimilar organisms and create more problems than it would solve. Conn and Dimmick² proposed that at least one group of these soil organisms the morphology of which shows some resemblances to *Corynebacteria* should be placed in a separate genus, for which they proposed to revive the old name *Arthrobacter*. The type species suggested by Conn and Dimmick was *Arthrobacter globiformis*, originally described by Conn³ as *Bacterium globiforme*.

In previous work we have noted that strains of *Corynebacterium* are characterized by a distinctive pattern of sugar and amino-acid components in their cell wall namely arabinose and galactose as sugars and alamae, glutamic acid and DL-diaminopimelic acid as the principle amino acids. Furthermore this pattern of cell wall components is shared by strains of *Mycobacterium* and *Nocardia*⁴.

We now report briefly the results of cell wall analysis on 7 strains of *Arthrobacter*, and our findings would seem to indicate that there is no close relationship between these organisms and the *Corynebacteria* proper. The material for analysis was kindly provided by Dr. Gareth Morris of the Biochemistry Department, Oxford, in the form of freeze-dried suspensions. These were resuspended in saline and the cell wall fractions were prepared hydrolysed and examined as previously described⁴. The purified cell wall fractions were also tested for their susceptibility to lysozyme digestion by suspending them in *M/30* phosphate buffer pH 0.3 + lysozyme 100 µg/ml and incubating at 40°. The progress of lysis was estimated roughly by comparing each treated suspension with a control suspension in the same buffer without lysozyme.

Table 1 CELL WALL COMPOSITION IN STRAINS OF *Arthrobacter*, AND THE EFFECTS OF LYSOZYME ON THE ISOLATED CELL WALLS

| | | Cell wall components present | | | | | | | | | | DAP isomers | | Effects of Lysozyme | |
|--|--------------|------------------------------|-----------|---------|---------|-------------|---------------|--------------|---------|---------------|--------|-------------|-----|------------------------|-----------|
| | | Arabinose | Galactose | Glucose | Mannose | Glucosamine | Galactosamine | Muramic acid | Alanine | Glutamic acid | Lysine | Glycine | DL | | LL |
| <i>Arthrobacter globiformis</i> | N C I B 8602 | — | ++ | — | — | + | — | + | +++ | +++ | +++ | | | | 2 hr |
| <i>Arthrobacter citreus</i> | N C I B 8915 | — | ++ | — | — | + | — | + | +++ | +++ | +++ | | | | No effect |
| <i>Arthrobacter ureafaciens</i> | N C I B 8916 | — | +++ | — | + | + | — | + | +++ | +++ | +++ | | | | " |
| <i>Arthrobacter pascens</i> | N C I B 8910 | — | +++ | Tr | Tr | + | + | + | +++ | +++ | +++ | | | | " |
| <i>Arthrobacter aurescens</i> | N C I B 8912 | — | +++ | — | + | + | + | + | +++ | +++ | +++ | | | | " |
| <i>Arthrobacter simplex</i> | N C I B 8913 | — | +++ | — | + | + | + | + | +++ | +++ | +++ | +++ | | +++ | 7 min |
| <i>Arthrobacter tumescens</i> | N C I B 8914 | — | + | + | + | + | + | + | +++ | +++ | +++ | +++ | | +++ | 7 min |
| <i>Corynebacterium diphtheriae</i> (results taken from Cummins and Harris ref 4) | | | | | | | | | | | | | | | |
| | | +++ | ++ | — | + | + | — | + | +++ | +++ | | | +++ | | Not done |

In recording the amino-acids trace amounts have been ignored to avoid undue complication

The results of cell-wall analysis and the effects of lysozyme are shown in Table 1. From our previous results⁴ it appeared that the amino acid pattern of the cell walls is of significance at approximately generic level, and in these 7 strains there are 2 distinct groups in terms of the principal amino acids of the cell wall. One, comprising 5 strains including *A. globiformis*, has alanine, glutamic acid and lysine as the principal amino-acids of the wall. The other is composed of the 2 strains called *A. simplex*, N C I B 8913 and *A. tumescens* N C I B 8914, both of which have 4 amino-acids in the wall, that is, alanine, glutamic acid, glycine and LL-DAP.

In commenting on these results, it may be noted first that the cell-wall composition of these strains of *Arthrobacter* follows the general patterns already established for other Gram-positive bacteria⁴, and secondly that the 7 strains examined differ from the *Corynebacteria* both as to the sugars and the amino-acids of their cell walls. This can be seen from Table 1 where the cell-wall composition of *C. diphtheriae* is included for comparison. The fact that of the 7 strains examined 2 differ from the others in amino-acid pattern suggests that the organisms at present classified in *Arthrobacter*⁵ may still be of mixed origin. However, the first 5 strains in Table 1 seem to form a fairly homogeneous group which moreover contains a representative of the type species, *A. globiformis*. It is of interest that the cell-wall pattern of these 5 strains bears a considerable resemblance to that of *Actinomyces israeli* where the principal components found were galactose, glucosamine, muramic acid, alanine, glutamic acid and lysine⁴. That of the 2 aberrant strains however (*Arthrobacter simplex* and *A. tumescens*) is very similar to the pattern of components found in *Streptomyces* or *Propionibacterium*.

The activity of lysozyme on these cell-wall fractions was investigated in the hope that it might reinforce the cell-wall findings, but the results seem merely to provide another example of the fact that it is not possible to determine whether or not the cell walls of a given species will be lysozyme sensitive merely by a knowledge of the components present⁶. There seems to be no qualitative difference between the cell walls of *Arthrobacter globiformis* 8602 and those of *A. citreus* 8915, yet the former are attacked by lysozyme (although slowly) while the latter are unaffected. The difference may lie in the O-acyl content of the walls, as has been demonstrated for lysozyme-sensitive and lysozyme-resistant strains of *Micrococcus lysodeikticus* by Brumfitt, Wardlaw and Park⁷. The

cell walls of *Arthrobacter tumescens* seem to be highly sensitive to lysozyme, and it was obvious from the decrease in turbidity that a considerable amount of lysis had occurred within 1–2 min, although it was not judged complete until some minutes later, when the originally turbid suspension had become water clear.

We must thank Dr Gareth Morris for providing the freeze-dried suspensions of *Arthrobacter*, and Miss Sylvia Start for technical assistance in the preparation of chromatograms.

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Formation of Streptolysin S by Streptococcal Protoplasts

As has been reported previously the production of a hemolytic toxin, streptolysin S, by streptococci is greatly stimulated by adding oligonucleotides with high guanylic acid content¹.

In order to study the mechanism of streptolysin S formation, an attempt has been made to simplify the method of its formation and we have succeeded in producing the toxin with streptococcal protoplasts.

Strain S No. 8, group A hemolytic streptococcus was grown in a horse heart infusion broth (a modified Todd-Hewitt medium) for 15 hr at 37°C. 5 ml of this culture was inoculated into 100 ml of the fresh medium having the same composition and incubated for 6 hr at 37°C. The cells were harvested by centrifugation and washed twice with phosphate saline (pH 7.0). The protoplasts were prepared by incubating the washed cells with a partially purified lytic enzyme from a bacteriophage lysate of group C streptococci² in 0.5 M sodium succinate (pH 7.0) for 20 min at 20°C. The conversion to protoplasts was tested both by osmotic rupture in a hypotonic

Table 1 FORMATION OF STREPTOLYSIN S BY PROTOPLASTS AND INTACT CELLS

| | Time of incubation (min.) | Amount of hemolysin (H.U.) [*] | | |
|-------------|---------------------------|---|------|--------------------------------------|
| | | Active fraction | Core | Active fraction + casein hydrolysate |
| Protoplasts | 30 | 4 | 3 | 2 |
| | 60 | 40 | 32 | 20 |
| | 90 | 70 | 70 | 40 |
| | 120 | 88 | 43 | 43 |
| Intact cell | 150 | 84 | 32 | 70 |
| | 60 | 11 | 20 | 9 |
| | 90 | 32 | 30 | 12 |
| | 120 | 35 | 25 | 10 |
| | 150 | 40 | 61 | 16 |
| | 180 | 61 | 32 | 12 |

* The hemolytic unit (H.U.) is the amount of hemolysin which will lyse half the erythrocytes contained in 1 ml of phosphate-buffered saline (pH 7.0) in 2 hr at 37°C.

medium and by observation through a phase contrast microscope. The protoplasts were collected by centrifugation at 4,000 r.p.m. for 10 min in the cold and resuspended (concentration of protoplasts 10 mgm dry weight per ml) in the reaction medium containing sodium succinate (pH 7.0) 0.5 M magnesium sulphate 0.002 M, potassium phosphate (pH 7.0) 0.03 M, maltose 0.005 M and oligo nucleotide fraction¹ (the material of yeast ribonucleic acid (core) resistant to pancreatic ribonuclease) 200 µgm/ml or 100 µgm/ml of the active fraction of core obtained by chromatography on an 'ECTEOLA' cellulose column. The suspension was incubated at 37°C and at appropriate intervals an aliquot was withdrawn, chilled at -20°C and centrifuged at 4,000 r.p.m. for 10 min in the cold. The hemolytic activities in the supernatants were determined using a freshly prepared 3 per cent rabbit erythrocytes suspension. A control experiment was carried out in the same conditions with intact cells in place of protoplasts.

Table 1 shows that protoplasts can produce more toxin more rapidly than intact cells under these conditions.

Addition of an amino acid mixture ('Difco' casein hydrolysate) at a concentration of 1 mgm/ml inhibited toxin formation in both protoplasts and intact cells.

Gooder and Maxted² recently reported that the streptococcal protoplasts could be obtained with either 2 M sucrose or 2 M sodium chloride as suspending media. In our case however the formation of streptolysin S was strongly inhibited in these hypertonic media and 1.6 M sucrose, 10 per cent poly ethyleneglycol, 0.5 potassium chloride and 0.5 potassium monohydrogen phosphate failed to support the protoplasts of this bacterium. Such media as 0.5 M fumarate, malate, malonate, citrate and tartrate supported the protoplasts but succinate is most satisfactory in view of the inhibitory effect of other salts on toxin formation.

We wish to thank Dr W. R. Maxted for the gift of group C streptococcus and its phage.

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Growth of *Bacterium coli* and *Staphylococcus albus* in Heavy Water

In the mid 1930's when heavy water became available, workers experimenting on its biological effects reported delayed growth, complete inhibition and morphological changes in many types of organisms including bacteria^{1, 2}. Some reported normal growth³. Recently Walker and Syrett⁴ confirmed the inhibition of autotrophic growth of *Chlorella* by heavy water but found less inhibition in the presence of glucose.

Growth of two strains of bacteria in buffered nutrient heavy water broth prepared by redissolving lyophilized aqueous nutrient broth in 99.8 per cent heavy water (Norsk Hydro) was compared with their growth in aqueous medium and in medium with various concentrations of heavy water. Small inocula were prepared by growing and suitably diluting overnight cultures of the test organism in the experimental medium.

In heavy water the growth of both strains was slower than in ordinary water. The specific growth rate in ordinary water was 2.0 times greater for *Staphylococcus albus* and 2.5 times for *Bacterium coli*. Even after repeated subculture in 99.8 per cent heavy water medium the organisms were morphologically indistinguishable from those grown in ordinary water and the colonial morphology was unaltered.

In lower concentrations of heavy water the doubling time was roughly proportional to the antilogarithm of the concentration of heavy water.

The addition of glucose to heavy water broth produced an effect no greater than in ordinary water broth and *Bacterium coli* was able to grow in a 99.8 per cent heavy water medium with glucose and ammonia as sole carbon and nitrogen sources.

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GEOLOGY

Indications of Glaciation in the Siwalik System in India

THE Indian sub continent was not subjected to glacial conditions during the Quaternary Era but its highlands, namely the higher ranges of the Himalayas up to the latitude of about 33 degrees were.

The Great Ice age is believed to have commenced everywhere during Lower Pleistocene times, as proved by the occurrence of glacial deposits lying directly over the Pliocene rocks. de Terra, who has studied the glacial geology of the Himalayas, is of the opinion that the Boulder Conglomerate, the uppermost member of the Siwalik system, corresponds to the second or the Mindel stage of the glacial cycle and the Interglacial interval immediately following it and is therefore, of middle Pleistocene age. If this is so, the underlying Tatar and Pinjar stages should represent the first ice advance and belong to lower Pleistocene.

Accepting this suggestion Pilgrim¹ considers the Pinjar and Tatar stages as belonging to the upper Pliocene and not to the lower Pleistocene particularly

in view of the unconformity that de Terra presumes to exist between the Boulder-Conglomerate and the Pinjor stage. It is very important that both de Terra and Pilgrim make no mention of any evidence of glaciation in the Pinjor or the Tatrot stages. Hopwood and Lewis³ consider the Pinjor zone as lower Pleistocene on fossil evidence alone.

I have studied the Pinjor zone where it is exposed near the village of Khanpur, close to Jammu, latitude 33° N and longitude 75° E approximately. The basal clayey bed of the zone is overlain by a fairly thick conglomerate bed. The conglomerate consists mostly of pre-cambrian quartzitic pebbles and boulders, a few pebbles and boulders of the Panjal trap, Permian limestone and the Murree sandstone, all held together by a coarse arenaceous matrix, containing undecomposed grains of feldspar. The peculiarity of most of the pebbles and boulders in the conglomerate is that they possess a fairly high degree of surface-polish, unlike other pebbles and boulders in the beds below or above. The Panjal trap boulders also exhibit good faceting and fine glacial striations. The high degree of polish of the quartzitic boulders seems to indicate what might be termed 'silt-polishing'. This term has been used by Grinlinton⁴ during his researches in the Liddar valley. I am thus led to conclude that the Pinjor zone belongs to the first interglacial period and the underlying Tatrot zone to the first glacial period. On glacial evidence, therefore, the Tatrot and Pinjor zones are of lower Pleistocene age.

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AGRICULTURE

Influence of Site and Season on Agricultural Variety Trials

IN recent work at the National Institute of Agricultural Botany¹ the variation between centres and seasons has been studied in large numbers of cereal variety trials. It was found that the standard deviation of relative yields for wheat, barley and oat varieties in England and Wales is of the order of 10 per cent, when based on results from several centres in one or more seasons, but may be influenced by the actual varieties in trial. Comparable figures for this between trials 'error' have now been obtained for relative yields of roots and dry-matter in fodder beet (12 per cent), dry-matter yields of lucerne from single cuts (11 per cent), yields of maincrop potatoes (14 per cent), and of marketable heads of winter cauliflowers (16 per cent). In the absence of clear guidance from plant physiologists as to the critical conditions determining yield in each crop, attempts to relate these differences in relative varietal performance to particular environmental factors have not often been successful with the 20-40 results usually available for each pair of varieties. There is at present, therefore, little practicable alternative to basing varietal advice to farmers on national average results, although the search for environmental adaptation continues.

The differences in error according to the particular varieties in trial confirm Salmon's finding² for wheat in America that year-variety interactions are not

always homogeneous and imply the need for caution in using the analysis of variance for variety trial series. Such caution is also necessary for physiological considerations do not necessarily support the underlying mathematical assumption of the analysis of variance that varietal differences are additive: it seems perhaps more probable that differences between varieties will be, for example, greater where the general level of yield is high.

There are other important implications for agricultural variety testing procedures. At least 20 trials over a representative range of centres and seasons are thus usually necessary to obtain significance at $P 0.05$ for a 5 per cent difference in yield between two cereal varieties. A lower between-trials error, leading to significance from fewer trials, is not necessarily a matter for congratulation, but suggests that the trial centres or seasons may not have been sufficiently representative.

If yield results from single cereal trials are to be considered as having validity beyond the particular field and season of the trial, the standard error of the mean variety yields from that one trial should not be considered as less than about 10 per cent. Much greater internal precision within individual trials is, therefore, uneconomic. Engledow and Yule³ have pointed out that it is "no use spending great pains on the endeavour to reduce the effects of one sort of error (within trial) when another is left uncontrolled". They were discussing seasonal differences: differences between centres are no less important. To illustrate this, a series of 21 spring oat trials with 6 replications of 4 varieties in 1/48-acre plots at 7 centres over 3 years has been analysed to study the effect of reducing numbers of replications as follows:

| No. of replications in each of 21 trials | 6 | 5 | 4 | 3 | 2 | 1 |
|---|------|------|------|------|------|------|
| Standard deviation of variety yield as percentage mean plot yield | 11.5 | 11.3 | 11.2 | 11.1 | 11.2 | 12.4 |

Varietal differences were significant at $P 0.001$ with only one replicate at each centre. Similarly my colleague, C G Finch has recently undertaken four trials of summer cauliflowers in one season, each with single plots of 101 varieties: the significant difference between the proportions of perfect heads was 17.8 per cent, compared with figures of between 12.8 and 20.0 per cent from the means of five trials each with 6 replications in earlier years.

In variety trials adequate and substantial replication between centres and seasons is therefore essential, and 2 or 3 replications within each of the centres is likely to be sufficient for yield assessment. The long-established practice of testing varieties at representative centres for several seasons is thus amply justified. The results now reported emphasize that when seed or facilities are limited, it is more important to cover the main environmental conditions than to achieve high accuracy in individual trials.

Similar conclusions may well apply to other types of agricultural investigation for which it might also be profitable to examine the variation between centres and seasons under British conditions.

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CONFERENCES BIG OR SMALL?

MORE science means more information, in the form of books, journals and conferences. No scientist needs to be reminded of this. It was estimated recently that to keep up with all the current work a physiologist would have to read nearly four hundred papers a day. Sir George Thomson has even gone so far as to suggest that it is the impossibility of absorbing the necessary information that will ultimately halt scientific progress. Communication is therefore a subject that we cannot afford to neglect. The purposes of books and journals are, or should be, obvious; but the functions of conferences are more complicated.

Scientific conferences grew as an answer to the problem of assimilating in a reasonable time the vast quantities of information scattered throughout the journals. They do provide an answer—the meeting together of workers in similar fields and the collection of their ideas are the obvious advantages. But is it the best answer? The basis of a conference is the presentation of papers but why bother to read them? The distribution of all the papers to all the members would serve the same purpose. It would even have advantages. It is much easier to read a foreign language than to follow it by ear, and it is difficult to grasp a complicated argument at a single hearing. In fact, something of the sort often happens when preprints are issued or when the proceedings are published in book form afterwards.

The preprint was introduced to save time. If all his audience are armed with his complete paper, there is no need for a speaker to give more than a summary. This frees time for discussion or, more frequently, more papers. But the possibility of discussion is the great advantage of conferences. Questions can be asked and suggestions made in print, but it is a very slow business and what takes months in the journals may take only minutes in the conference room. Conferences have other advantages, of course. Meeting other workers in one's own field is an obvious one. But this is really an extension of the main advantage—one meets in order to discuss.

Conferences are getting bigger. The Fourth International Congress of Biochemistry held in Vienna last September was attended by nearly five thousand scientists and the published proceedings run to fifteen volumes. Two thousand one hundred papers were submitted at the Second Geneva Conference on the Peaceful Uses of Atomic Energy, and there are thirty three volumes of proceedings. These two examples are exceptions, but they do represent a real trend, at least in international conferences. The question is whether this trend is a good thing. Are bigger conferences necessarily better? In particular, are they better with regard to the advantages that conferences have over other methods of communication? The answer is, surely, no. It has already been pointed out that the great asset of conferences is discussion, and the value of a discussion is usually inversely proportional to the size of the

group. There is such a press of papers that it is difficult to find time to read them, let alone discuss them. Furthermore most big conferences have to split up into sections which meet at the same time, and so it is impossible for an active member of a section to get any idea of the conference as a whole. 'Interdisciplinary cross fertilization', as it is unhappily called, does not take place.

Fortunately, many people are aware of these points, in particular, some of the research foundations, such as the Ciba Foundation in Britain which recently celebrated its tenth anniversary, and the Josiah Macy Jr. Foundation in the United States, deserve mention. Both these organizations sponsor symposia. Membership of a symposium is restricted to a small number of experts, so that profitable discussions are possible. Afterwards, the complete proceedings are published. It is a pity that there are so few institutions of this type interested in the physical sciences, most of them are biological, with a bias towards medicine.

The Gordon Research Conferences, many of which are held every year in the United States, illustrate yet another approach. They cover both the physical and biological sciences, and the membership of any one conference is restricted to a hundred. They are 'intended as a means of disseminating information which otherwise would not be realized through the normal channels of publication and scientific meetings'. They differ from other conferences in that nothing is published, and no information may be disclosed without the speaker's consent. At first this may seem odd in connexion with a conference "intended as a means of disseminating scientific information", but it enables those present to speculate freely without feeling that hundreds of critical readers will later censure them for making suggestions not backed up by adequate evidence. Speculation is a vital part of science, so it is desirable that there should be some means whereby people can do so together as well as alone. A series of meetings of the Gordon type has recently been established in Britain. The first Miller conference*, on radiation chemistry was held at Portmerrion in North Wales during April 20-24 and was a success. The conferences have been named after the late Dr N. Miller, of the University of Edinburgh, who did much to help establish them.

Big conferences are obviously here to stay. Many important aspects of them have not been discussed here, such as their significance as social events which promote international understanding, though it is to be hoped that the tendency to compete for national prestige, evident at some recent conferences, will not have the opposite effect. Nevertheless the small informal gathering, where ideas are exchanged as freely as facts, should not be neglected.

* Further information about the Miller conferences can be obtained from the chairman of the next meeting, which is to be held in 1961—Prof. F. S. Dainton, School of Chemistry, The University, Leeds 2.

HISTORY OF COSMOLOGY

Le Système du Monde

Histoire des Doctrines Cosmologiques de Platon à Copernic, Tome 10 Par Prof Pierre Duhem Pp 528 (Paris Hermann, 1959) n p

THE great work of the late French historian of science, Pierre Duhem, on the history of cosmology from Plato to Copernicus, is now completed by the publication of Volumes 9 and 10. It will be remembered that only the first five volumes were published during the author's life in the years 1914-17. At the time there was no possibility of publishing the extant material for the remaining volumes, and it seemed that the historians of science would have to become resigned to the valuable work remaining a torso for ever. However, after the Second World War circumstances were ameliorated and so the rather rare situation could arise of the missing volumes appearing some forty years after the beginning of publication. On a previous occasion comment has been made upon the unavoidable drawback of the work becoming somewhat antiquated in the meantime. This, however, is only a slight disadvantage in comparison to the immense value to be attributed to Duhem's pioneering work, which forms the beginning of the modern interest in medieval natural science.

Of the new volumes, Volume 9 brings to completion the subject-matter of Volumes 7 and 8, mainly consisting of the Parisian physics of the fourteenth century. First, the theory of the tides is dealt with from William of Auvergne to Pierre d'Ailly, then follows the equilibrium of the Earth and the oceans, with an introduction to the idea of their centre of gravity of Greek and Arab commentators of Aristotle, the origins of geology, including the theory of the small movements of the Earth. Hereafter the important question of the rotation of the Earth is tackled, the discussion of which was inaugurated by Duhem in 1909 in his epoch-making article on Oresme as a precursor of Copernicus, in the *Revue Générale des Sciences*. This article is substantially reproduced here and is supplemented by a discussion of the views of that other great figure of medieval physics, Jean Buridan. The author repeats his former conclusion that the daily rotation of the Earth was duly discussed in the Parisian school of the fourteenth century and that in particular Oresme deserves credit for his anticipation of the ideas of Copernicus on the Earth's daily rotation. In the final chapter of Volume 9 the problems of the plurality of worlds in connexion with the possibility of the vacuum and with the variability of gravity with the distance to the centre of the world are discussed.

In Volume 10 it becomes quite clear that it is not offered to us as a complete work, but only as a compilation of fragments in greater or lesser degree of perfection. The title of the whole of Volume 10 was not chosen by Duhem himself but was added by the editors, who hoped to sum up by it the principal contents of the volume. It announces a treatment of fifteenth-century cosmology and of the schools and universities in which it was developed. The decline of the University of Paris in the first half of the fifteenth century is dealt with rather elaborately, but the treatment of the subsequent developments leaves something to be desired. The German universities of that century receive full attention, but the English and Italian ones remain somewhat in the background, although Paul of Venice (Paolo Nicoletti) has an extensive chapter

devoted to him. This is also the case of Nicolaus of Cusa, the German cardinal, whose ideas are expounded at length. Finally, there are chapters on the Viennese astronomer Purbach and Regiomontanus and on the fourteenth-century humanists Petrarca and L. Bruni, which, however, are far from dealing exhaustively with the relation of humanism to medieval philosophy.

The treatment is everywhere extremely clear and interesting, one regrets that the work was not completed by its author. E J DIJKSTERHUIS

RUSSIAN VIEW OF SPACE FLIGHT

Sputniks and After

By Karl Gilzin. Translated from the Russian by Pauline Rose. Pp 285+25 photographs (London Macdonald and Co (Publishers), Ltd, 1959) 21s net

KARL GILZIN, a lecturer at the Moscow Aviation Institute, gives here a popular account of the past, present and probable future of space flight. Brooding over the whole story is the spirit of Tsiolkovski, the 'father of astronautics', who foresaw in remarkable detail the techniques likely to prove most efficacious in space flight. Since British and American authors have scarcely done justice to this Russian pioneer, the eulogy in the present book will do no harm. It also serves to remind us how the Russians have created, around the name of Tsiolkovski as patron saint, a mystique of space flight which is unparalleled in the Western world. It is no accident that experiments with animals, a necessary prelude to manned space travel, have figured so largely in the Soviet rocket and satellite programmes, or that *Sputnik 1* was launched within a month of the centenary of Tsiolkovski's birth.

The subject-matter of the book can be divided into three sections, past, present and future. The first section expounds the principles of space flight and traces the development of rockets and other power units in fair detail, though with a pro Russian bias. Tsiolkovski figures in the history of the gas-turbine engine, but not Whittle. The second section, covering present developments, though it includes a good chapter on the atmosphere, is disappointing in detail: there is no new information on the Sputniks, and the meagre report of the results obtained from them (which appears to date from mid-1958) is, a little surprisingly, based largely on British radio observations reported in *Nature*. The last section is an excellent preview of space flight, which ends with an imaginary but realistic excursion to the Moon by a party of school-children.

The material is presented in an easy, expert manner and the book is well illustrated and technically reliable. There are a number of lapses and inconsistencies, however. For example, the rocket of *Sputnik 1* is on p 117 said to have completed its 900th circuit of the Earth on December 2, 1957, when it really came down on the previous day, as is implied on p 131, on p 139 Jodrell Bank is described as an Irish radio observatory, a peccadillo startling to parochial ears, and the last paragraph on p 102 does not follow from the one before.

The translation is competent, but too overloaded with abstract nouns to be called graceful, and the phraseology sometimes conflicts with established usage: 'thrust' sometimes masquerades as 'traction', and 'solid fuel' as 'dry fuel'. D G KING-HELE

VAPOUR-LIQUID EQUILIBRIUM TREATISE

Vapour-Liquid Equilibrium

By Eduard Hala, Jiří Pick, Vojtěch Fried and Otakar Vilim. Translated by G. Standart (Czechoslovak Academy of Sciences Monographs and Source Material Chemical Section) Pp xvii+402 (London and New York Pergamon Press, 1958) 90s. net.

THE authors have made an effort to produce a comprehensive treatise on all aspects of vapour-liquid equilibrium, and certainly this is the most complete work yet to appear on the subject. It is divided into three parts, covering respectively the thermodynamic basis for correlation of data, experimental techniques of measurement, and an up-to-date survey of the relevant literature. The theoretical basis of the subject is developed in four chapters, starting with general thermodynamic relations in the first chapter, introducing the concept of ideal solutions in the second, and finally dealing with real solutions in the third and fourth.

Although the content of Chapter 1 may be found in any text-book on thermodynamics, and will be considered elementary by most readers, it is useful to have such a summary of the relations to hand, and it also serves to introduce the symbols and nomenclature—we learn, for example, that the Gibbs free energy is to be referred to as the 'free enthalpy'. It is a pity that the chapter should be marred by the common student's error made in passing from expressions involving 'number of moles' to those involving 'mole fraction'. In spite of the warning at the foot of page 10, the authors themselves fall into the trap on page 11 in obtaining equation I-47. The same error is made later in the first expression of equation I-255 on page 70, while equation I-257 on the same page is not deducible from equation I-148, but rather follows directly from equation I-147. In a similar way, equation I-141 on page 38 is in fact correct, and is not obtained, as stated, from the erroneous equation I-47. In all these cases, confusion would be avoided if the complete set of variables involved were given for each equation, rather than simply indicating the constancy of pressure and temperature. In Chapter 2, the properties of ideal solutions are adequately dealt with, and Chapter 3 introduces the concepts of activity and activity coefficient, and develops the relevant thermodynamic relations. The major part of Chapter 4 is concerned with integrations of the Gibbs-Duhem equation, and this is probably the most valuable section of the whole book. The treatment is systematized in the way first presented by Wohl, and forms an excellent summary of the many empirical relations now existing, including those due to Van Laar, Margules, Scatchard and Hamer, and Redlich and Kister. It is a pity that Wohl's own contribution is represented only by his earlier work, and that no mention is made of his 1953 paper. The value of this section is enhanced by the inclusion of many worked numerical examples of the application of these equations, together with comparisons of the results with direct experimental data, as well as a summarized presentation of all the relations in tabular form. Thus although the authors have wisely refrained from attempting a general assessment of the relative values of these relations, they have made it easy for the reader to make his own comparisons for any specific case.

The authors show good practical sense in following up this survey with a discussion of methods for deriving complete equilibrium data from indirect measurements, again fully supported by numerical examples. Here one could perhaps wish for a little more discussion on the relative suitability of the methods for numerical solution of these particular differential equations, since two methods have been introduced somewhat arbitrarily in the examples. Some discussion of the magnitude of the errors involved in the different methods would also be welcome. On reading this chapter one is left with the impression that, since the Gibbs-Duhem equation is obeyed, all the correlations are at least thermodynamically consistent. The limitation of the Gibbs-Duhem equation, as an expression of variation with composition of a single phase at constant pressure and temperature, is explicitly stated in the earlier chapters. However, as is frequently done, it is later assumed in some applications to hold along the equilibrium line, which for binary mixtures must involve variation of either temperature or pressure. It is only fair to the authors to say that in each case this assumption is noted but its significance and the approximation involved are rarely sufficiently stressed, and are more often glossed over, as in the case of the derivation of the expressions for limiting relative volatilities on page 45.

In view of the detailed treatment accorded to these integrations of the Gibbs-Duhem equation, it is disappointing to find only a cursory treatment of alternative methods of correlating equilibrium data. The effect of non-ideality of the vapour phase is disposed of in less than eight pages, which also contain the only reference to equilibrium ratios, or K values. Surely the Benedict equation, and all that arises from it, is worth more than a passing reference? The law of corresponding states is illustrated by two numerical examples, but the treatment is wholly inadequate. The reader will find no mention of the 'convergence pressure' concept, nor indeed is any indication given of the difficulties arising in correlating equilibrium data when the temperature is above the critical temperature of one or more of the components. Here the absence of vapour pressure makes impossible the application of the Gibbs-Duhem integrations, or even the ideal solution laws.

Part 3 is concerned with laboratory techniques, and should be considered as a review of a wide range of techniques rather than as a detailed discussion and assessment of the different methods. The five chapters cover criteria of purity, temperature and pressure measurement, vapour pressure and vapour-liquid equilibrium determinations. In each case a good variety of techniques is presented and although there is seldom an adequate assessment of precision and the treatment is sometimes superficial—for example, the dead weight piston pressure-balance is dealt with in six lines—there are usually sufficient references to the literature to enable one to obtain all the information required.

The authors state in their preface that they have deliberately avoided description of current laboratory equipment, and on these grounds have excluded thermometers. This does not seem logical for a book which includes chapters on measurement of temperature and pressure and discusses manostats in some detail. One cannot deny the usefulness of these in directing attention to points which so many workers overlook and in view of the authoritative treatment

establishing its aims and staking its frontiers. Embryology, in the strict sense, is no longer granted automatic precedence, nor is morphogenesis the key problem. Events in any part of the ontogenetic cycle are seen in terms of the contribution they can make to an understanding of the whole.

These meetings were thus, if anything, even less restricted in scope than might be suggested by the titles of the volumes in which they are reported. Though there is remarkably little repetition of one in another, between them they touch upon a substantial fraction of all experimental biology. However, it was not intended that the series should be comprehensive and there are, inevitably, many gaps, some premeditated and others contingent upon the informal nature of the discussions. This is not a fault, but it does mean that some of the reports will be of most value to those already familiar with the background to the themes discussed. This is true, for example, of "Cytodifferentiation" and of "Environmental Influences on Prenatal Development", both of which contain stimulating presentations of recently discovered facts and recently developed ideas. On the other hand, the more formal reviews in "Regeneration in Vertebrates" provide excellent and comprehensive surveys of a few selected experimental situations.

These seven volumes do indeed vary greatly in character, partly because the meetings themselves took different forms and partly by editorial decision. At the one extreme (for example, in "Embryonic Nutrition") we are offered an orthodox sequence of papers and discussions of them, with a complete list of the authorities referred to. At the other (in "Immunology and Development") the identities of discussion leaders, participants, and absent authorities are not defined and their work is merged into a sort of collective stream-of-consciousness report. Both volumes are successful, but their usefulness is clearly of different kinds.

Formal considerations apart, it must be confessed that the series, viewed as a whole, lacks the intellectual coherence that the "unity of subject matter" claimed for it by its organizer, Paul Weiss, might lead one to expect. We have not yet a continuous spectrum of problems in developmental biology. But these meetings certainly reflected real progress towards a consciously unified approach to developmental processes, a progress that will be further stimulated by the publication of their proceedings.

D R NEWTH

THE HETEROGENEITY OF HUMAN HÆMOGLOBIN

Abnormal Hæmoglobins

A Symposium Organized by the Council for International Organizations of Medical Sciences. Edited by J H P Jonxis and J F Delafresnaye. Pp ix+427 (Oxford: Blackwell Scientific Publications, Springfield, Ill: Charles C Thomas, 1959) 45s net.

THIS volume contains the papers and discussions of a symposium on abnormal hæmoglobins held in Istanbul in September 1957. Since Pauling's demonstration in 1949 of an electrophoretically distinct hæmoglobin in sickle-cell anaemia, the dis-

covery of new variants has proceeded with increasing momentum so that, at present, 15 hæmoglobins have been designated by letters of the alphabet. Four sub-fractions of normal adult human hæmoglobins, A_1 , A_2 , A_3 , A_4 (A_2'), and one normal foetal hæmoglobin are now known. The complexity of the situation is illustrated by reports of a further seven variants which are given provisional names derived from the place of discovery, in order to avoid confusion of the nomenclature.

The interest in abnormal hæmoglobins is spreading throughout the world, and involves many scientific disciplines. It is this widespread multidisciplinary interest which has brought the subject within the ambit of the Council for International Organizations of Medical Sciences. Participants in the symposium included eminent workers of international repute, and others who have become recognized for their work in their own geographical localities. The papers have been grouped under two main headings: "Biological Considerations" and the "Geography of Hæmoglobins". Itano (United States) opens the symposium with an introductory discourse on the "Genetic and Physical Factors in the Heterogeneity of Hæmoglobin". The identification of human hæmoglobins is described by Huisman (Holland), though practical details of technique are not given. This paper is supplemented by Cabannes and Portier (Algiers) with a description of their electrophoretic experiences of the newly discovered hæmoglobins. Two groups of workers using two different techniques bring forth evidence that the alkali-resistant hæmoglobin of thalassaemia is not foetal hæmoglobin—a view not held by the majority of authorities. Derrion (France) bases his evidence on solubility experiments, while Dianoco and Castay (Tunis) describe immunological differences using a complement fixation test for the detection of hæmoglobin antibodies. Clinical and hæmatological aspects of the various hæmoglobin syndromes are described by Zuelzler (United States). Chapters on foetal and sickle cell hæmoglobin are provided by Jonxis (Holland) and Vandepitte (Belgian Congo) respectively. Fessas (Greece) described the alterations of the hæmoglobin pattern in thalassaemia. The first section is concluded by chapters on the genetic aspects by Neel (United States) and on the hæmoglobin types of animals by Huisman (Holland) and his colleagues.

In the part on geography, the following authors have dealt with the position of abnormal hæmoglobins in their region: Aksoy (Turkey), Pouya (Iran), Silvestrom and Bianco (Italy), Fessas (Greece), Vandepitte (Belgian Congo), Portier, Cabannes and Duzer (Algiers), Edington (Ghana), Chatterjee (India), de Silva, Jonxis and Wickramasinghe (Ceylon), Na Nakorn (Thailand), and Lie Injo Luan Eng (Indonesia). Prof Jonxis contributes some interesting comparisons of the frequencies of the sickle cell and hæmoglobin C traits in the Dutch colonies of Curacao and Surinam. Two chapters by Lehmann (United Kingdom) put the subject of hæmoglobin variants in their proper geographical perspective.

The nomenclature of the newer hæmoglobin variants $H-N$ is given in an appendix, together with the studies required before a new hæmoglobin can be designated.

This volume will provide a useful account of the abnormal hæmoglobin situation up to early 1958, whether the reader be a hæmatologist, physician, biochemist, geneticist or anthropologist.

J A M AGER

A Handbook of Lattice Spacings and Structures of Metals and Alloys

By Dr W B Pearson (International Series of Monographs on Metal Physics and Physical Metallurgy, Vol 4) Pp x+1044 (London and New York Pergamon Press, 1958) 262s 6d

THIS is a formidable work of more than 1,000 pages. It is divided into two parts. The first part is an account of the methods used in the accurate determination of lattice spacings and crystal structures, and of the significance of the results in connection with the location of phase boundaries, the application of electron theory to metals and alloys, and the effect of magnetic properties on lattice spacings. A brief mention is also made of the role of lattice parameter measurements in miscellaneous fields such as thermal expansion and superconductivity.

The second part occupies most of the book, and consists of a collection of crystallographic data. This includes the lattice spacings and crystal structures of the elements, of binary, ternary and quaternary alloys, and of borides, hydrides, carbides, nitrides and oxides. The largest section in this part is an alphabetical index of the work on metals and alloys. For each alloy system a brief description of the equilibrium diagram is given, together with a critical assessment of the various lattice parameters obtained by different workers. Sufficient practical information on the methods of obtaining the data is given to make it unnecessary in most cases to refer to the original papers. References are included up to 1957.

The labour involved in producing this work must have been considerable, and the author is to be congratulated on the result. It will prove to be of great value to the research worker, and should be in the library of all people who are interested in the physics of metals. The book is unfortunately very expensive. J A CATTERALL

The Birds of Sydney (County of Cumberland), New South Wales

By K A Hindwood and A R McGill Pp iii+128+10 plates (Sydney: Royal Zoological Society of New South Wales, 1958) 12s 6d

THE Sydney Basin is essentially Triassic in origin and was formed by successive lake deposits overlying coal measures of Permian age. Above the coal is red shale, and above this there lies a tough sandstone surmounted by a final capping of grey shale. Here and there erosion has bared the underlying structures; in fact, the city of Sydney is built on and partly of Hawkesbury sandstone. Each geological type supports its own characteristic flora and, correspondingly, fauna. The red shale of the deep valleys has attracted an Indo-Malayan vegetation, as well as a fauna partly of northern affinity. The flowering heaths of the sandstone support many honey-eating animals and others, and in the open forests of the surviving top-shale is found a fauna which is often closer allied to that of the dry interior than to the animals in the cool valleys nearby.

Messrs Hindwood and McGill have compiled a useful list of the 377 species of birds—both land and marine—native to this zoologically fascinating region. Under each name are five or six lines, mentioning salient points of description and the localities in which each species can be found. The compilation, therefore, remains of strictly local interest, and this is a pity. The area abounds with problems relating

to the wider aspects of avian zoogeography, ecology and dispersal and it is regrettable that no attempt has been made to get to grips with such matters. The book is illustrated with a map of the area and excellent photographs of about thirty species.

A J MARSHALL

Food for Survival after a Disaster

By Dr R C Hutchinson Pp ix+90+6 plates (Carlton, N 3 Melbourne University Press, London Cambridge University Press, 1959) 13s 6d

THE disaster envisaged in the title is that of shipwreck forced plane landing, or vehicle breakdown in a desert area, rather than the large scale disaster of modern war, and the information given is primarily that which would be of the greatest value to individuals or small groups of survivors trying to keep alive under adverse conditions in strange surroundings. In addition to this, however, the book also contains much pertinent detail on de salting kuts and on the selection and packaging of survival rations which would be of great use to those planning scientific expeditions and to commercial shipping and airline companies who may not have access to pamphlets prepared for the Armed Forces.

The author claims to speak from personal experience as "a survivor on both land and sea", and has certainly condensed a wealth of material into a very small space and presented it in a most readable form. The chapter on "Possible Supplementary Sources of Food" is a whole lesson in ecology in itself and one that should stimulate the interest of any school boy. Decidedly a book to be recommended to all inveterate travellers: the day might well come when they would owe their lives to what they had learnt from its pages.

M W GRANT

From Microphone to Ear

Modern Sound Recording and Reproduction Technique By G Slot Second, revised and enlarged edition. Pp ix+258 (Eindhoven Philips Technical Library London Cleaver Hume Press, Ltd 1959) 21s

THIS book might well be entitled *Gramophones, from A to Z*, for it seems to contain everything, even (p 82) how to remove gin spots from your records! It is obviously written by an enthusiast for enthusiasts, and its quality has been well preserved in the excellent translation. Many an amateur constructor, "hi fi" or stereophony fan, or even the intelligent listener with a curiosity to learn more of what gets the music on to the records and out of the loudspeaker, will find plenty of reading here. Recording techniques, studio work, tracking theory, loudspeaker dynamics, cabinet design, motor construction, care of records, negative feedback, tape recorders, sound effects, automatic record changers, needles hum—the lot.

With this enormous coverage the treatment of much of the material will seem shallow to professionals and it would be easy to be critical, but purposeless. The book is informative, practical, well written and illustrated by many simple line diagrams and photographs. It makes a welcome and timely appearance in these days of such increased demand for better musical recording and reproduction. Many enthusiasts want to assess the merits of this technique and that, or to judge the quality of their equipment, or to improve it: this book will help them.

COLIN CHERRY

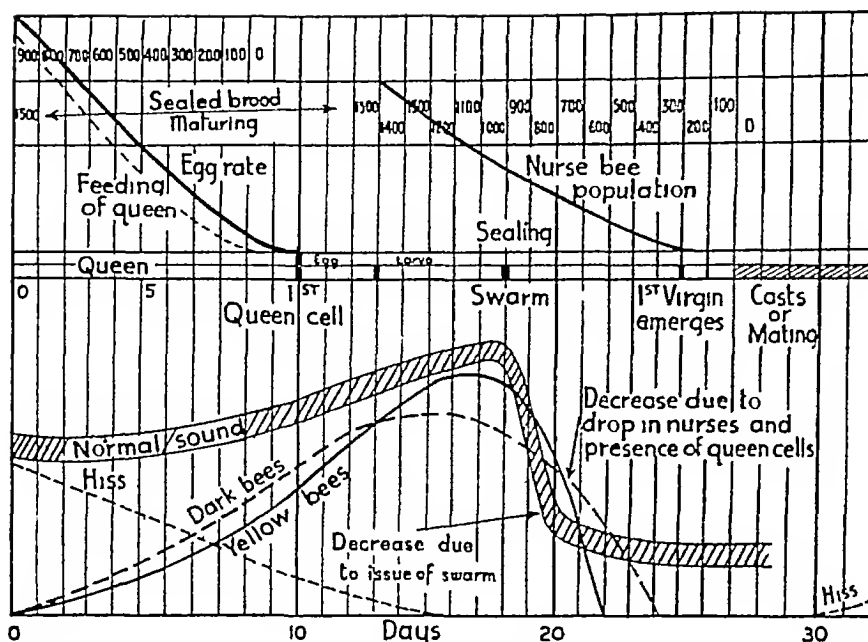


Fig 3 Swarm cycle

warble. Furthermore, the warble 'radiates' from the queen, which is usually at the top of the brood-box, away from the entrance.

Disturbance was eliminated, and the relative volume of the warble increased by placing a microphone permanently inside the hive at the top, but the adverse conditions of heat and humidity destroyed the (crystal) microphone fairly quickly, and the running cost of one microphone per hive per season was excessive.

A scheme which has proved successful and economical utilizes a hole in the back of the brood-box at the

top, with an internal screen of perforated zinc, and plugged with a rubber bung. This bung is removed and the microphone, mounted in an identical bung, plugged in. This third plan also removes a disadvantage of the second, namely, the variability of microphones, especially after some weeks in the hive.

Headphones, of the familiar stethophone pattern, are used as a detector, but later development may permit the use of a visual indicator, at an increased cost. An automatic alarm system is also possible for use in large centralized apiaries.

The 'Apidictor' was primarily visualized as a swarm predictor, for which it has obvious economic advantages, but it has a great range of other uses. It removes almost completely the uncertainty of queen introduction and queen cell acceptance, it detects abnormalities such as queen failure, that is,

drone breeding, and it enables an accurate check to be made of the health of the colony in winter, even during heavy frost.

I wish to acknowledge the enthusiastic and skilled co-operation of many friends, but particularly of Mr E F Birch of Horeford, who has been working with me since 1951, and of Mr C B Dennis of Harrow, who has co-operated with me for the past three years. I also wish to thank Messrs Wayne Kerr Laboratories of Surrey, for invaluable technical assistance.

¹ British Patent No. 720,007 (1958).

SEARCHING FOR INTERSTELLAR COMMUNICATIONS

By GIUSEPPE COCCONI* and PHILIP MORRISON†

Cornell University, Ithaca, New York

NO theories yet exist which enable a reliable estimate of the probabilities of (1) planet formation, (2) origin of life, (3) evolution of societies possessing advanced scientific capabilities. In the absence of such theories, our environment suggests that stars of the main sequence with a lifetime of many billions of years can possess planets, that of a small set of such planets two (Earth and very probably Mars) support life, that life on one such planet includes a society recently capable of considerable scientific investigation. The lifetime of such societies is not known, but it seems unwarranted to deny that among such societies some might maintain themselves for times very long compared to the time of human history, perhaps for times comparable with geological time. It follows, then, that near some star rather like the Sun there are civilizations with scientific interests and with technical possibilities much greater than those now available to us.

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To the beings of such a society, our Sun must appear as a likely site for the evolution of a new society. It is highly probable that for a long time they will have been expecting the development of science near the Sun. We shall assume that long ago they established a channel of communication that would one day become known to us, and that they look forward patiently to the answering signals from the Sun which would make known to them that a new society has entered the community of intelligence. What sort of a channel would it be?

The Optimum Channel

Interstellar communication across the galactic plasma without dispersion in direction and flight-time is practical, so far as we know, only with electromagnetic waves.

Since the object of those who operate the source is to find a newly evolved society, we may presume that the channel used will be one that places a minimum burden of frequency and angular discrimi-

nation on the detector. Moreover, the channel must not be highly attenuated in space or in the Earth's atmosphere. Radio frequencies below ~ 1 Mc/s, and all frequencies higher than molecular absorption lines near 30,000 Mc/s, up to cosmic ray gamma energies are suspect of absorption in planetary atmospheres. The band widths which seem physically possible in the near visible or gamma-ray domains demand either very great power at the source or very complicated techniques. The wide radio band from, say, 1 Mc to 10^4 Mc/s, remains as the rational choice.

In the radio region, the source must compete with two backgrounds: (1) the emission of its own local star (we assume that the detector's angular resolution is unable to separate source from star since the source is likely to lie within a second of arc of its nearby star); (2) the galactic emission along the line of sight.

Let us examine the frequency dependence of these backgrounds. A star similar to the quiet Sun would emit a power which produces at a distance R (in metres) a flux of

$$10^{-15} f^2 / R^2 \quad \text{W m}^{-2} (\text{c/s})^{-1}$$

If this flux is detected by a mirror of diameter l_d the received power is the above flux multiplied by l_d^2 .

The more or less isotropic part of the galactic background yields a received power equal to

$$\left(\frac{10^{-15}}{f} \right) \left(\frac{\lambda}{l_d} \right)^2 (l_d)^2 \quad \text{W (c/s)}^{-1}$$

where the first factor arises from the spectrum of the galactic continuum, the second from the angular resolution, and the third from the area of the detector. Thus a minimum in spurious background is defined by equating these two terms. The minimum lies at

$$f_{\min} \approx 10^4 \left(\frac{R}{l_d} \right)^{2/3} \text{ c/s}$$

With $R \approx 10$ light years $\approx 10^{17}$ m. and $l_d \approx 10^2$ m. $f_{\min} \approx 10^{16}$ c/s.

The source is likely to emit in the region of this broad minimum.

At what frequency shall we look? A long spectrum search for a weak signal of unknown frequency is difficult. But, just in the most favoured radio region there lies a unique, objective standard of frequency which must be known to every observer in the universe: the outstanding radio emission line at 1,420 Mc/s ($\lambda = 21$ cm) of neutral hydrogen. It is reasonable to expect that sensitive receivers for this frequency will be made at an early stage of the development of radio astronomy. That would be the expectation of the operators of the assumed source and the present state of terrestrial instruments indeed justifies the expectation. Therefore we think it most promising to search in the neighbourhood of 1,420 Mc/s.

Power Demands of the Source

The galactic background around the 21-cm. line amounts to:

$$\frac{dW_b}{dS d\Omega df} \approx 10^{-11} \text{ W m}^{-2} \text{ ster}^{-1} (\text{c/s})^{-1}$$

for about two thirds of the directions in the sky. In the directions near the plane of the galaxy there is a background up to forty times higher. It is thus economical to examine first those nearby stars which are in directions far from the galactic plane.

If at the source a mirror is used l_s metres in diameter, then the power required for it to generate in our detector a signal as large as the galactic background is

$$\frac{dW_s}{df} = \frac{dW_b}{dS d\Omega df} \left(\frac{\lambda}{l_s} \right)^2 \left(\frac{\lambda}{l_d} \right)^2 R^2 = 10^{-11} R^2 / l_s^2 l_d^2 \quad \text{W (c/s)}^{-1}$$

For source and receiver with mirrors like those at Jodrell Bank ($l_s \approx 80$ m), and for a distance $R \approx 10$ light years, the power at the source required is $10^3 \text{ W (c/s)}^{-1}$, which would tax our present technical possibilities. However if the size of the two mirrors is that of the telescope already planned by the U.S. Naval Research Laboratory ($l_s \approx 200$ m), the power needed is a factor of 40 lower, which would fall within even our limited capabilities.

We have assumed that the source is beaming towards all the sun-like stars in its galactic neighbourhood. The support of say, 100 different beams of the kind we have described does not seem an impossible burden on a society more advanced than our own. (Upon detecting one signal, even we would quickly establish many search beams.) We can then hope to see a beam toward us from any suitable star within some tens of light years.

Signal Location and Band-Width

In all directions outside the plane of the galaxy the 21-cm. emission line does not emerge from the general background. For stars in directions far from the galactic plane search should then be made around that wave length. However, the unknown Doppler shifts which arise from the motion of unseen planets suggest that the observed emission might be shifted up or down from the natural co-moving atomic frequency by $\pm \sim 300$ kc/s (± 100 km s $^{-1}$). Closer to the galactic plane, where the 21 cm. line is strong, the source frequency would presumably move off to the wing of the natural line background as observed from the direction of the Sun.

So far as the duration of the scanning is concerned the receiver band width appears to be unimportant. The usual radiometer relation for fluctuations in the background applies here, that is:

$$\frac{\Delta B}{B} \propto \sqrt{\frac{1}{\Delta f \Delta t}}$$

where Δf is the band width of the detector and τ the time constant of the post-detection recording equipment. On the other hand, the background accepted by the receiver is

$$B = \frac{dW_b}{df} \Delta f \quad \text{and} \quad \propto \frac{\Delta f}{(\Delta B)^2}$$

If we set ΔB equal to some fixed value then the search time T required to examine the band F within which we postulated the signal to lie is given by

$$T = \frac{F\tau}{\Delta f} \propto \frac{F}{(\Delta B)^2}$$

independent of receiver band width Δf .

Of course, the smaller the band width chosen the weaker the signal which can be detected provided $\Delta f \gg \Delta f_s$. It looks reasonable for a first effort to choose a band width Δf normal in 21 cm. practice but an integration time τ longer than usual. A star

settings should cover the frequency range F using an integration time of minutes or hours

Nature of the Signal and Possible Sources

No guesswork here is as good as finding the signal. We expect that the signal will be pulse-modulated with a speed not very fast or very slow compared to a second, on grounds of band-width and of rotations. A message is likely to continue for a time measured in years, since no answer can return in any event for some ten years. It will then repeat, from the beginning. Possibly it will contain different types of signals alternating throughout the years. For indisputable identification as an artificial signal, one signal might contain, for example, a sequence of small prime numbers of pulses, or simple arithmetical sums.

The first effort should be devoted to examining the closest likely stars. Among the stars within 15 light years, seven have luminosity and lifetime similar to those of our Sun. Four of these lie in the directions of low background. They are τ Ceti, θ , Eridani,

ϵ Eridani, and ϵ Indi. All these happen to have southern declinations. Three others, α Centauri, 70 Ophiucus and 61 Cygni, lie near the galactic plane and therefore stand against higher backgrounds. There are about a hundred stars of the appropriate luminosity among the stars of known spectral type within some fifty light years. All main-sequence dwarfs between perhaps G0 and K2 with visual magnitudes less than about +6 are candidates.

The reader may seek to consign these speculations wholly to the domain of science-fiction. We submit, rather, that the foregoing line of argument demonstrates that the presence of interstellar signals is entirely consistent with all we now know, and that if signals are present the means of detecting them is now at hand. Few will deny the profound importance, practical and philosophical, which the detection of interstellar communications would have. We therefore feel that a discriminating search for signals deserves a considerable effort. The probability of success is difficult to estimate, but if we never search, the chance of success is zero.

METABOLIC CHANGES INDUCED IN MAMMALIAN ERYTHROCYTES BY WHOLE-BODY X-IRRADIATION

By PROF. D. A. RAPPOPORT and B. W. SEWELL

Department of Biochemistry, Baylor University College of Medicine, Houston, Texas

APPPLICATION of X-rays and radium in medicine, after their discovery during 1895-96, established their effectiveness in diagnosis and treatment of disease. Only somewhat later were the lethal and injurious properties of these penetrating rays recognized¹. Since then, large groups of men have become exposed more frequently to man-made radiation. These additional exposures to penetrating radiation have magnified the need for a reliable indicator of radiation-induced tissue damage. What is precisely needed is a simple and accurate indicator which would correlate biological damage with the radiation dose¹.

The requirements of an ideal biological radiation indicator are that (a) a tissue or tissue component should show changes over extended periods following whole-body irradiation, (b) this change can be quantitatively measured. It is also important that tissue samples should be available for intermittent sampling without injury to the subject and without alteration in the system under examination.

Choice of Erythrocytes

Certain generalizations can be used in considering this problem in order to initiate a working hypothesis. Tentatively it can be assumed that any radiation absorbed by cells will cause changes in the cell enzymes², but that the detection of these changes is dependent on (a) the sensitivity to radiation of a particular enzyme system under evaluation and (b) the degree of sensitivity of the analytical methods employed.

Implicit in the above specifications is the fact that the tissue must be incapable of extensive internal repair if it is to reflect any post-irradiation changes

This immediately eliminates tissues with large populations of mitotic cells and suggests erythrocytes as the tissue component of choice. In man the erythrocyte has a life-span of 110-120 days³, in the rat this span is 49-55 days⁴, in other mammals erythrocyte life spans are between these values⁵. Since mammalian erythrocytes are enucleated, no resyntheses of proteins can occur, and any radiation damage incurred on the enzyme-proteins, such as denaturation or rupture of peptide linkage, should be detectable by changes in enzymic reactions. This rationale suggests the erythrocyte enzymes for examination as a test system.

If the hypothesis is held that any absorbed radiation will affect enzymes in all cells, how is it that no enzymic changes have been observed in erythrocytes after moderate whole-body irradiation? This may be explained on the basis that up to the present time few erythrocyte enzymes have been tested after radiation treatment. Erythrocyte enzymology has now been more thoroughly explored^{6,7}. With the complete elucidation of glycolysis, the hexosemonophosphate shunt, the transketolase and transaldolase enzymes, and nucleoside phosphorylase in erythrocyte extracts, re-examination of the radiation effect on these enzyme systems is in order.

Nucleoside Metabolism

Investigators concerned with the preservation of blood have found that when inosine or adenosine is added to blood the integrity of the erythrocytes is maintained during storage and their survival following transfusion is improved⁸. This was attributed to the resynthesis of metabolites essential for erythrocyte integrity.

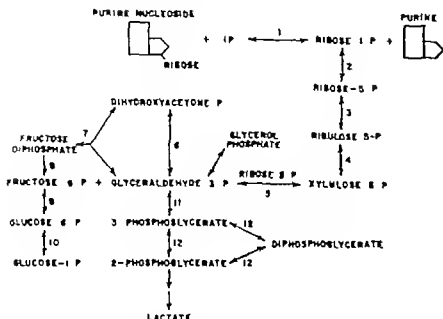


Fig. 1. Diagrammatic representation of the metabolic reactions of purine nucleosides in erythrocytes. The enzymes involved are: (1) nucleoside phosphorylase, (2) phosphoribomutase, (3) phosphoribosyltransferase, (4) phosphoketopentosephosphatase, (5) transketolase, (6) triosephosphate isomerase, (7) aldolase, (8) fructose diphosphatase, (9) phosphoglucose isomerase, (10) phosphoglucose mutase, (11) triosephosphate dehydrogenase, (12) phosphoglycerate kinase.

The enzymes responsible for nucleoside metabolism within the erythrocyte are in the soluble portion of the cell. The reactions which they catalyse are diagrammatically illustrated in Fig. 1. First, the nucleoside in presence of phosphate is converted to ribose 1-phosphate and a purine base by a nucleoside phosphorylase¹. Later, the pentose phosphate is transformed to a variety of phosphate esters via the actions of transketolase, transaldolase and the glycolytic enzymes².

When considering nucleoside metabolism in erythrocytes as a system for evaluation of X-ray effects it can be assumed that if any enzyme among the group of interdependent reactions is inhibited there will be an accumulation of substrate and a change in the yield of phosphate esters. Complex multiple enzyme systems, such as are involved in erythrocyte metabolism of nucleosides, have certain disadvantages as well as advantages in studies of radiation effects. The disadvantage in such systems is that it may be difficult to determine which particular enzyme was affected by the radiation. However, the advantage in using a multiple enzyme system is that this increases the opportunity of finding one or more enzymes sensitive to absorbed radiation.

Erythrocyte Turnover

In the studies on the enzymic changes at prolonged post-irradiation intervals, time of residence of the circulating erythrocyte is a major factor for consideration. This requires that the maximum post-irradiation time interval used for evaluation must be within the period when the irradiated erythrocyte population is not markedly altered. This can be calculated from the erythrocyte life-span.

Inbred strains of rats are convenient for radiological studies. The 'mean life-span' of rat erythrocytes as well as the 'half-clearance time' can be used to estimate changes in erythrocyte population. The 'mean life span' of an erythrocyte is the average interval of time any erythrocytes will remain in circulation; 'half-clearance time' is that time interval at which 50 per cent of the circulating erythrocytes will disappear from circulation. Bolohor and Harriss³ have recently reported the 'mean life

span' of the rat erythrocyte as 40-55 days. The 'half-clearance time' was determined as 20.7 ± 2.5 days.

Since these observations are based on the mean life span and half-clearance time of erythrocytes in the normal rats, it is important to know how these figures are altered in X-irradiated rats. Total body X-irradiation of rats in excess of 300 r causes complete inactivation of marrow and stops the extrusion of erythrocytes into circulation⁴. However, the life span and half-clearance time of the circulating erythrocytes remain relatively the same as in the unirradiated animals¹¹. There is evidence that random (non senescent) destruction of erythrocytes, which in the normal rat is approximately 0.48 per cent per day¹², is increased in the irradiated animals but the magnitude of this change is unknown¹¹.

Recognizing the prolonged inactivation of marrow after an X-ray dose of 300 r or higher, we see that the erythrocyte population will consist only of irradiated cells up to and even beyond a two week period, since no new cells are extruded by marrow during this time. However due to internal hemorrhages and other undefined factors, random non senescent loss of erythrocytes will be increased¹¹. This will cause a drop in the number of red cells; however, loss of plasma into tissue and dehydration due to vomiting and diarrhoea will tend to decrease plasma volume, hence there may be no net change in hematocrit values¹¹.

The above discussion can be summarized by the conclusion that following total body radiation with doses at and above 300 r the erythrocyte population remains relatively undiluted and the life span and half-clearance time remain approximately the same as in the unirradiated rat, with the exception that there is an increased random loss of erythrocytes which cannot be quantitatively evaluated at present.

It is tentatively concluded that the erythrocyte is a promising tissue component as an internal mammalian X-ray indicator, since (a) it has a wide variety of enzymes among which some may be sensitive to radiation, (b) it cannot replace altered enzyme proteins, (c) it has a long life-span even in irradiated animals, (d) it is accessible for repeated sampling.

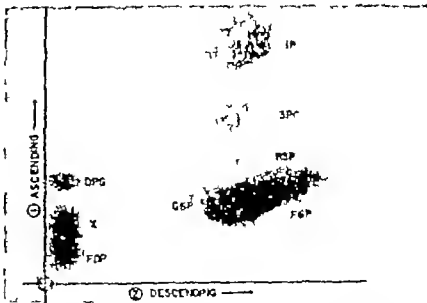


Fig. 2. Radioautogram of phosphate esters separated by two-dimensional paper chromatography: (1) ascending with ethyl acetate, acetic acid and water (8:3:1) and (2) descending with methyl ethyl ketone, methyl cellosolve, ammonia and water (7:2:0.7:2.3). R5P, ribose 5-phosphate; F6P, fructose 6-phosphate; G6P, glucose 6-phosphate; and others.

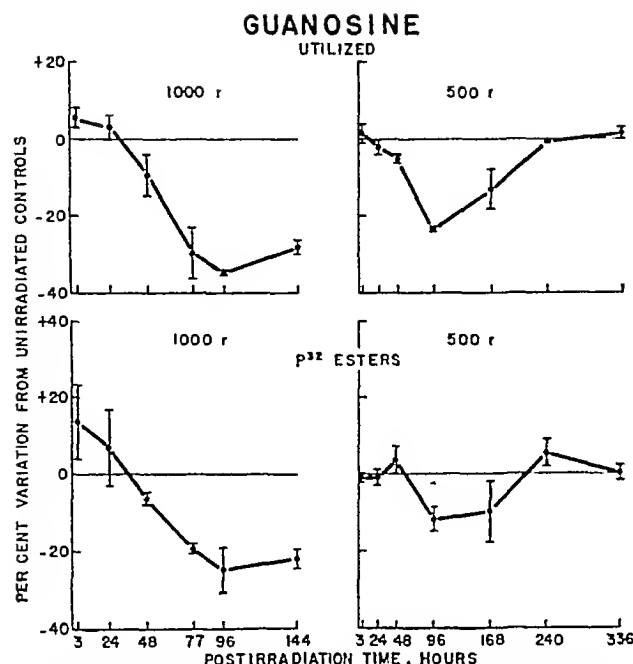


Fig 3 Comparative utilization of guanosine and formation of phosphate esters by rat erythrocyte extracts from rats irradiated with 1,000 and 500 r X-rays, respectively

The concepts discussed above were tested by measuring the changes in nucleoside metabolism by erythrocyte extracts from irradiated and unirradiated rats. Our results established that following 1,000 r whole-body X-irradiation the utilization of purine nucleosides was markedly depressed up to 144 hr after irradiation. Whole body irradiation of 500 r also depressed purine nucleoside metabolism for a period of 96 hr, when the metabolism began to increase and by 240 hr reached the level of substrate utilization by erythrocyte extracts from unirradiated controls. These results establish that erythrocyte enzymes are affected by moderate whole-body radiation and that these changes are detectable over a period from one to two weeks after irradiation.

Experimental Results

Erythrocytes from irradiated and unirradiated Sprague-Dawley rats were separated from white cells and plasma, lysed in water, dialysed overnight, extracts were then prepared by centrifugation. These extracts were incubated for 2 hr in *tris* buffer at pH 7.4 with either guanosine, inosine, or adenosine in the presence of inorganic phosphate labelled with phosphorus-32 and magnesium chloride. The detailed procedures and techniques will be described elsewhere¹². After incubation, the remaining purine nucleoside was analysed, total organic phosphate was determined, and the nature of the individual phosphate esters formed was established by means of paper chromatography¹³.

The reactions studied in these incubations are represented schematically in Fig 1 and the phosphate esters actually formed from guanosine and labelled inorganic phosphate are shown by the radioautogram in Fig 2. The same phosphate esters were also obtained from incubations of inosine and adenosine. Enzyme activity of erythrocyte extracts from rats irradiated with 1,000 r or 500 r to the whole body were compared with extracts from unirradiated controls. A decrease in substrate utilization and phosphate ester formation was observed. The results

of these experiments are illustrated in Figs 3, 4 and 5.

Erythrocyte extracts from rats treated with 1,000 r showed enhanced utilization of guanosine up to 24 hr after irradiation (Fig 3), but afterwards both guanosine utilization and phosphate ester formation decreased and at 96 hr reached a minimum value and remained at this level until the death of the animals in 7-8 days. Extracts from the rats treated with 500 r showed a decrease in guanosine utilization in 24 hr after irradiation and this reduced enzyme activity continued until the ninety-sixth hour (Fig 3, these are similar to the results with the 1,000 r extracts). Afterwards, the utilization of guanosine increased again and in 240 hr the level of substrate utilization was equal to that of the controls. Almost identical results were obtained with inosine, as shown in Fig 4. However, utilization of inosine by erythrocyte extracts from 500 r treated rats did not reach the level of inosine utilization by the controls until 336 hr after irradiation. Experiments with adenosine utilization showed results similar to those of inosine.

Significance of Results

These experiments establish that erythrocyte enzymes are affected by lethal (1,000 r) and sublethal (500 r) whole-body X-irradiation. Also the inhibitory effect of radiation persists for seven days or longer depending on the X-ray dose. Since the same enzymes are involved in the metabolism of guanosine, inosine or adenosine, one would expect radiation to influence these reactions in a similar way, as they did (Figs 3, 4 and 5).

Although nucleoside metabolism by the erythrocyte extracts from rats treated with 1,000 r was inhibited during their survival (7-8 days), the extracts from the rats treated with 500 r X-rays showed a marked inhibition for the initial interval up to 7 days after radiation. This was followed by the recovery of enzyme activity by 7-10 or 14 days post-irradiation. This recovery of activity suggests that with 500 r whole-body radiation the inhibition was not due to

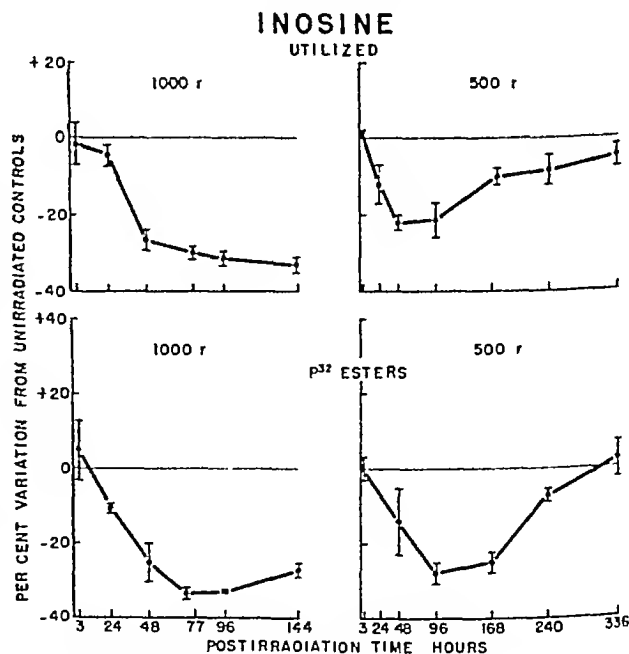


Fig 4 Comparative utilization of inosine by rat erythrocyte extracts

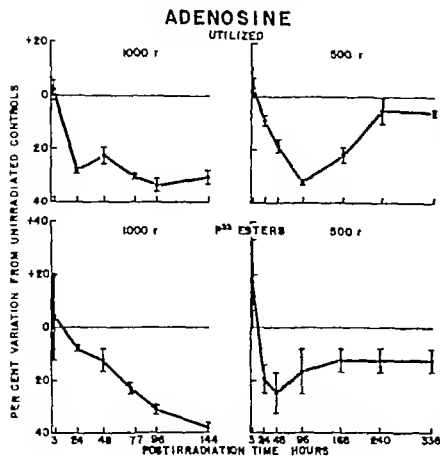


Fig 5 Comparative utilization of adenosine by rat erythrocyte extracts

irreversible protein damage, but probably to the oxidation of some essential sulphhydryl groups to disulphides. Since the erythrocytes contain glutathione, it is likely that the disulphide groups were gradually reduced by the glutathione during the period of recovery of enzyme activity.

Although the radiation does affect the erythrocyte metabolism, how useful is this information in evaluating erythrocyte metabolism as a biological radiation indicator? Data from Figs 3, 4 and 5 also show that the degree of inhibition, particularly for guanosine and inosine metabolism (Figs 3 and 4), is appreciably

greater at 48 hr after 1000 r irradiation than after 500 r treatment. Adenosine metabolism decreased in 24 hr to a greater extent in the rats treated with 1000 r than in those receiving 500 r. The variations in erythrocyte activity described above following 1000 r and 500 r irradiation are only the initial observations. Additional data will be necessary to establish the relationship between whole-body radiation dose and degree of enzyme inhibition in erythrocyte extracts. The present results suggest that the metabolism of nucleosides following radiation can serve as a gross biological indicator. This information may encourage other investigators to examine the erythrocyte metabolism in other species, particularly cancer patients requiring total body radiation treatment, in order to ascertain whether X ray induced inhibition of rat erythrocyte metabolism also occurs in other animals as well as in man.

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THE CHEMISTRY OF CLOTHING*

EVEN though clothing is one of the essential needs of human beings, it is only some fifty years since chemists and physicists, in their professional capacity first began to give any serious thought to the subject, or even to the textile fabrics from which most clothes are made. Almost everyone is of course, interested in the aesthetics of clothing and the fashion and style of garments often reflect the spirit of the times. In the past half century, however, quite outstanding progress has been made not only in providing new materials for garments, but also in understanding more precisely what is required of clothing to be worn under various climatic conditions. It was fitting, therefore, that at the York meeting of the British Association on the occasion of Section B (Chemistry) was devoted to a symposium entitled "The Chemistry of Clothing."

* Based on the following four papers presented at the York meeting of the British Association for the Advancement of Science
 "Physical Aspects of Clothing for Comfort" by Mr W H Rees (British Cotton Industry Research Association)
 "The Chemical Treatment of Apparel Fabrics" by Prof G S Whewell (professor of textile technology University of Leeds)
 "Recent Advances in the Application of Cellulose Man-Made Fibres to Clothing" by Dr H A Thomas (Messrs Courtauld Ltd.)
 "The Use of Synthetic Hydrophobic Fibres in Clothing" by Mr A B Thompson (Messrs. Imperial Chemical Industries Ltd. Fibres Division)

The scope of the symposium was rather wider than its title implied for much of the work which has been carried out is more accurately described as applied physics. The principles on which the comfort and usefulness of clothing are based were discussed by Mr W H Rees of the British Cotton Industry Research Association. He pointed out that in cold climates clothing acts as an insulator, thereby reducing heat lost from the body to a level which can be counterbalanced by body metabolism. Since textile fibres are better conductors than air, the greater the amount of air entrapped by a fabric the more effective will it be as an insulator. Rees indicated that only about 6 per cent of the volume of a blanket is occupied by fibres, the remainder being air. In more compact structures this volume of air is reduced, but in most apparel fabrics it is of the order of two-thirds. It is important that the entrapped air should be undisturbed and, consequently, apparel fabrics for use in windy weather should be constructed so that the wind is kept out. Again, if the air in the fabric is replaced by water, as in heavy rain, the efficiency of the fabric as an insulator will fall. According to Rees therefore, clothing to be worn in wet windy conditions should comprise 'a windproof waterproof

and vapour permeable outer garment and an ample supply of inner garments having a large air content"

Body heat is also lost by radiation in the far infra-red region. All textiles, whatever their colour, are virtually black bodies, with high emissivities, at least ten times as great as that of a metallic surface. To minimize radiation losses garments have, therefore, been lined with aluminium foil. The heat loss is markedly reduced, but if the layer of foil is continuous, the fabric becomes harsh and unsatisfactory and is impermeable to water vapour. By an ingenious method of perforating the film, however, it has been possible to produce in the laboratories of the British Cotton Industry Research Association a fabric which has the usual textile properties but which is extremely effective in cutting down losses by radiation.

In hot climates clothing must reflect away solar radiation and assist in keeping the body cool by the evaporation of sweat. Reflection of radiation is clearly determined partly by the colour of the fabric, lighter coloured materials being the more effective. A white fabric will reflect away two-thirds of the incident radiation and a black one only about one-tenth. Mr Rees has also examined the reflecting power of cotton fabrics dyed the same colour but with different types of dyes, and has found considerable differences in the infra-red. This indicates that although the reflecting power for radiations in the visible region are the same for all the fabrics, those in the infra-red are different. The chemical constitution of the dye is, therefore, important in determining the reflecting power of dyed fabrics. As would be expected, fabrics coated with aluminium foil are excellent reflectors, and if they are produced by the British Cotton Industry Research Association technique their textile properties are not impaired. In addition to being good reflectors, hot weather garments should also assist in the evaporation of sweat, and those worn next to the skin should, therefore, be absorbent and of open structure.

Modern clothing must have many characteristics other than that of being comfortable to wear. It must be aesthetically satisfying and must often have specific properties such as being fireproof, lustrous, mothproof or waterproof. In addition it must retain its appearance and essential properties during wear and after being washed or dry-cleaned. The necessity for garments to retain their essential properties throughout their life is becoming increasingly important and was stressed several times during the symposium.

Although some garments are made from skins, leather, felt and plastics, most are made from knitted, woven or bonded textiles. Fabrics available to the clothing manufacturer may contain both natural and man-made fibres. Garment manufacturing has been, however, largely based on natural fibre fabrics, but with the advent of man-made fibres, the resources of the clothing designer have been greatly increased, for there is an ever growing production of new fibres and fabrics with interesting and novel characteristics. It was clearly not possible to discuss in the symposium new developments in all types of synthetic fibres and attention was concentrated upon specific fibre types. It must be stressed, however, that progress in the production of other fibres, for example, the acrylics, the polyolefines, and those based on fully acetylated cellulose, has been equally rapid. The development of man-made fibres has made possible the production of fabrics and garments with per-

formance characteristics formerly considered to be unattainable. Of particular importance has been the production of fabrics which are light in weight but yet are strong and durable, and of fabrics which are easily washed and do not require ironing to restore their attractive appearance. These developments have, of course, stimulated research in the treatment and modification of fabrics made from natural fibres so that these materials also can be given some of the attractive characteristics of fabrics made from the newer fibres.

The man-made fibres can be divided into two groups—those which absorb considerable amounts of moisture, for example, viscose rayon, and those which do not, such as 'Terylene' and nylon.

Older forms of viscose rayon had several defects, but now a wide range of improved regenerated cellulose fibres can be obtained. It is well known that fibres made by the viscose process have a 'skin and core' structure. The ratio between the amounts of skin and core may, however, be altered by controlling the conditions of ventilation and coagulation, and other desirable properties can be given to the filaments by stretching them immediately after they have been formed. Some of the newer products obtained by such techniques have extremely interesting properties. For example, fibres composed entirely of 'skin' are exceptionally tough and resistant to abrasion wet or dry, being stronger than cotton when wet. Filaments which are all core are obtained by spinning into a solution of ammonium sulphate and stretching the filaments by 50–100 per cent. These filaments are characterized by high strength and low extensibility when wet and are useful for making fabrics which do not shrink or stretch when they are washed. Moreover, by adjusting the spinning conditions so that one side of the fibre has a thick skin and the other a thin skin, asymmetric fibres are obtained. Because of the different swelling properties of the two sides, these fibres are crimped, and even if the crimp is pulled out during processing it will reappear on after wards wetting the fibre. Provided that appropriate stable pigments can be ground sufficiently finely to prevent blocking the holes in the spinnerets 'spun dyed' fibres can be produced by almost any spinning process by incorporating the pigment in the dope before it is extruded. The spun-dyed viscose rayons have been found to have some unexpected properties, for not only are the colours very fast to repeated washing and to exposure to bright sunlight, but the dispersed pigments also protect the fibre from photodegradation and deterioration in industrial atmospheres.

The introduction of the hydrophobic apparel fibres was a great step forward in textile science and technology. As Mr A. B. Thompson pointed out, a good textile fibre must be soft without being too extensible, that is to say, it must be intermediate between a glass and a rubber. It must be elastic rather than plastic, although a plastic state is needed to ensure a satisfactory response to ironing and pressing which are essential in garment making, and often for the subsequent care of apparel fabrics. Natural fibres meet the latter requirements because they can be made plastic by application of heat and moisture. The hydrophobic fibres are much less affected by moisture and consequently retain their elasticity during use, and to achieve the plastic state heat is necessary. In general, therefore, the elastic state required in use and the plastic state needed for

ironing etc., are quite distinct. This separation of the semi-flexible elastic state required in use from the more flexible plastic state needed for shaping and pressing enables garments made from the hydrophobic fibres to retain their smart appearance during wear and to be pressed or creased permanently when required.

Each natural or man-made fibre has its own characteristics. Many apparel fabrics are therefore made from blends of different fibres, the blend being selected so that advantage is taken of the desirable properties of each of the components. Of particular significance is the blending of hydrophobic and hydrophilic fibres to produce fabrics which are light, durable, and easily cared for, but yet comfortable to wear.

Almost all fabrics are improved by suitable chemical treatment. The changes brought about must however, be permanent. Processes of this type were discussed by Prof C S Whewell, emphasis being laid on developments in the production of crease-resistant,

'drip-dry' and minimum-care fabrics, the permanent pleating of wool fabrics, methods for obtaining textile fabrics which do not shrink or expand when they are washed, and the production of fabrics which are permanently mothproof, fireproof and waterproof.

The four papers presented at the symposium formed a useful indication of some of the important trends in the production of better apparel fabrics and garments. The craft of the tailor and the cloth designer is now being supplemented by the skill and resources of the scientist. This combined approach to the problems associated with clothing is comparatively new, but the success which has so far been achieved is ample proof of the value of the collaboration. The opportunities for research and development in this field are indeed exciting. Perhaps a future meeting of the British Association will be the occasion on which the results and achievements will be discussed.

C S WHEWELL

RESEARCH IN THE ANTARCTIC DURING 1960

British Programme

THE Falkland Islands Dependencies Survey maintains a number of permanent scientific stations within the Falkland Islands Dependencies sector of the Antarctic. Many of these have been in continuous occupation since 1944. During the International Geophysical Year they played their part with the stations of other nations in the general co-ordinated plan. At the end of 1958 the Royal Society station at Halley Bay was handed over to the Survey and will continue to work like that of the other stations of the Falkland Islands Dependencies Survey, into the indefinite future.

The main geophysical stations are at the Argentine Islands and Halley Bay, the two being separated by about 1,000 miles. At both, daily upper air soundings will continue, as will the surface meteorological work which is common to all bases except Port Lockroy. Fluxplates and solarimeters will be in use for the study of radiation balance, and both stations will continue ozone observations using the Dobson spectrophotometer.

The ionospheric work at Port Lockroy only 40 miles from the Argentine Islands, will continue in operation as will the recording of whistlers which forms a part of the programme initiated from Dartmouth College, New Hampshire.

At Halley Bay the ionospheric equipment was not in use last year but is to be brought into commission again for 1960. On the other hand it has been decided to abandon the seismological work there but to continue using the Willmore short period seismographs at the Argentine Islands.

Because of the geomagnetic latitudes of the stations of the Falkland Islands Dependencies Survey, very few auroral displays are observed except at Halley Bay. There an all-sky camera will continue in operation and other studies include a small glaciological programme, observations of sea-ice growth and of the measurements of marine currents.

In the coming year an attempt will be made to recover cosmic spherules falling on the ice sheet,

and also to obtain samples from deep within the ice. Since there can be no dilution by other sedimentary materials it may prove possible to determine a rate of deposition for this cosmic material.

The other bases extend from South Georgia where there is a purely meteorological station through the South Orkneys and the South Shetlands along the coast of Graham Land to about lat 68° S. All are manned throughout the year, the number of men varying between five and eighteen. During the summer, work is to be carried out from the ships operating in the area. These will be R.R.S. *John Biscoe*, R.R.S. *Shackleton*, H.M.S. *Protector* and the Danish vessel *Kista Dan* chartered for the season.

John Biscoe will be committed almost entirely to relief and restoring the bases, but it is hoped to operate a wave-recorder on board to investigate the damping effect of pack ice. This is not only of academic interest but will also be valuable when forecasting the break-up of the sea ice. All bases maintain constant sea-ice observations which already provide a background upon which seasonal probability charts are being built up. If the protective effect of large areas of drifting pack can be assessed, ice forecasts for shipping will be materially assisted.

Shackleton will be extending hydrographic surveys along the west coast of Graham Land and around the South Shetland Islands. In addition, she has been fitted to tow a proton resonance magnetometer so that investigation of the Scotia Arc can be begun. This work will tie up with the magnetic traverses already in progress from Hope Bay in the Trinity Peninsula area. A Worden gravimeter will also be carried and put ashore for gravity observations at as many points as possible.

H.M.S. *Protector* carries helicopters and these will be used to extend the tellurometer survey where the landing of men and instruments cannot be made in any other way.

The task of the *Kista Dan* is to re-establish the southernmost base on Stonington Island which had to be evacuated last year because of bad ice con-

ditions. She will be carrying two aircraft which can be used for the transport of men and material, but if the ship is held up by bad ice conditions their first task will be to re-supply the base. Then reconnaissance flights are to be made southward to select a site for a field hut which will be flown in at the end of the season. Both aircraft will winter at the base and can therefore support field parties making topographical and geological surveys in the remoter regions during the early part of the 1960-61 season. The *Beaver* aircraft is fitted with a Williamson vertical camera so that photographic cover can be obtained over the more inaccessible areas.

Geological and topographic surveys will also continue from a number of other stations and, in addition to the glaciological programme at Halley Bay, glaciologists will be working from Hope Bay, Admiralty Bay and King George Island.

In the coming year biological work will have less emphasis than in some years, but the marking and population counts of fur seals and elephant seals will continue. A small project concerned with soil ecology is to begin at Signy Island. Also at Halley Bay, where there is a rookery of 10,000 emperor penguins, a biologist has been appointed to continue the study of the species. In particular, an examination of the endocrinology of the bird and a further collection of embryological material will be made.

In each southern summer, ice conditions are different, and it is this which often hinders the planned programme. Last year was a bad year, this year we hope for better things, but in any event it is certain that the only way to succeed is to keep up the pressure and be ready to take advantage of any relaxation which Nature may afford.

VIVIAN FUCHS

American Programme

A STATEMENT released by the National Science Foundation gives details of grants for scientific investigations either in or associated with Antarctic regions. Logistic support will again be the responsibility of a U.S. Navy support force under Rear Admiral David M. Tyree, who has recently taken over from Rear Admiral George J. Dufek. The grants total 3,170,069 dollars, of which approximately one-third goes to support the meteorological programme and one quarter to glaciological projects. Greater emphasis than formerly is placed on geology, cartography and biology, which is in accord with the recommendations of the Special Committee on Antarctic Research of the International Council of Scientific Unions.

Among new projects mentioned are a United States scientific expedition to the Bellinghousen Sea which will include specialists in biology, geology, cartography and oceanography.

The International Geophysical Year pattern of over snow traverse operations will be continued in Mario Byrd Land and Victoria Land. Biological investigations on the ecology of the Ross Sea area and on land invertebrates of the McMurdo Sound and Hallett areas will be helped by the recently established U.S. Antarctic Biological Research Laboratory at McMurdo.

The investigations will be spread over seven Antarctic stations of which three are fully and one jointly under the direction of the United States. Co-operation with other countries in these investigations in both scientific and logistic spheres has been a notable feature of the U.S. Antarctic effort, and this appears likely to continue.

NEWS and VIEWS

The Third Russian Space Rocket

A MULTI-STAGE space rocket was launched in the U.S.S.R. at about 02h UT on October 4. When the last stage, weighing 1,553 kgm (3,424 lb) without fuel, had reached a speed slightly less than escape speed from the Earth, an instrumented vehicle weighing 278.5 kgm (614 lb) separated from it. This vehicle entered an elongated elliptic orbit which took it into the vicinity of the Moon. Its nearest approach to the Moon occurred at 14h 16m UT on October 6, when it was about 7,000 km (4,300 miles) from the surface of the Moon, at selenographic longitude 137° W and latitude 12° S. After leaving the vicinity of the Moon, the vehicle entered a new elliptic orbit about the Earth, with an apogee distance of 470,000 km (292,000 miles) from the surface of the Earth, attained at about 00h UT on October 11, and a perigee distance of 40,000 km (25,000 miles), attained at about 17h UT on October 18. The orbit is inclined at about 75° to the Earth's equator and the period of revolution is about 15.4 days. The vehicle has been designated Earth-satellite 1959 0. The orbit of the spent rocket is not known. The instrumented vehicle, which the Russians have referred to as an "automatic interplanetary station", carried apparatus to photograph the part of the Moon which is never seen from the Earth, and also

apparently performed other scientific experiments, of which details have not yet been given. The vehicle had radio transmitters operating on 39 986 Mc/s and 183.6 Mc/s, the power being supplied partly by chemical and partly by solar batteries.

Research Association of British Paint, Colour and Varnish Manufacturers Dr L. A. Jordan, CBE

DR LOUIS ARNOLD JORDAN, the founder-director of the Research Association of British Paint, Colour and Varnish Manufacturers, has relinquished his appointment after thirty-three years. The Paint Research Station at Toddington, at present being further extended, stands in testimony to his achievement. Educated at Alderman Newton's Greencoat Foundation School, Leicester, he proceeded as a Royal scholar in 1910 to the Royal College of Science, where he was Tyndall prize-man in physics and Frank Hatton prize-man in chemistry. He received the D.Sc. (London) in 1921. During the First World War he was concerned with explosives, and certain 'gas' problems, thence to Boots Pure Drug Co., Ltd., and later to the British Xylonite Co., Ltd., to start an investigation which resulted in the establishment of the British synthetic camphor industry. From 1923 until the establishment of the Paint Research Association in 1926 he was scientific adviser

to the State of Bhopal, Central India. He returned to India in 1955 at the invitation of the Government of India to inquire into matters touching the development of the lac industries. In fact, he is widely travelled (another recent journey having been to Brazil to advise on organized research in paint and related matters) and is well known internationally, for example, through his work for the Organic Coatings Division of the Applied Chemistry Section of the International Union of Pure and Applied Chemistry.

Dr Jordan has given extensive service to the Oil and Colour Chemists Association (he was president during 1947-49) and to numerous other scientific and technical organizations. He was chairman of the council of the Society of Chemical Industry during 1952-53 and medalist of the Society in 1953. As one of the Jubilee Memorial lecturers of the Society (1944) he chose as his subject "Paint the Art and Science", reflecting his interest in the artistic as well as in the industrial and scientific aspects of paint and painting, an interest culminating in 1958 in his appointment as professor of chemistry at the Royal Academy of Arts. His work for technical education stands high in achievement and personal satisfaction. He has for long been chairman of the City and Guilds Advisory Committee on Paint Technology and his period as a Surrey county councillor (1948-58) provided opportunities for contributions in a wider field of technical studies. He is now chairman of the governors of the Kingston Technical College, a governor of the Brunel College of Technology, and a member of the Regional Advisory Council for Technological Education for London and the Home Counties Region. He has recently been appointed to the senate of the University of London.

Botany at Hull

Prof R D'O Good

PROF RONALD GOOD, who has retired from the chair of botany in the University of Hull was head of the Department of Botany from the foundation of the University College in 1928. After serving in the First World War, followed by a brilliant period at Downing College, Cambridge he held an appointment at the British Museum (Natural History). At Hull he had much to do with the organization and equipment of his department as well as teaching but he has also been active as a researcher and writer. His book on the "Geography of the Flowering Plants" has had a wide circulation and is regarded as one of the chief works on the subject while his "Handbook of the Dorset Flora" is an outstanding ecological study.

Prof N F Robertson

DR N F ROBERTSON, who has succeeded Prof Good has been on the staff of the Cambridge Botany School since 1948. His interest in mycology was first aroused by Dr Malcolm Wilson at the University of Edinburgh. After graduating there in 1944, Dr Robertson was appointed a Colonial Office probationer and studied at the University of Cambridge, at Rothamsted Experimental Station and in the United States before proceeding to the West African Cacao Research Institute at Tafe late in 1946. He worked there, in collaboration with Dr A. F. Potton, on insect transmission of the swollen shoot disease. Dr Robertson's first research problem at Cambridge was concerned with mycorrhizal infection of the Scots pine, and he made a notable contribution to the subject by showing that the behaviour of the mycor-

rhizal fungus was closely related to that of the specialized root disease fungi affecting tree crops. More recently, Dr Robertson has turned his attention to the physiology of fungal branch systems in culture and has made what may eventually prove to be the first experimental approach to the morphogenesis of asexual spore production. With his research students Dr Robertson has explored a much wider field, ranging from the physiology and genetics of the *Fusaria* in laboratory experiments to the behaviour of *Fusarium* wilt diseases and potato blight in the field. The University of Hull is doubly fortunate in securing Dr Robertson as professor of botany, because he has distinguished himself at Cambridge not only by his research but also as a teacher, and by the full share he has taken in other duties in the Department of Botany, where he will be greatly missed.

The World Veterinary Association

Prof W I B Beveridge

AT the recent International Veterinary Congress in Madrid a World Veterinary Association was established. The main purposes of the Association are to unify the veterinary profession throughout the world by providing a central link for national veterinary associations and the exchange of information on matters of veterinary interest. The organs of the Association are the congress and the permanent committee.

Prof W I B Beveridge, professor of animal pathology, University of Cambridge, has been elected president of the Permanent Committee of the newly founded World Veterinary Association. He has had a distinguished career as a veterinarian who gave outstanding service to his profession in Australia and in the United Kingdom. After graduating at the University of Sydney, he was a member of the research staff of the McMaster Animal Health Laboratory in Sydney during 1931-41. During two years of that time he was the holder of a Commonwealth Fund Fellowship at the Rockefeller Institute, Princeton, and the Bureau of Animal Industry, Washington. From 1941 until his appointment as professor of animal pathology in Cambridge he worked at the Walter and Eliza Hall Institute in Melbourne. Together with Sir Macfarlane Burnet he worked on viral diseases in man and published several outstanding papers concerning cultivation of viruses. In Cambridge Prof Beveridge's researches are mainly concerned with viral diseases of respiratory systems in animals. Unfortunately his scientific work there was very much interrupted by administrative duties associated with the establishment of the new Veterinary School which was opened by H M the Queen and the Duke of Edinburgh in October 1955. He is the author of the book, "The Art of Scientific Investigation". Both on account of his outstanding reputation and his interest in international co-operation, he will be a most welcome president of the newly founded World Veterinary Association.

Amendments to the U.S. Atomic Energy Act

IN a report by the United States Atomic Energy Commission (The Indemnification of Atomic Energy Activities and Operations of Advisory Committee on Reactor Safeguards, 1958-59 Report of the Joint Committee on Atomic Energy on Operations under Section 170 of the Atomic Energy Act of 1954 as Amended Pp iii+74 Washington DC: United

States Atomic Energy Commission, 1959), details are given of the proposed regulations approving the form of nuclear energy liability insurance policies and Commission indemnity agreements. Amendments to the indemnity proposals of the Atomic Energy Act, 1954, which it is proposed to submit to Congress, exclude liability for damage to property located at the site of, or used in connexion with, the licensed activity, and would authorize the Commission to fill a gap for a sufficient period of time in which to give the licensee reasonable opportunity to furnish the required protection. The Commission is also studying the possible gaps resulting from the 'common occurrence' provision, and has entered into a contract for a study of criticality hazards as part of its continuing study of the problem of extending indemnity to materials licensees. As regards foreign liability problems, the efforts of the Commission have been directed primarily to encouragement and support of the efforts of other governments to enact their own legislation and effect international arrangements.

Scientific Staff In New Zealand

DURING the past twelve months six officers of the Ruakura Animal Research Station in New Zealand have resigned to accept posts in Australia. All have received an increase of salary of £A500 to £A1,000 on taking up their new posts. The maxima attached to their new position in Australia is, in all cases about twice that offered for the positions they vacated in New Zealand. Another 25 individuals have resigned from Government laboratories or science departments of New Zealand universities during the past three years to accept overseas posts, mainly in Australia. This figure does not include graduates in science who have gone overseas for advanced training.

Both Government departments and the universities experience great difficulty in replacing the losses of scientific staff with persons of the desired quality. The Soil Bureau of the Department of Scientific and Industrial Research has been seeking pedologists for some time without success, and advertisements for mycologists, entomologists, mathematicians and physiologists have failed to attract any applicants or applicants of the desired qualifications and calibre. Whereas five years ago there were usually a number of highly qualified applicants for each vacancy from which selection could be made, the position has changed so that to day only one or two such applicants and sometimes none at all apply for advertised positions.

Scientific Research in British Universities

"SCIENTIFIC Research in British Universities, 1958-59", based, as in previous years, on material collected by the British Council from heads of departments of the universities, who are alone responsible for the entries, now runs to 446 pages (pp. xi+446. London: H.M. Stationery Office, 1959. 25s. net). These brief notes on scientific research in progress during the 1958-59 session indicate the nature of the projects in sufficient detail to show the scope of the research. Entries are arranged in alphabetical order of university or university college, and under each institution the arrangement is alphabetically by subject. The head of the department is named, with those permanent members of staff actually engaged in supervising research. There are alphabetical name and subject indexes.

Registration of Scientific and Technical Persons, 1958

FRESH and renewed registrations for all professional classes covered by the Technical and Scientific Register of the Ministry of Labour, with the exception of mathematicians and physicists, steadily increased during 1958, according to the Ministry's annual report. At the end of December, registrations, including those seeking a change as well as those employed, were 29 per cent higher than in December 1957, a significant part of the increase comprising registrations of men in the middle age groups seeking better positions before age restricted their prospects and from ex-regular members of the Forces who had retired or anticipated premature retirement. At December 8, 1958, of 4,556 on the register, compared with 3,538 in 1957, 1,326 were unemployed. Premature retirements from the Services reached a peak during the year, but the Regular Forces Resettlement Service, set up by the Ministry, received encouraging support from industry and commerce, and there was no significant increase at the end of the year in the number of such applicants unemployed. The report also directs attention to the establishment in July 1958 by the British Employers' Confederation, the Trades Union Congress and the boards of the nationalized industries, of the Industrial Training Council in accordance with the recommendation of the Carr Committee. This Council has undertaken as its first task the encouragement of industry generally to take advantage of the opportunities provided by the 'bulge' of school leavers to expand apprenticeship schemes and other forms of training. Thirty-two appointments were made to the general factory inspectorate, and with five applicants awaiting appointment, the number of vacancies at the end of the year was nine. Five additional appointments were made to the Engineering and Chemical Branches of the inspectorate. On the advice of the National Advisory Committee on the Employment of Older Men and Women, the Ministry is discussing with the Department of Scientific and Industrial Research and the Medical Research Council arrangements to ensure co-operation between the Ministry, industry and research organizations and to stimulate research into problems of employment of older workers.

Rubber Research

THE twenty-second "Annual Report on the Progress of Rubber Technology" covers the progress of rubber technology during the year 1958 (edited by Dr T. J. Drakeley. Pp. ix+125+xii. Cambridge: W. Hoffer and Sons, Ltd., 1959. Published for the Institution of the Rubber Industry). The report contains twenty-three sections, by different contributors, covering all aspects of the technology of rubber-like materials, both natural and synthetic, ranging from surgical goods to the use of rubber in roads. The report also includes sections on historical and economic aspects, planting and production of natural rubber, fibres and fabrics used in conjunction with rubber, compounding ingredients and, for the first time, a separate section on the manufacture of synthetic rubbers. The introduction of this latter section is timely since 1958 saw the opening in Italy, Germany and the United Kingdom of the first major European plants for the production of general-purpose synthetic rubber. Synthetic elastomers are now firmly established as a large and important part of the rubber industry. Already approximately 65 per cent of American new-rubber consumption consists

of synthetics the corresponding figure for the rest of the world (excluding Communist countries) is 25 per cent but this is likely to increase with the opening of the new plants. The year does not appear to have produced any outstanding new technical developments but rather a steady improvement of materials and techniques. The report contains more than one thousand references to scientific and technical publications, although, as is inevitable in a work of this kind, there is some overlapping from section to section.

Aerial Photographic Exhibition of Quarries and Mines

A SPECIAL exhibition of aerial photographs of quarries and mines opened at the Geological Museum Exhibition Road London, S W 7, on October 16. Admission is free. The exhibition will remain open for several months. The photographs show past and present surface aspects and effects of quarrying and mining in the United Kingdom and illustrate the great variety of useful rocks and minerals found in Britain. All the photographs are from the Cambridge University Collection, an extensive library of air photographs specially selected to meet needs of teaching and research. They have been taken during recent years by Dr J. K. S. St Joseph, curator in aerial photography at Cambridge from aircraft of the Royal Air Force on training flights.

Petroleum Industry in Great Britain

THE Petroleum Information Bureau has published under the title 'U.K. Petroleum Industry Statistics relating to Consumption and Refinery Production 1957 and 1958' (Pp 10 London Petroleum Information Bureau, 1959) figures covering all petroleum products, whether imported or from indigenous sources, as well as substitutes such as benzole and hydrogenated spirits. Refinery production figures do not count further treatment of finished products for special grades. The figures relate to 1957 and 1958 in which deliveries and consumption of petroleum products totalled 24,784,586 tons and 31,065,020 tons respectively.

New Journal of Glass Technology

MORE and more problems in the physics and chemistry of glasses are being investigated in laboratories all over the world. At present the results are published in many non-specialized journals and the time has come to provide a vehicle for these papers. The Society of Glass Technology has therefore decided that from February 1960 its *Journal* should be published in two parts. These will be called *Glass Technology* and *Physics and Chemistry of Glasses*. Both journals will contain papers, abstracts, communications to the editor and book reviews. Arrangements are being made with the Abstracting Board of the International Council of Scientific Unions to ensure that papers published in these new journals will be abstracted as widely as possible and also that the abstract sections will be comprehensive. *Glass Technology* will contain reports of applied science in the glass industry, and subjects considered suitable include control of batch compositions, corrosion of refractories, design, operation and performance of furnaces, methods of chemical and physical testing, melting processes, statistical analysis of industrial experimentation. In *Physics and Chemistry of Glasses* will be published reports of original studies of the physics and chemistry of glasses, both experi-

mental and theoretical. Possible subjects include electrical properties, infra red absorption relaxation processes, thermodynamics of the glassy state; viscosity, X ray diffraction. Copies of the Society's notes for authors are available from Prof R. W. Douglas, Society of Glass Technology, Thornton, Hallam Gate Road Sheffield 10.

Plant Nematology

IT is now recognized that eelworm diseases are among the most important problems in plant health and there has been a rapid increase in the study of plant parasitic nematodes in all countries where the growing of plants has become an organized industry. Unfortunately, there is a shortage of trained specialists in nematology and of introductory literature on the subject. The Ministry of Agriculture's new Technical Bulletin No 7 (Pp vii+175+12 plates London H.M. Stationery Office, 1959 6s 6d not) provides a general introduction and is based on the lectures given at a special training course held at the National Agricultural Advisory Service regional headquarters, Bristol, in 1958. It also reviews the more important nematode problems in British agriculture and is in part designed as a companion volume to Technical Bulletin No 2 (Laboratory Methods for Work with Plant and Soil Nematodes). Although primarily designed for non-nematologists it should also be of interest to agricultural entomologists, plant pathologists and others who have to advise on eelworm problems and also to students and teachers of zoology, agriculture and parasitology. It contains 21 articles by research and advisory workers, arranged in six main sections covering the general structure and classification of nematodes, the more important genera, several practical and research problems with eelworms, control and cultural studies.

Sea Fisheries Research in East Africa

THE annual report for 1958 of the East African Marine Fisheries Research Organization (pp 20 Nairobi Government Printer 1959 4s) is one that reflects great credit on the small staff at Zanzibar. Research on the fish and fish stocks of the Indian Ocean first at Mauritius and now at Zanzibar has been the post-war concern of the director, Dr R. H. Wheeler, and it is good to learn from him that the phase during which it has been of first necessity to identify species is passing. In spite of the need to do systematic work Dr Wheeler, operating from Mauritius with a small converted fishing vessel had already discovered a large and potentially rewarding fishery in the neighbour hood of Seychelles Banks. The same vessel was transferred to Zanzibar, but during 1957 it was replaced by a large and more serviceable trawler the *Manihine*. Among other tasks assigned to *Manihine* was floating long line fishing for yellow fin tuna and striped marlin. Using seven miles of line and two hundred and fifty hooks on or below the thermocline at 50-70 fathoms, heavy catches were made. These results are most encouraging for all those who wish to see the Colonies, Dependencies and emerging Commonwealth countries of Africa break into the oceanic resources of pelagic fish now so largely in the hands of the Japanese.

Translocation of Amino-Acids

THE translocation of carbon 14 labelled amino acids and nucleides in the stems of young *Solanum*

plants has been investigated by C D Nelson and P R Gorham (*Canadian J Bot*, 37, 3, 431 (1959)) with the following results. In all, the translocation of each of seven amino-acids and three amides was measured for periods of 5 minutes or less after introduction through the cut petiole of a primary leaf. The compounds used were asparagine, uracil, glutamic acid, glutamine, glycine, norleucine, arginine, serine, alanine and aspartic acid. During the short times of these experiments it was found that each compound was translocated downwards as such. The amount of carbon-14 in the stem decreased logarithmically from the point of introduction. Each compound was translocated with unchanged velocity past a short section of stem killed with steam. There was no translocation of aspartic acid through a stem that had an entire internode killed with steam. Potassium cyanide ($10^{-2} M$) did not inhibit the velocity of translocation of any of the compounds although the logarithmic pattern of distribution of arginine was altered. The minimum velocity of translocation was different for each compound and varied between 350 cm per hr for asparagine and 1400 cm per hr for aspartic acid. The authors have also reported on the physiological control of the distribution of these substances (*Canadian J Bot*, 37, 3, 439 (1959)). From the point of introduction, translocation of each amino-acid or amide was mainly downward towards the root, very little was translocated upward. Both excision of the roots and chilling decreased the velocity of downward translocation of aspartic acid, indicating that the roots exert a strong 'demand' which favours translocation in a downward direction more than an upward direction in the stem.

Volcanic Activity on the Moon

In a brief article, N A Kezyrev (*Priroda*, 3, 84, 1959) describes his observations of the Moon since 1955 and provides a critical examination of the records of the Alphonse crater on November 3, 1958. In his opinion the spectrographic evidence suggests strongly that an eruption of volcanic ash did take place on that date on the Moon. This eruption was followed by the emission of gases containing C_2 molecules.

Astronomische Gesellschaft Star Catalogues

BETWEEN 1868 and 1908 the Astronomische Gesellschaft organized the production of a catalogue of all the stars brighter than the ninth magnitude in the northern sky. A dozen observatories shared in this work, the observations being made visually using meridian circles. It was later decided to repeat the whole programme photographically, and new observations were obtained during the years 1928-32. The Hamburg Observatory photographed the sky north of $+20^\circ$ declination, the Bonn Observatory that from $+20^\circ$ to -2° . Observations of 14,000 reference stars were made at several observatories. The measurement of the photographs and the reduction of the measures have been in progress since 1932, and publication of the results began in 1951. The results are contained in a fifteen-volume catalogue, and the last five volumes of this catalogue have recently been published. The catalogue contains the positions of 180,000 stars down to magnitude 11.5. No proper motions for the stars were deduced because it was impossible to free the earlier catalogues from systematic errors. The homogeneity of the results of this large undertaking represents one of its most important features, and the catalogue is, and will remain, a

landmark in positional astronomy. The catalogue is known as the AGK2.

It has been decided to repeat the whole catalogue with a mean epoch of about 1960. 18,000 secondary reference stars are being observed at various observatories, the photography is being performed at Hamburg and 1,939 plates will be required. It is hoped to have positions and proper motions for all the 180,000 stars by 1965. This new catalogue, the AGK3, will enable astronomers to determine the systematic errors of old catalogues, connect the proper motions of the bright stars with those of fainter stars measured relative to the extragalactic nebulae, and provide much data for geodetic purposes.

Courses in Chemical Engineering

A NEW pamphlet, "Scheme for a Full-time Course in Chemical Engineering" (pp 16. London: Institution of Chemical Engineers, 1959. 2s.), is a revised version of the "Scheme for a Degree Course in Chemical Engineering", originally issued in 1944, and takes account of current developments in teaching chemical engineering at technical colleges. The course covers three years, and although in the first two years most of the time is spent on physical, organic and inorganic chemistry, the physics of solids, electricity, and mathematics, fluid mechanics, heat and mass transfer, the design and construction of process plant, power thermodynamics and engineering drawing are introduced at this stage and not left until the final year. In this year the course comprises fluid and particle mechanics, heat and mass transfer, separation processes, applied chemical thermodynamics and kinetics, fuels and combustion and design problems. Practical experience in works is regarded as an essential adjunct to the course, and the economic aspect should be introduced into lectures on chemical process principles in the first year. The course should not be so rigid as to preclude transfer to chemical engineering in the earlier years by students who have commenced studies in a cognate faculty.

Talanta Medal

THE board of editors of *Talanta* announces a new award to be known as the Talanta Medal. The publishers, Pergamon Press, are providing the funds for this Medal, which will have a value of 100 guineas and which will be awarded for outstanding contributions to analytical chemistry. The Medal will not normally be awarded more frequently than once a year, but no attempt will be made to award it at any stated intervals. This award will be either to analytical chemists who are responsible for major developments in the subject or to scientists whose work is judged to have contributed in a substantial way to the developments in the field of analytical chemistry. Applications should be sent to the editors of *Talanta*, c/o Pergamon Press, 4-5 Fitzroy Square, London, W 1.

Perkin Centenary Trust

THE programme of awards for the year 1960-61 will include one Perkin Centenary Fellowship, valued at not less than £600 a year, which is available to a graduate for advanced studies, and two Perkin Centenary Scholarships at £300 a year, which are intended to give young persons employed in the industries concerned with the manufacture or the application of colouring matters the opportunity of full-time education at a university or technical

collegiate. Applications are invited for the Perkin Trust Travel Grants from teachers concerned in the study of any aspects of the manufacture or applications of colouring matters at a university or technical college or other institute. The purpose of the grants is to enable teachers to make short visits to comparable institutions overseas to widen their experience. The secretary to the trustees is Dr J R Ruck Keene, to whom inquiries relating to awards should be addressed at the Chemical Society, Burlington House, London, W1.

Harkness Fellowships of the Commonwealth Fund

THE awards bearing since 1925 the title Commonwealth Fund Fellowships were renamed in 1953 the Harkness Fellowships of the Commonwealth Fund. All Fellowships are tenable in the United States and are offered, in separate series to candidates from the United Kingdom, Australia and New Zealand and Western Europe. The Fund, an American philanthropic foundation, believes that international understanding may be promoted by opportunities for education and travel in the United States. Thirty Fellowships are offered in 1960 to candidates from the United Kingdom who are British subjects and are either graduates or have experience in government service, the professions, the creative arts, journalism, branches of business or industry. Forms of application, which must be returned before December 1, can be obtained from the Warden, Harkness House, 38 Upper Brook Street, London, W1 from whom further details can be obtained.

British Institution of Radio Engineers Awards

THE Council of the British Institution of Radio Engineers has announced the award of a number of premiums for outstanding papers published in the Institution's *Journal* during 1958. The senior award, the Clerk Maxwell Premium, goes to Mr C Powell and Mr D A Hendley (Doeca Navigator Co Ltd) for the paper, "Docta: A Long Range Radio Navigation Aid", Heinrich Hertz Premium to Mr K. Foster (Cossor Radar and Electronics Ltd) for the paper, "The Characteristic Impedance and Phase Velocity of High-Q Triplate Line" for the third successive year the Sir Louis Sterling Premium to Dr A van Weel (Philips, Eindhoven) for his paper, "Design of Detector Stages for Signals with Symmetrical or Asymmetrical Side Bands", Sir J O Bose Premium to Dr B Ramachandra Rao Dr M Srirama Rao and Mr C Abhirama Reddy, from Andhra University, South India, for their paper entitled "Magneto ionic Fading in Pulsed Radio Waves reflected at Virtual Incidence from the Ionosphere", Brabazon Premium to Prof D G Tucker, Dr V G Wolsey, Mr R Kendall and Mr D E N Davies for their associated papers entitled "Electronic Sector Scanning" and "Radar Systems with Electronic Sector Scanning", and Varcon Premium to Dr Morton B Prince and Mr M Wolf, of Hoffman Electronics Inc, Evanston, Illinois U.S.A., for their paper "New Developments in Silicon Photo voltaic Devices".

Volume Fifty of the "Large Soviet Encyclopedia" ("Bolshaya Sovetskaya Entsiklopediya")

This volume, part of a set of fifty, could not be sold separately when it was originally issued. In 1957, however, a special edition of 100,000 copies was printed which could be sold separately. Thus this finely printed and bound volume of 764 pages

can be purchased in Britain for the sum of £2. It contains summary articles or reviews of all aspects of the Soviet Union and thus it is an invaluable reference book for anyone interested in this subject. It is illustrated by a large number of folding and text maps, plates, text figures and tables. Scientific workers will be interested in the following chapters: 3, geography, geology, climate, soils, vegetable and animal worlds of the Soviet Union; 4, population; 5, history; 9, economics; 12, education; 13, science. Chapters which follow deal with literature, arts and other subjects. Chronological tables and a name index are placed at the end.

Announcements

DR A J P MARTIN, of Elstree Herts, Dr R L M Syngé, of the Rowett Research Institute, Bucksburn, Aberdeenshire and Dr A. T. James of the National Institute for Medical Research, Mill Hill have been awarded John Price Wetherill medals of the Franklin Institute for their development of gas-liquid (partition) chromatography.

At the sixth annual general meeting of the Association of Clinical Biochemists, held at the Royal College of Surgeons, London, on October 3, the following officers were elected: *President* Dr C P Stewart, *Chairman*, Dr A L Latner, *Hon Treasurer* Dr J H Wilkinson, *Hon Secretary* Dr A. L. Tarnoky, Royal Berkshire Hospital, Reading.

A REGIONAL training course for laboratory technicians sponsored jointly by the University Institute of Chemistry, Lahore, and the Unesco South Asia Science Co-operation Office will be held at the University Institute of Chemistry, Lahore, Pakistan during November 23-December 10. Inquiries should be addressed to the Unesco South Asia Science Co-operation Office, 21 Curzon Road, New Delhi, India.

In a written answer in the House of Commons on July 30, the Chancellor of the Exchequer stated that to assist the Government in making a review of the control of public expenditure he was appointing a small group to make a full examination of the whole problem, in consultation with all major departments, and to formulate proposals. Lord Plowden would take general charge of this work and besides senior officials from departments, including the Treasury, the group would include two or three persons from outside the Government service.

THE Chemical Society has announced that applications for Research Fund grants should be submitted not later than November 14. Further information can be obtained from the General Secretary, Chemical Society, Burlington House, London W1.

THE Institute of Physics is organizing a conference during November 13-14 on "Structure Analysis and Experimental Techniques". The conference is to be held at the Institution of Civil Engineers, Great George Street, London SW1. Further information can be obtained from Dr P. T. Davies, "Shell" Research, Ltd, Thornton Research Centre, P O Box 1, Chester.

ERRATUM In the communication entitled "Prevention of the Onset of Seed Dormancy by Gibberellic Acid" by Dr M. Black and J. M. Naylor in *Nature* of August 8, p. 468, in the legend to Fig. 1 for '3 replicates each comprising 50 embryos' read '2 replicates each comprising 50 embryos'.

SCIENTISTS IN THE PUBLIC SERVICE IN BRITAIN

SPECIAL PROMOTIONS

FURTHER posts have been created in the Civil Service as in previous years under provisions included in the White Paper on the Scientific Civil Service (Cmd 6679, 1945) to provide for the promotion of individual research workers of exceptional merit. The promotions were effective from July 1, and include the following

Deputy Chief Scientific Officer

DR J S HEY joined the Army Operational Research Group in 1940, becoming its head in 1949. In 1952 he formed a research section of what is now the Royal Radar Establishment. Both before and since going to Malvern, he made exceptionally distinguished pioneering contributions to radio astronomy which were the basis for his D.Sc. His work for the Ministry of Supply has also included important contributions on the mechanism of electromagnetic scattering and the ionization associated with discontinuities in hypersonic gas flows, all marked by originality and simple elegance in experimental technique. He is a Fellow of the Physical Society and the Royal Astronomical Society, has served on the Council of the latter and was this year awarded the Eddington Medal. He serves on Commissions of the International Astronomical Union.

DR H G HOPKINS was at the Royal Aircraft Establishment during the war years, working primarily on the theory of elastic stability and of stress distribution in aircraft structure. In 1946 he returned to academic teaching and research. He joined the Armaments Research Development Establishment in 1954 and has been concerned with damage to structures, camouflet and crater formation in soils and dynamic studies in metal plasticity.

MR D H SADLER is superintendent of H.M. Nautical Almanac Office, the work of which is divided between the highest theoretical and numerical requirements of fundamental astronomy and celestial mechanics and the practical requirements of astronomical navigation. It was largely due to him that the Royal Air Force had such excellent almanacs and tables during the Second World War. Since then the provision for astronomical navigation, both at sea and in the air, has been much expanded and is now completely unified with that in the United States. Mr Sadler has contributed much to the theoretical side of navigation and has been awarded the premier awards of both the British (Gold Medal, 1957) and the American (Thurloew Award, 1948). Institutes of Navigation, he was president of the British Institute during the period 1955-56. He is at present general secretary of the International Astronomical Union, and he was secretary of the Royal Astronomical Society during 1939-47. During the Second World War he also directed the computational side of the highly successful Admiralty Computing Service.

Senior Principal Scientific Officer

MR J M CRADDOCK is serving in the assistant directorate of Dynamical Research in the Meteorological

Office of the Air Ministry and is engaged on research into the problem of long-range weather forecasting.

MR F J BRADSHAW, of the Metallurgy Department, Royal Aircraft Establishment, is a fertile research worker on the physics of metals.

MR A G EARL, of the Guided Weapons Department, Royal Aircraft Establishment, is a research engineer who has studied the fuel system and control systems of guided missiles.

DR H KOLSKY, of the Armament Research and Development Establishment, after a distinguished outside career devoted mainly to the mechanics of solids, has recently joined Dr Hopkins at Fort Halstead.

DR E H MANSFIELD, of the Structures Department, Royal Aircraft Establishment, has studied mathematical aspects of aircraft structural research, most recently in connexion with the effects of kinetic heating.

DR A H COOK (National Physical Laboratory, Standards Division) is primarily engaged in the accurate measurement in absolute terms of certain physical quantities and constants.

MR C G GILES (Road Research Laboratory) has conducted research aimed at finding ways of reducing the number of road accidents due to skidding.

DR A C HULME (Ditton Laboratory of the Food Investigation Board, now of the Agricultural Research Council) works on various aspects of the biochemistry and physiology of apples and other fruits, especially on biochemical changes in respiration during storage.

MR A SILVERLEAF (National Physical Laboratory, Ship Division) is in charge of the group responsible for research and design in the fields of ship propulsion, cavitation and vibration.

DR E H RHODERICK joined the Services Electronics Research Laboratory in 1955 and is working at present on very fast switching for computers using superconductors.

MR S B KENDRICK, of the Naval Construction Research Establishment, is an authority on the design of submarine pressure hulls.

Similar promotions have been made by

(1) U.K. Atomic Energy Authority
Deputy Chief Scientific Officer

DR G E BACON spent the war years at the Telecommunications Research Establishment on the development of ground radar equipment, particularly aerial systems. In 1946 he joined the Atomic Energy Research Establishment at Harwell, where he has worked on the application of X-ray and neutron diffraction to the study of the solid state. He is known especially for his work on the structural crystallography of graphite and for neutron studies of hydrogen bonds and thermal motion in hydrated and organic substances.

Dr W B THOMPSON took up a Harwell Senior Fellowship in 1950 and is now the senior theoretical physicist working on the problems of fusion reactors. His section of the Theoretical Physics Division carries out mathematical investigation into the stability of high current gas discharges, on the rates of loss of heat from gases at temperatures of more than a million degrees centigrade, and on the effects of magnetic fields on the bulk and particle motions of highly ionized plasmas. The work includes interpretation of the many fundamental experiments in this field carried on in all parts of the world and assessment of its significance to the building of a theory good enough to allow final success in the fusion reactor field.

Mr R W WALKINSHAW is one of Britain's leading particle accelerator theoreticians, joining the Telecommunications Research Establishment in 1940 where he carried out theoretical research on radar and on high-energy particle accelerators. He has worked at the Atomic Energy Research Establishment, Harwell since 1951. His section of the Theoretical Physics Division is very closely associated with the Rutherford Laboratory of the new National Institute for Nuclear Research, and has been engaged principally on the large 7,000 MeV proton synchrotron which is still under construction. In addition to this continuing task, the group is charged with the duty of conceiving new types of accelerating machines and specifying designs for other machines of tested types.

Senior Principal Scientific Officer

Dr K. W. BAGNALL is at Harwell in charge of a section of the Radiochemistry Branch of the Chemistry Division which is concerned with research into the chemistry of the actinide and other heavy elements. At present, the main interest is in protactinium.

Dr A M LANE is part of the team of theoreticians whose task it is to ensure that the Atomic Energy Authority is fully armed with the most up to date and reliable knowledge of nuclear physics.

(2) Agricultural Research Council Deputy Chief Scientific Officer

Dr R L MITCHELL joined the staff of the Macaulay Institute for Soil Research Aberdeen, in 1937. He

is deputy director of the Institute and head of the Department of Spectrochemistry. Dr Mitchell has been responsible for the development of spectrochemical methods applicable to the analysis of soils, plants and related materials, involving the evolution of techniques and equipment for arc, spark and flame emission methods. The chemical concentration technique is now quite widely used throughout the world and many overseas workers have visited the Macaulay Institute to study the spectrochemical methods developed by Dr Mitchell and his co-workers. More than sixty publications describe methods employed and the valuable results obtained in the study of trace element relationships in soils and plants and of the geochemical background to their occurrence. The work of his department also includes the use of infra red and ultra-violet absorption methods for the examination of organic and inorganic soil constituents.

Senior Principal Scientific Officers

Dr N J BERRIDGE is a member of the staff of the National Institute for Research in Dairying and is well known as an authority on rennin.

Dr ALAN ROBERTSON, of the Agricultural Research Unit of Animal Genetics, Edinburgh is widely recognized as one of the most successful students of the rapidly expanding subject of population genetics.

Dr V P WHITTAKER, of the Agricultural Research Institute of Animal Physiology, Babraham Cambridge, has done outstanding research in the cholinesterase field.

(3) Development Commission Senior Principal Scientific Officer

Dr J W G LUND is in charge of the Freshwater Biological Association and has made important contributions to the understanding of the factors which by controlling the annual phytoplankton cycle determine the fertility of lakes and reservoirs.

(4) Nature Conservancy Senior Principal Scientific Officer

Mr J G SKELLAM is head of the Biometrics Branch of the Nature Conservancy, contributing to mathematical biology, and in particular to theoretical study of population dynamics and statistical ecology.

CONCEPTION OF EVOLUTION

MEETING IN PARIS

THE Muséum National d'Histoire Naturelle celebrated on June 5 the anniversaries of the "Procédures et Fondations de l'évolutionnisme—Buffon Lamarck, Darwin" the 250th anniversary of Buffon's birth the 150th anniversary of the publication of Lamarck's "Philosophie zoologique", and the centenary of Darwin's "Origin of Species". The meeting was held in the famous Grand Amphithéâtre planned during Buffon's administration, and which reconducted about four years ago, is again used for its original purpose. A large and distinguished audience including many famous scientists, some of whom have long been retired, was present.

Prof Roger Heim, director of the Museum, gave an opening discourse, first summarizing the pre-Buffon period with his customary clarity and grasp of essentials. If in this he appeared to stress the views of naturalists of the old Jardin du Roi it was inevitable, for naturalist philosophers were almost confined to France at the time—and to the Garden. There were clear statements about transformism before Buffon, and equally there was a belief in the fixity of species after him. An upholder of this was Bosc, one of the founders of the Linnean Society of Paris in 1788 the same year as that of London was started. One of the first acts of the society

was to petition for the erection of monuments in the Garden to the memory of famous scientists, beginning with that of Linnæus, later destroyed by *sans-culottes*.

Prof Jean Piveteau, of the Sorbonne, a well-known authority on Buffon, gave an account of his personality with particular reference to his ideas on evolution, how they developed and how, at times, they seemed incompatible. A valuable commentary gave the reasons for this, both psychological and diplomatic. Few men are so misjudged in Great Britain as Buffon. He had an enormous influence on the thought of his time. He was a man of wide scientific attainments and in every way a man of the world. His Discourse on Style, delivered on his admittance to the Academy of Sciences in August 1753, has given him his place in literature. This celebrated discourse was read at the meeting by M. Toni Taffin of the Comédie-Française. The audience was obviously thrilled to hear the sonorous phrases which probably all had read—there were at least sixty editions of it in the nineteenth century.

Dr J. Ramsbottom followed with an account of the lives and work of Jean Lamarck and Charles Darwin. Lamarck first postulated progressive evolution, Darwin put the doctrine of evolution on so sound a basis that it became generally accepted. It was a pleasing acknowledgment of Darwin's epoch-making "Origin of Species" that he should be given a prominent place in what was essentially a celebration of French achievements; moreover, it was logical in realizing that it was the book and not the preliminary announcement of natural selection which was important. So Lamarck and Darwin could be spoken of as searchers after truth without some of the nonsense which has been allowed to belittle the former. Comparing the basic ideas of the two—Lamarck held that an organism in a changing environment is stimulated to vary, Darwin that variation is independent of the environment. For both the environment—adaptive, physical and biotic factors, the last including competition, parasitism, etc.—is all-important. Natural selection is not active like artificial selection, but passive: an organism can live under certain conditions, or it cannot. Lamarck suggested that the simpler animals and plants would provide instructive facts. Evidence accumulated since the introduction of pure culture methods suggests that environmental conditions can produce definite inheritable changes, though not necessarily of the kind Lamarck propounded. The boosting up of penicillin production in *Penicillium chrysogenum* has much in common with what Darwin considered to be the effects of domestication.

Mme G. Duprat, librarian to the Museum, then gave an account of the career of P. J. Redouté,

born in 1759, who was artist to the Garden and painted many of the famous *vélins*. She showed a series of projections of portraits of Redouté and a large number of his paintings, several of which were of specimens from the Royal Botanic Garden at Kew. An exhibition was arranged in the corridor adjoining the amphitheatre showing many of Redouté's original paintings and a number of his published plates, also an announcement of his lectures. The Muséum d'Histoire Naturelle, as one of its main functions, acts as a teaching university. There are at present 24 professors who give courses of lectures covering a very wide field, but there are no degrees awarded as the result of examinations. The system is *sui generis*.

Prof H. V. Vallois, director of the Musée de l'Homme—attached to the Natural History Museum—gave a history of the Société d'Anthropologie, founded in 1857. In spite of the date the Society's beginning was in no way connected with the publication of the "Origin of Species"; indeed, it preceded it by six months. Social and physical anthropology in the widest sense have been the scope of the Society, and its activities, as outlined, make an impressive history. It is noteworthy how Darwin's name became increasingly prominent after the publication of his "Descent of Man" in 1871. Cuvier, the great exponent of catastrophism, died in 1832, but though there was no successor to stamp out heresies his influence was such that Lamarck's beliefs were still discredited and it was not until Darwin amassed and arranged the evidence that inquiries about the status of fossil man became scientifically respectable.

The last paper, by M. Franck Bourdier, assistant chief of the Service de Muséologie, dealt with the French forerunners of evolution. They make an imposing list far outnumbering the combined total from all other countries. The notion of permanent change in organisms and that of evolutionary sequence stood out clearly. It would be useful to distinguish between them, possibly by speaking of the first as transformism and the second as evolution.

In an adjoining corridor an exhibit was arranged where the matter of this lecture could be studied at leisure and in greater detail. Here again Darwin was included as the end of the old period or as the beginning of the new.

In addition to this intellectual feast and as part of the anniversaries, an excellent exhibition was staged in the gallery of the Botanical Museum, dealing with the history of the doctrine of evolution and illustrating development up to and including man. Specimens, casts, models, photographs and all the modern methods of display provided a most instructive and convincing story.

J. RAMSBOTTOM

X-RAY MICROSCOPY AND X-RAY MICROANALYSIS

THE second International Symposium on X-ray Microscopy and X-ray Microanalysis was an independent meeting held in Stockholm in 1959, and sponsored by the same three laboratories as were responsible for arranging the first Symposium, held in Cambridge in 1956: the Department of Medical Physics, Karolinska Institutet, Stockholm, the Departments of Physics and Biophysics, Stanford University, California, and the Electron Microscope

Section of the Cavendish Laboratory, Cambridge. The attendance of 180 was 50 per cent greater than that at the previous meeting, although the number of papers presented (74) was not appreciably greater than before (66). The participants were drawn from seventeen different countries and from 120 different laboratories.

The programme was divided according to the nature of the physical techniques employed. X-ray

absorption microradiography, X ray emission micro analysis, and X ray microdiffraction analysis. Each division was sub-divided into sections on methodological aspects and equipment, technical applications and biological applications. The number of communications under these three cross-divisions was 43, 10 and 21, respectively, showing that the development of techniques is still enjoying most attention and that their application in biology and medicine is ahead of that in mineralogy and metallurgy.

In absorption microradiography, interest was mainly in the relative merits of the contact and projection techniques, only two contributions being concerned with the reflexion method, in which the correction of aberrations is still the main problem. For qualitative microscopy, all three methods at present have about the same limit of resolving power, at about 0.25μ . H. H. Patton (Stanford University) has investigated a number of alternatives to the photographic emulsion for recording the X ray image in contact microradiography, including radiosensitive dyes and plastics, some of which give images which can be enlarged in the electron microscope. J. H. Auld and J. F. McNeil (Aeronautical Research and Defence Standards Laboratories, Australia) showed that xerography with liquid developers allows a resolution comparable with that given by ultra fine grained X ray films and at exposure times similar to those of the fastest X ray films. In the projection method, improvements are being made in the technique of focusing at very high resolution (W. C. Nixon, Cavendish Laboratory) and in obtaining improved contrast (S. P. Ong and J. B. Le Poole, Delft). The main emphasis, however, was on the perfection of the absorption procedure for micro analysis, whether of particular elements (sulphur, phosphorus, calcium) or simply of the dry weight of biological tissues. The contact method has been developed for this purpose especially in Swedish laboratories, and improvements in the technique were described by Howling and Fitzgerald (New York), Hyden and Larsson (Gothenburg), Lindström and Holm (Stockholm) and Müller and Sandritter (Frankfurt am Main). The accuracy of analysis varies between 5 and 10 per cent, depending on the nature of the specimen. A detailed study of all the factors involved is being made by Henke (Pomona College, California), using red blood cells as standard specimen. In the projection method direct measurements can be made with a counter on the enlarged X ray image, thus eliminating the stages of photography and microphotometry, so that the accuracy of analysis is better. In determinations of calcium in bone, Long (Cavendish Laboratory, Cambridge) obtained 2-3 per cent accuracy. The smallest area which can be analysed is a few microns in diameter in either method, the limit being set by the light spot in microphotometry and by the counter aperture in projection recording. The ultimate mass sensitivity is of order 10^{-11} - 10^{-12} gm, since sections thinner than 10μ cannot be used.

The applications of absorption microradiography, by one or the other experimental technique covered a wide range of subjects. In the inorganic sciences, papers were concerned with mineral dressing, petrography and mineralogy, in biology and medicine, with bone (six papers), vascular systems (five papers), other animal tissues (four papers) including a wide survey by Saunders of Dalhousie University), plant tissues (two papers) and foraminifera (one paper). Most of this work was qualitative, only Lindström

(Stockholm) and Sissons (Institute of Orthopaedics, London) describing quantitative applications.

X ray emission microanalysis is more definitely a quantitative method, and rapid progress is being made with its development now that its value in metallurgy and mineralogy has been demonstrated. In biological research, where compounds rather than elements are of interest, its scope is much more restricted. The mechanism of emission is more complicated than that of absorption and in practice results are subject to a variety of corrections. The efficiency of X ray production by direct electron excitation was discussed by Archard (Associated Electrical Industries Research Laboratory, Aldermaston) and by Cosslett (Cavendish Laboratory, Cambridge), and the corrections for absorption and fluorescence by Philibert (Institut de Recherches de la Sidérurgie, Paris) and by Austin, Richard and Schwartz (Battelle Institute, Columbus). The factors limiting the spatial resolution (or localization) of the method were discussed by Duncumb (Cavendish Laboratory, Cambridge) the main factor being the very rapid decrease in electron beam current as the focal spot is reduced to less than 1μ in diameter. At present the practical limit is about 0.25μ , and further improvement must wait upon developments of the electron source, electron lenses and recording system. A great gain is attainable if a proportional counter can be used for wave length discrimination instead of a crystal spectrometer, and Dolby and Cosslett reported promising results with a counter of wide collection angle coupled to an electrical network which can separate the pulses produced by neighbouring elements in the periodic table.

Improvements in the design of microanalysers were reported from the laboratories of Associated Electrical Industries (Aldermaston) and Tube Investments (Hinxton) and from the Cavendish Laboratory. The Associated Electrical Industries instrument is now being manufactured by Metropolitan Vickers and the first model was on view during the meeting. The production of the scanning microanalyser developed in the Cavendish and Tube Investments laboratories, which displays images of the distribution of selected elements in the specimen was announced by the Cambridge Instrument Company. The original static spot instrument of Castaing is in production in France, and two similar instruments are now being commercially made in the United States. This activity has been stimulated by the great interest now shown in the method by metallurgists and mineralogists which was reflected in the papers on applications by Austin Long, Melford (Tube Investments) and Philibert. All elements with atomic number greater than 11 (sodium) can already be analysed, with an accuracy in favourable cases of better than 0.1 per cent. Since the localization of the analysis can be smaller than 1μ , in depth as well as in diameter, this corresponds to a minimum detectable mass of about 10^{-14} gm. As the range of applications is extended however it is becoming clear that the limits of accuracy must be more closely investigated in each special type of alloy or mineral. The work of Philibert on light alloys showed that very careful correction needs to be made for fluorescence effects as well as for absorption of X rays from one constituent by the others present. To reduce such corrections to a minimum it will be desirable to build up a collection of reference standards so that one may be selected which is as close as possible in composition to the specimen under

investigation. Comparison of the results obtained in three different laboratories, on the variation of nickel content across taenite inclusions in the same type of meteorite, indicated that standard methods of preparing the specimen must also be worked out. It was unfortunate that only an extended abstract was available of what would have been a most interesting paper by Borovski (Institute of Metallurgy, Moscow), who has independently developed the X-ray micro-analyser for metallurgical research. It appears that he has made great progress not only with standardizing the procedures, but also in the automatic recording of concentration curves. His main interest is in diffusion problems and in transfer processes between solid and liquid media.

In summary, it can be said that the omission microanalyser is leaving the stage of being an interesting piece of gadgetry and is now having to prove itself as a routine research tool, in the course of which its capabilities and limitations will become more clearly defined. In particular, it remains to be seen how far it can help in some of the main problems of ferrous metallurgy: exploratory determinations of carbon have already been made by Dolby, but what the limits of accuracy may be and whether carbon and nitrogen can be distinguished from each other are problems still to be solved.

The Symposium ended with two sessions on micro-diffraction, which becomes increasingly related techni-

cally to X-ray microscopical methods as the advantages of using micro-focus tubes are more widely appreciated. Further developments were described in the tubes themselves and in the spectrometers and micro-beam cameras used with them. The value of the method, especially in reducing exposure time to more practical limits when only very small crystals are available, emerged strongly from the work of Fournier (Centre National pour la Recherche Scientifique, Paris) on crystals from tumours, Mrs Kennard (National Institute for Medical Research, London) on a number of clinical problems, Skortchily (Textile Physics Laboratory, Leeds) on keratinization of hair, and Wylio (Royal College of Technology, Glasgow) on the growth of crystals in balsa wood. Quite different techniques have been developed for investigating dislocations and other substructures in metals, by combining Bragg diffraction with X-ray microscopy. Extensions and applications of this 'Berg-Barrett' method were described by Newkirk (General Electric Laboratories, Schenectady) and Weissmann (Rutgers University, New Jersey). Shimoda and colleagues (Osaka University) had used a transmission variant of the method to investigate the recrystallization of zirconium and its alloys on the micro-scale.

A third symposium is planned for 1962, and will probably be held at Stanford University, California.

V. E. COSELY

THE BRITISH GELATINE AND GLUE RESEARCH ASSOCIATION

THE seventeenth meeting of the Research Panel of the British Gelatine and Glue Research Association was held on June 25, with Mr S. G. Hudson (Richard Hodgson and Sons, Ltd.) in the chair. In the morning a review of certain aspects of the research of the Association was given by Mr A. G. Ward, for whom it was the last meeting as director of research, and in the afternoon a discussion on gelation took place, with the main contribution from Mr J. W. Janus (Kodak, Ltd.).

The review by Mr Ward was entitled "The Present Position in Gelatine and Glue Research". The paper opened with a reference to a previous review given by the author to the second Research Panel meeting nine years earlier, in which considerable attention was given to those methods of polymer physics and chemistry which were applicable to the study of gelatin. The expansion of research on gelatin now made it necessary to limit the paper to the central problem of the structure of the molecules of the many different types of gelatin. This largely left on one side research on the collagen-gelatin conversion and also on gelation, except where these subjects threw light on the molecular structure of gelatin.

The chemical composition of gelatine, and animal glue, were shown to depend on the amino acid composition of the gelatin itself, that is to say, of the collagen breakdown products, and on the occurrence and composition of rather small amounts of non-gelatin constituents. Separation procedures such as adsorption on activated charcoal, or 'IRC50' resin, enabled small quantities of gelatin-free impurities to be obtained and analysed, and examination of fractions prepared with isopropyl alcohol showed that about 1

per cent of degraded protein, other than gelatin, might also be present in the residue from fractionation. Using hydroxyproline content as a measure of purity, it was suggested that a total of 3 per cent of organic impurities might be present, although the variation in hydroxyproline content could equally be the result of small differences in composition between gelatin molecules.

Revision of figures for the amide content of gelatines enabled very good agreement to be obtained between the analytical figures for the ionizable groups in gelatin and the results of titration curve determinations. This shows that, within experimental error, all the carboxyl amino and guanidino groups are free to ionize and are not cross-linked. The accuracy attained did not make it possible to exclude the occurrence of a small number of cross links involving these groups.

The properties of preparations of well-characterized soluble collagen extracted from calfskin, carp swim bladder tunic and codskin, by Doty and co-workers, and their conversion of the soluble collagens to gelatin, could be explained in terms of dissociation of the triple-helix collagen structure. The gelatins obtained would, on this view, be single chains, free of cross-links. In contrast, first extract alkali process gelatins have been shown by Courts and Stainsby, using end-groups and light scattering determinations of molecular weight, to be multichain, at least for the higher molecular weights. The relation between these results was discussed.

The problem of explaining the reduction in gel-forming ability in gelatine caused by neutral and alkaline degradation, although not by acid degradation, as distinct from any effect due to the reduction

in molecular weight, still remained to be solved. Suggested explanations were put forward in terms of internal arrangements of the protein chains which upset the ordered arrangement required for a gel bond, or alternatively, that intra molecular cross linking occurs progressively on heating under neutral or alkaline conditions, and interferes with subsequent gel formation.

After a brief discussion Dr A Courts (British Gelatine and Glue Research Association), in moving a vote of thanks, expressed the appreciation of the staff of the help given to them by Mr Ward in his term of office. Mr C F C Simeons (British Gelatine Works, Ltd.), in seconding, added the thanks of the gelatine and glue industry.

Mr Janus, in opening the discussion on gelation, gave a short paper on "The Formation and Structure of Gelatin Gels". He described the measured properties of gels, the rigidity of the matured gel, the melting point and the setting time from the sol state, and showed how these depended on solution pH. He emphasized that setting might occur in a short time even at room temperature, whereas the gel rigidity increased over long periods at 0°C. The melting point was, however, much less influenced by low temperature maturing.

The influence of guanidino content on setting time and melting point was made clear, but not that on low temperature rigidity. Interference with setting can also be secured by alkaline copper solutions which

are presumed to interact with the >CO groups of the backbone. An interaction between guanidinium groups and the backbone was therefore postulated as the mechanism of the early stage of setting. To explain the continued growth of rigidity at low temperatures, reversion to the helical structure was suggested, and support was drawn from the optical rotation changes.

Dr R Collison (British Baking Industries Research Association) presented a short paper by Dr G A H Elton and himself on "The Swelling of Starch". In this he described the swelling of the granules in water as the temperature is raised, and effects on the mechanical properties. He also mentioned the action of surface active agents in controlling swelling probably by forming a hydrophobic layer on the granules.

Mr D D Carruthers (University of Durham) described measurements on gelatin gels at high frequency and discussed the dependence on temperature of the mechanical properties.

The general discussion was opened by Dr G Stainby (British Gelatine and Glue Research Association), who emphasized the difficulty of establishing precisely the mechanism of gelation. The vote of thanks to Mr Janus and the other speakers was moved by Mr E Bradbury (British Cotton Industry Research Association) and seconded by Dr A Jobling (British Glues and Chemicals, Ltd.).

ALAN G WARD

THE TORRY RESEARCH STATION, ABERDEEN

THE Torry Research Station in Aberdeen of the Department of Scientific and Industrial Research, which was set up in 1930 together with its sub station in Hull, the Humber Laboratory (opened in 1953) carries out research into the problems of fish preservation. The occasion of the open days during June 15-17 when the Station was on show to scientists, equipment manufacturers, the fish industry and the general public, provided an opportunity both of seeing the range of practically the whole of the research in the United Kingdom into fish technology and also of assessing how the treatment of the fish we eat is likely to change in years to come.

Although the fish industry has changed in numerous ways in the thirty years since Torry was opened it nevertheless remains largely "traditional", there are many small firms, mechanization to any substantial degree is found only in a few factories and with the exception of deep freezing, the methods of preservation used were familiar to our grandparents. Torry, which has been closely concerned in many of the changes which have occurred, is becoming more and more closely occupied with the technical development of the industry of the future. Changes are occurring at an increasing tempo and the next decade is likely to see a much greater alteration in both techniques and organization than the previous 30 years have done.

One of the major problems concerning our supply of white fish is that about half of it comes from Arctic waters. The fishing grounds are anything from three days to one week's steaming from the Humber ports, on which almost all the long distance trawlers are based, and this consequently sets a limit to the age

of the freshest fish that can be landed. Voyages are on an average of nearly three weeks duration and the fish caught first may therefore be 16-17 days old when it is landed. Cod and haddock even when properly stored in crushed ice remain in reasonably good edible condition for only 14-15 days. About 1 per cent per annum of the Arctic catch is in fact condemned at landing as unfit for human consumption. After landing the vicissitudes of the distribution chain may render possible fish unpleasant and good fish only possible.

Since the Second World War considerable attention has been paid at Torry to the problem of how to get fresher fish to the consumer. A promising solution is to build a trawler capable of freezing the first third of the catch. That the idea is practicable was shown in a full-scale trial carried out in 1955-56 under Torry's technical supervision and financed jointly by the Distant Water Vessel Owners' Development Committee, the White Fish Authority and H.M. Government. A Grimsby trawler was fitted with vertical plate freezers developed at Torry and capable of operating satisfactorily in the exacting conditions of Arctic fishing, and with a -30°C cold store. The frozen fish was distributed to consumers through out the country whose reactions were almost universally favourable. The latest development is the design of a vessel of normal size and cost which would show attractive economic advantages over existing high speed trawlers. Such a vessel would be a trifle slower than the latter, the extra 1-2 knots of which are disproportionately expensive to obtain. It could spend rather longer on the fishing grounds and therefore land a greater weight of fish. The frozen part of

the catch could be used to even out the supply from the summer glut to winter dearth

Another possible way of slowing down the rate of spoilage of fish is to use antibiotics such as chlortetracycline and oxytetracycline. Much of the pioneer work has been carried out in Canada, where their use is now permitted, but they may not yet be used in the United Kingdom. One of the major tasks in hand is to determine the quantities of these substances likely to get into and remain in the flesh after various types of storage, processing and cooking. Even those antibiotics most effective in fish preservation have limitations, there is little difference in the flavour of fish stored in plain water ice and in antibiotic ice up to about the tenth day, so that no more could be done than to keep fish that would otherwise become poor or very poor in a passable, but not really fresh, state.

A recent survey carried out by staff of the Humber Laboratory and workers seconded by the White Fish Authority of the temperatures of fish during distribution from unloading from the trawler to sale from the fishmonger's slab has stimulated considerable interest within the trade and is already bringing about improvements in practice. It represents another approach to the same problem of how the quality of fish reaching the consumer can be raised. This survey is probably the first large scale attempt in any country to obtain first-hand field data of this kind. It is typical of much of the work carried out at Torry, since it was made possible only by the co-operation of the industry and was initiated by discussion with representatives of the fish trade.

The Station necessarily supplements such practical applied investigations and development work with a considerable volume of basic research. Thus, a greater understanding is being sought of the detailed structure and composition of fish tissues, and of their behaviour during processing such as freezing and cold storage, smoking and drying. Knowledge is also being acquired of the composition of the bacterial flora of fish and the nature of the species mainly responsible for spoilage. Studies since the War have contributed to improvements in the taxonomy of the marine bacteria mainly concerned and in the building up of a type culture collection now of international reputation.

Solid progress in recent years in the characterization and estimation of the so-called 'extractives' of fish muscle is providing a clearer insight into the autolytic changes that take place immediately after death and during bacterial spoilage. This work is of particular importance in understanding the various physico-chemical changes that occur during dehydration, freezing and subsequent storage of fish, as well as the factors which give rise to different types of spoilage flora under various conditions. Recent years have also seen the accumulation of new knowledge of the main proteins of fish muscle which is serving in particular to explain the causes of textural change during freezing, cold storage and dehydration. Mention should be made of the work on the Maillard 'browning' reactions which occur in dehydrated fish muscle.

Considerable attention has been given to the prevention of oxidative rancidity in cold-stored fatty fish. Fish fats are highly unsaturated, and frozen fatty fish such as herring remain in really edible condition for a shorter period than white fish. The rate of oxidation of fish fat can be slowed down by 'glazing', this consists of dipping the frozen fish in

water so that a layer of ice is formed around the outside. Drying of fish in cold store hastens the development of rancidity, even more important, therefore, is to store fatty fish under conditions where drying is at a minimum. Current work on the oxidation process may eventually lead to economic improvements. It has been found that fat oxidation is catalysed by haematin pigments in the red lateral muscle which is present in a well-defined form only in fatty fish.

Nevertheless, there are limits to the cold-storage period even of species like cod which contain considerably less than 1 per cent fat in the muscle, the fat becomes oxidized and there are progressive changes in the protein structure common to all fish. Recently, a new method has been devised for assessing the development of toughness in cold stored fish. This depends upon the fact that although fresh unfrozen muscle can be mincerated in dilute formalin solution to give a thick opaque suspension, there is a tendency for the fibres of frozen fish to resist minceration and this resistance increases as a function both of storage time and of storage temperature. By determining the amount of light transmitted by the 'soup' of fish fibres produced under standard conditions it has been found possible to relate samples to a standard time/temperature curve. This test, the validity of which requires further checking to cover a number of variables, is so simple that it could easily be adopted by the fish freezing firms which, with one or two notable exceptions, do not employ scientifically trained staff and do not possess quality control or development laboratories.

Fish freezes more rapidly than it thaws, due to the difference of thermal conductivity through frozen and unfrozen tissue. For example, a block of fillets 4 in. thick may freeze in 4 hr. or so but may take 20 hr. to thaw out in air at ambient temperatures. A number of firms use large quantities of frozen fish for their products, for example, there is a variety of ready cooked fish products prepared initially from frozen fish and sold in frozen consumer packs, and the kippering industry uses large amounts of frozen herring when fresh herring is not available. At present, fish is thawed on a large scale, either by merely leaving the frozen blocks in air or by spraying with cold water. The latter method, if it is carelessly carried out, may adversely affect the quality of the product, and both methods are time- and labour-consuming. Attempts by workers in other countries to apply dielectric heating have not been successful, mainly due to 'runaway' heating. This is the condition in which there is progressively increasing absorption of the available power in warm spots in the blocks, which become cooked, this is at the expense of the cooler portions, which remain frozen. Recently this difficulty has been overcome and commercially available equipment has been slightly modified, a pilot plant has been running at Torry without trouble for the past six months or so. Blocks of frozen fish can be evenly thawed in about 15 min. The technological implications of this work are very wide indeed.

The commercial smoking of fish is still largely carried out in the traditional smoking kiln which was developed during the early Middle Ages. This is merely a chimney in which brined fish is hung and a sawdust and wood-chip fire lighted on the floor. The operation takes anything up to 12 hr. or more to complete. The irregularity of natural convection, and the effect of warm humid weather on the functioning

of the kiln, render fish smoking an art which is difficult to practise. In 1939 a mechanical kiln was developed at Torry which amplified the process and made it much easier to control. Although the industry was at first slow to adopt the new kilns, an increasing number of firms are now doing so. Intriguing possibilities are, however, now being suggested as a result of basic physical and chemical work on the composition of wood smoke. It has been shown that virtually all the smoke constituents on smoked fish are derived from the invisible vapour phase and not the visible particulate phase. The practicability of smoking fish with 'smokeless' smoke and further developments as well are envisaged.

There is a continuous programme of work at Torry on the improvement of the efficiency of conventional fish meal plant. Emphasis is put upon methods of

increasing production, plant efficiency and nutritive value of the product.

It is important to stress that the high standing of the Torry Research Station within the fish industry itself is very largely due to the considerable amount of consultation and discussion which takes place with the industry and not less important, the very good relationship built up between individual scientists and various people 'in the trade'. Much of the development and survey work carried out within the past ten years would have been quite impossible without the close and friendly co-operation of the industry, on this personal contact between government research workers and the industry the future development of this relatively undeveloped and traditional industry, without any research organization of its own, depends. G. H. O. BURGESS

FISHERY RESEARCH

DR BREDER has prepared a valuable review of work on social grouping in fish*. It also contains new data, though it is sometimes a little difficult to pick these out. He discusses in detail the various types of groups, the aggregation, where the individuals are not 'polarized', the school, where they are, and the pod, where the fish are in physical contact. These types of groups are illustrated by outstandingly good photographs, those of pods and fish in 'orderly files' being the most interesting.

Descriptions of new work are mainly of the effect of light intensity and colour on a number of species and the analysis of the internal structure of schools. In the experiments on the effect of the wave-length of light the fish were given a choice between different colours, the intensity of the different colours being equated photometrically. No attempt was made by determining the spectral sensitivity of the fish, to equate the subjective intensity, or intensity as it appeared to the fish. Of particular interest are Dr Broder's discussions on the leadership of schools, the school as a super-organism and the evolution of schooling behaviour. There is also a section on schooling in terms of cybernetics, where the point is made that the survival of a species which has grouping tendencies should perhaps be considered from the

point of view of how they have got over the danger involved, rather than that such tendencies automatically have survival value.

Dr Loukashkin and Dr Grant's work on *Sardinops caerulea**, a species of great commercial importance, has much in common with Dr Broder's but is more limited in extent. It is again well illustrated with photographs. Like other clupeoids, *Sardinops* is not an easy subject for experiment but results have been obtained which show the importance of light for the maintenance of school formation and that fright reactions are elicited by red lights and by flashing white lights. When given the choice between red, green, blue and white light, the fish avoided red and preferred blue and green to white. As in Dr Broder's work this technique has a limitation in that the intensities of the different colours were not equated subjectively but only photometrically.

This type of behaviour work, which may be considered important as an aspect of fisheries research is now being produced in much greater quantity than before the War, and it is particularly welcome to the fisheries research worker when it is concerned with species of commercial importance.

J. H. S. BLAXTER

* Bulletin of the American Museum of Natural History. Vol. 117. Article 6. Studies on Social Groupings in Fishes. By O. M. Breder, Jr. Pp. 893-482 + plates 70-80. (New York: American Museum of Natural History 1959.) 1.50 dollars.

* Proceedings of the California Academy of Sciences. Vol. 29. No. 15. Behavior and Reactions of the Pacific Sardine *Sardinops caerulea* (Olivier) Under the Influence of White and Colored Lights and Darkness. By A. B. Loukashkin and N. Grant. Pp. 509-518. (San Francisco: California Academy of Sciences 1959.)

THE ONTARIO RESEARCH FOUNDATION

THE annual report of the Ontario Research Foundation for 1958 (pp. 36 Toronto: Ontario Research Foundation, 1959) includes, besides the report of the director, Dr H. B. Speakman, a summary of the work of the various sections, a list of papers published during the year, the financial statement and details of the Board of Governors and professional and technical staff. There is also a list of grants for postgraduate studies in science for the period 1958-60, for which grants in 1958 totalled 145,204 dollars. In biochemistry three major projects, dealing with the development of an all temperature biscuit spread for the Defence Research Medical

Laboratories, tea, and the recovery of pure individual amino acids from wheat gluten after hydrolysis, were completed, and two major studies are in progress under the Rice Mills Fellowship. In chemistry, activity was maintained at a high level. The three-year survey of air pollution of the Hamilton area was completed while the development of gas chromatography proceeds apace. In a study of factors controlling the crystallinity of polymers, techniques developed for preparing polymers of butane with 50 per cent of crystallinity are being used to study the relation between the type of catalyst and polymer structure. A novel ion-exchange process for recovering ammonia

from ammonia-base waste sulphite-liquor has been developed and a pilot plant constructed. A comprehensive study has been continued of various sulphite-liquors and their fractions and has led to a patent application, there have been utilization studies on by-product lignin from the manufacture of vanillin, while research on phosphate glasses has been continued in the $\text{Na}_2\text{O}-\text{P}_2\text{O}_5-\text{H}_2\text{O}$ system centred largely on the constitution of sodium acid glasses of intermediate composition, using filter paper chromatography.

In engineering and metallurgy basic research was directed at the concentration of hematite by a combination of magnetic and mechanical methods or by roasting methods followed by magnetic separation. In work on dry magnetic separators the 'Fast Eccentric Drum Separator' has been developed to the point of commercial production. In basic research on the fatigue of metals three stages have been distinguished: (a) the first four thousand cycles, (b) a slow steady decline in cyclograph (magnetic test), and (c) the last 15,000-20,000 cycles in which the final crack is developing. A precision camera was designed and built for stress determination in X-ray work.

In the Department of Parasitology most of the work was a continuation of earlier projects, and

persistent effort has provided an understanding of the prevalence and mode of transmission of some of the many parasites of Ontario's wild animals. Similar studies on wild birds are in progress, and during 1958 the blood parasite of ducks, *Leucocytozoon simondi*, was successfully grown on tissue culture in test-tubes. Continued studies of two types of blood parasites of birds have shown that certain types of black flies transmit them to ducks, while others transmit them to ruffed grouse. In physics some fundamental work dealing with beams of electrons has been planned, while other projects included development of an atmospheric X-ray spectrometer, design procedures for dynamic pressure stages, determination of gas density by electron beams and high energy applications of electron beams. The Department of Physiography completed an extensive study of the fine sand fraction of representative soils and a five year environmental study of soya bean is nearing completion. Research on the chemical modification of wool continued in the Department of Textiles as well as a study of the colour fastness of spun dyed viscose yarn. Good progress is reported in the standardization of women's and children's garment sizes for the Canadian Government Specifications Board.

INSTRUCTIONAL FILM RESEARCH IN PENNSYLVANIA

THE Pennsylvania Instructional Film Research Program was established in 1947 and terminated in 1955. Jointly sponsored by the U.S. Army and Navy, it represents the largest piece of co-ordinated research yet carried out on the teaching film. Accounts of the early part of the research have appeared in *Nature*¹. It is the purpose of this article to complete the outline record by reviewing the last reports—now gathered into one volume².

The later work follows directly on the earlier, confirming it, filling in details and dealing with specific problems. But some new and interesting notions of a general sort arise in this process. The very last studies, 100-104, deal with training aids such as models and other apparatus that are not films. Two of the studies, 46 and 50, are related to the use of films in psychotherapy. These two studies, as well as study 60, are concerned with films which influence attitude. The main classes of films dealt with in the research have been those which impart information and those which teach perceptual-motor skills.

A number of the studies yield information of general practical use. For example, study 37 by Philip Ash and Nathan Jaspen—see report *SDC* 269-7-37—examines optimum viewing conditions. Using a small rear projection daylight screen in teaching a performance skill—the assembly of a gun breech block—the optimum viewing area was found to be a sector 60° wide and 12 screen-widths deep. Increasing distance from the screen beyond 12 screen widths led to much sharper loss of teaching effectiveness than increasing angle of view beyond that of the 60° boundary. Outside the optimum viewing area loss was greater under daylight than under dark viewing conditions. These results may be compared with those found for a standard size screen and projector by J. J. Gibson³: he found that within a sector up

to 90° wide and 7 screen-widths deep there was no loss in teaching effectiveness.

The Pennsylvania film research organization has always stressed that teaching films should be tested "with adequate samples of appropriate target audiences using reliable and valid tests", rather than by viewing panels. Nevertheless, assessing teaching effectiveness by a viewing panel remains often the only practical alternative. Study 57 by L. P. Greenhill investigates such assessing, and recommends a particular type of film analysis form (or questionnaire), this panel testing procedure being used to select the best of several films, or to improve the teaching effectiveness of a film still under production. Study 59 by A. L. Edwards provides a statistical methodology which might be used when assessing films by the panel method. The report on study 48 about making simple demonstration films with untrained personnel includes—as an appendix—a 'manual for minimum film production'.

Infra-red photography offers an excellent means of recording audience reactions—of children and others—under conditions of little or no visibility. But infra-red motion photography is expensive. Study 56, by L. P. Greenhill, investigates the less costly use of infra-red memo motion photography. This is essentially time-lapse photography. The photographs were taken on 16 mm infra-red film at the rate of one a second, a rate which appears sufficiently frequent to show most types of human activity. The record was synchronized with the events on the screen, by the synchronous drive of camera and projector, and more satisfactorily by the use of a mirror reflecting a small image of the screen into the camera—so as to appear at one corner of each memo record frame.

In one of the earlier Pennsylvania studies⁴ it was found that a rating profile for a film, showing peaks for an audience reaction of 'I am learning' and

vallays for a reaction 'I am not learning', provided a valid index of learning. The subjectively based graph was found to be highly correlated with one based on the results of an objective learning test. This finding—although it has yet to be fully established—has considerable importance in connexion with film research, because it justifies a simple procedure in place of the present elaborate one of objective testing. In some measure it is further confirmed by study 55. In this study, by Richard M. Fletcher, it was found that a team of competent assessors could shorten film commentaries without reducing teaching effectiveness considerably more when aided by a learning profile than when not so aided—in one case 26 as against 11 per cent. However, Richard M. Fletcher says that the results of this study should be interpreted carefully. In an interesting discussion of results he considers the implications of the reactions 'I am learning' and 'I am not learning'.

The notion of 'realism' as a factor influencing the teaching effectiveness of films has received attention in early Pennsylvania studies, in relation to viewing angle⁴, stereoscopy⁶ and colour⁷. It emerges as a more conscious notion in the later work. In study 49 on the validity of pictorial tests and study 47 on the use of films in a Thematic Apperception Test, iconicity is considered. This term derives from C. Morris's work. 'A sign is iconic to the extent to which it itself has the properties of its denotata'.⁸ The study of the features and combinations of features that lead to life-likeness in films has been called by the present reviewer 'simulaeconomics'. In listing eight hypotheses of film research it is possibly significant that the director of the Pennsylvania research should have given the sign similarity hypothesis first. 'That films whose signals, signs and symbols have high degrees of similarity (iconicity) to the objects and situations which they represent will be more effective for most instructional purposes than films whose signals, signs and symbols have low degrees of iconicity'.⁹

Report 40 provides a valuable bibliography of production, utilization and research on instructional films. It contains about 600 references dating up to

the early part of 1952 arranged alphabetically by author.

One or two of the early Pennsylvania studies have been criticized on the grounds that they are directed towards findings that are obvious in the first place. Perhaps more justifiably one or two other of the Pennsylvania studies have been criticized because they have been concerned with teaching in general rather than teaching with films in particular. The Pennsylvania research includes relatively little basic research on the film medium itself. In general the method has been to carry out experiments using the prevailing current picture cum-commentary type of instructional film, and consequently to improve that type.

But such comment on isolated studies and minor aspects of the Pennsylvania research seems almost out of place in view of the enlightened way it has been directed and all it has accomplished. In 1947 there was no body of experimentally attested principles about teaching films and no proved techniques of film research which thanks to the Pennsylvania work exist now. This work—which might so easily have been restricted to fulfilling limited training needs—has yielded results of value to teachers generally and to psychologists. Credit is due to the associate directors C. R. Carpenter and L. P. Greenhull who with some of their staff now form an organization at Pennsylvania State University that has already investigated the use of closed circuit television in university teaching.

C. DENTON PEGGE

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BLOOD GROUPING OF THE REMAINS OF SWEDENBORG

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EMANUEL SWEDENBORG was born on January 29 1688 and died in London on March 29, 1772. He was interred in the vault of the Swedish church in London. His remains were disturbed on several occasions, an account of these was given by Hultkrantz¹. The coffin was first opened in 1790, and there is little doubt that this unauthorized action made the removal of the skull possible. The vault was opened at least nine times between this date and 1816. It has been suggested that a skull was stolen from the coffin on two occasions between 1816 and 1817. In consideration of the vogue enjoyed by phrenology at this time this is not a remarkable fact. On the first occasion the instigator was prob-

ably the famous phrenologist Captain Holm whose collection already included the skulls of Alexander Pope and Casimir Péricr. The presence of a Swedenborg skull in his collection was disclosed to his niece in 1845, but regarded as a family secret. There is some evidence that Holm introduced a substitute into the coffin. In a letter to *The Times* of April 4 1823 Hawkins states that the skull was removed in 1817, by Captain Granholm a Swedish sailor for financial gain. On his death this skull passed into the possession of Wahlén, pastor of the Swedish church in London. A skull claimed to be that of Swedenborg was in the collection of Charles Tulk MP, in the years prior to 1823 and it is thought

interest in this work. One of us (J A H) is indebted to the Medical Research Council for a Scholarship

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Hæmoglobin 'Bart's': a Fœtal Hæmoglobin without α -Chains

In a previous communication one of us reported¹ that normal fœtal hæmoglobin (*F*) consists of two kinds of polypeptide chains. One of these (α) is identical with the α -chain of adult hæmoglobin, while the other (γ) is different from its adult counterpart (β) and seems to be characteristic of the fœtal form (To avoid confusion in nomenclature of the hæmoglobin chains, it has been decided to call the chains of hæmoglobin *F*, α and γ and not α and β -fœtal as in ref 1.) A fœtal hæmoglobin with an abnormally high anodic electrophoretic mobility was discovered at St Bartholomew's Hospital in an infant whose red-cell morphology resembled that seen in thalassæmia.² It was called hæmoglobin 'Bart's'. We have now found that this consists of γ -chains only.

Fresh blood from an infant with hæmoglobin 'Bart's' was made available by the courtesy of Dr H Kohler, of Birmingham. A purified solution, containing about 4 mgm of hæmoglobin 'Bart's' in 15 ml, was obtained by elution from paper electrophoretograms. This solution was adjusted to pH 6.9 and heated

in a boiling water-bath for 20 min to precipitate the hæmoglobin. This was dissolved in 0.1N hydrochloric acid and the hæm extracted with acid acetone.³ The dried globin was suspended in 0.6 ml of 2 per cent ammonium bicarbonate buffer at pH 7.9, and digested by addition of 0.05 mgm of trypsin at 38°C. After 2 hr the solution was evaporated and re-evaporated from acetic acid to sublime the ammonium carbamate formed. A solution of chromatographically purified hæmoglobin *F* (ref 1) of the same concentration was treated in exactly the same way in a parallel experiment. The digests were compared with a normal tryptic digest⁴ of hæmoglobin *F* by both one dimensional paper electrophoresis at pH 6.4 and by fingerprinting.⁵

The 'fingerprint' of hæmoglobin 'Bart's' is shown in Fig 1 in comparison with those of hæmoglobin *F* and the α - and γ -chains of hæmoglobin *F* (ref 1). It is apparent that all the α -chain peptides are missing from hæmoglobin 'Bart's' and that it consists solely of γ -chains. Its sedimentation constant is indistinguishable from that of *A* (R A Kokwick), which suggests that its molecular weight is about 68,000 and the globin a tetramer.

Jones, Schroeder, Balog and Vinograd⁶ have found that hæmoglobin *H* consists solely of β -chains of adult hæmoglobin associated in a tetramer. Hæmoglobin 'Bart's', therefore, is the exact counterpart in the fœtal system of hæmoglobin *H* in the adult system. Hæmoglobin *H* is only found in the presence of the gene for thalassæmia. The blood picture of infants with hæmoglobin 'Bart's' is like that in thalassæmia, but this does not persist into later life, nor do the children develop an abnormal hæmoglobin. There are then two possible explanations for the production of an all γ -chain hæmoglobin. There may be an over-production of the γ -chains. However, from our present data we cannot be certain that there does not exist a small chemical difference between the γ -chains in hæmoglobin 'Bart's' and those in hæmoglobin *F*. Alternatively, the production of α -chains may be inhibited, in which case, since the children with hæmoglobin 'Bart's' do not develop hæmoglobin *H*, the α -chains of hæmoglobin *A* and *F*, although chemically identical, do not appear to be controlled by the same gene. Thus in a Greek boy with thalassæmia in whom, as is typical for this condition, hæmoglobin *F* had persisted beyond the age of infancy, a small amount of hæmoglobin 'Bart's' was

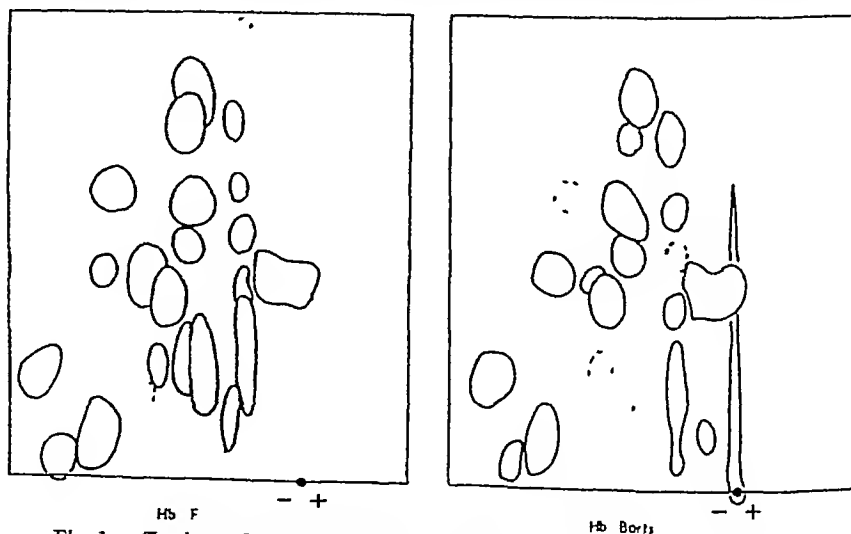


Fig 1. Tracings of fingerprints of the tryptic digestions of hæmoglobin 'Bart's' and hæmoglobin *F*.

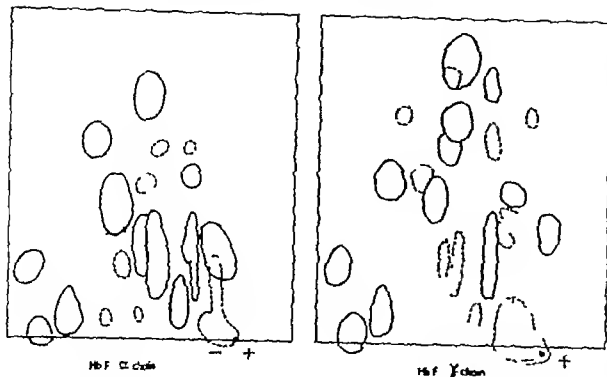


Fig. 2. Tracings of fingerprints of the tryptic digestions of the chains of hemoglobin F

also found but no haemoglobin H^a. This could be interpreted as demonstrating the independence of the production of the α chains for haemoglobins A and F. On the other hand in an adult woman from Israel with a thalassaemia like blood picture, more than 80 per cent of haemoglobin A and only traces of haemoglobin F were found, but 8 per cent of haemoglobin Bart's¹ and 5 per cent of haemoglobin H^a. Of her four children one also possessed haemoglobins A, Bart's¹ and H^a, but only a trace of F. This represents a strong inhibition of the fetal α -chain formation with only a weak inhibition of that of the α -chains for haemoglobin A.

Several infants with haemoglobin Bart's¹ have now been seen, always associated with normal haemoglobin F and it is interesting that in these infants the γ chains of fetal haemoglobin should be capable of a separate existence, even though α -chains are being produced for both haemoglobins A and F. No reports of haemoglobin consisting entirely of α -chains have yet appeared but it would not be surprising if such chains could also exist on their own.

One of us (J. A. H.) is grateful to the Medical Research Council for a scholarship.

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MECHANISM OF IMMUNOLOGICAL UNRESPONSIVENESS

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CONDITIONS of immunological unresponsiveness which vary in specificity, completeness and duration have been induced in newborn rabbits by administering small amounts of soluble proteins at birth¹⁻⁴, and in adult rabbits by the injection of massive doses⁵ of antigens, or by the prolonged administration of moderate amounts of antigens^{6,7}. In the hope of emphasizing pathways of antigen distribution that are essential for the establishment of an immune response studies were undertaken to determine whether the fate of labelled antigen in unresponsive rabbits differs from the fate in normal rabbits which are potentially responsive⁸. For this purpose, New Zealand white rabbits were rendered specifically unresponsive by means of repeated intraperitoneal injections of iodoproteins begun within 12 hr of birth⁹. The iodo-albumin and the iodo-bovine serum albumin which were injected contain 8-10 per cent of iodine and when injected intraperitoneally to normal adult rabbits they consistently evoke the production of precipitating humoral antibodies specific in part, for their determinant diiodotyrosine residues.

In no case, however, were precipitating antibodies found in the sera of rabbits which had been injected

repeatedly 4-6 months from the time of birth. The methods used to trace the iodoproteins were essentially the same as those employed in previous studies⁸. Preparations of the iodoproteins labelled with iodine 131 were injected intravenously to normal and unresponsive rabbits. Measurements were made after intervals of 2 min-24 hr of that portion of the persisting iodine 131 that was insoluble in aqueous 7 per cent trichloroacetic acid and in neutral alcohol and acetone. Because the radioactive iodine is an integral part of the determinant groups of the iodoproteins, it is felt that measurements of protein bound iodine 131 trace the fate of material that is potentially antigenic, possibly in contrast to measurements of the total persisting isotope. It was found that the labelled iodoproteins were eliminated from the blood and distributed among the organs of unresponsive rabbits in the same way as in normal adult rabbits. After a day, less than 0.5 per cent of the total injected iodoprotein remained in the blood of rabbits of both types. Since the inability to form antibody induced by the present procedures does not result in a persistence or 'tolerance' of the antigens in the unresponsive rabbits there is no evidence that the iodoproteins are 'recognized as self' by the unresponsive rabbits or that the unresponsiveness depends on a mechanism for eliminating the iodo-

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proteins more rapidly than normal. Inasmuch as the patterns of intracellular localization in the cytoplasmic granules of the livers and spleens of the unresponsive rabbits were exactly the same as those observed previously with iodo ovalbumin and certain azoproteins¹⁰, it is clear that the presence of foreign antigenic material in cytoplasmic granules, while possibly a condition that precedes or is necessary for antibody formation¹¹, is not in itself a condition that leads inevitably to the production of measurable amounts of precipitating antibody.

Of the many possible interpretations of these findings only one will be considered, namely, that the presence of antigen or haptene fragments of degraded antigen may actually function to forestall antibody formation. It is proposed that antibody formation is initiated as usual in a small number of susceptible cells whenever normal or unresponsive rabbits receive antigen. However, the first molecules of antibody that are formed are likely to encounter cytoplasmic granules that contain residual antigen derived from the final injection, or (in the case of unresponsive rabbits) partially degraded haptene residues remaining from previous injections of antigen. Intracellular antigen-antibody reactions at appropriate loci could release the hydrolytic enzymes that are normally retained within the membranes of granules such as the lysosomes¹².

If the damage inflicted on essential structures by the reaction itself, or by the enzymes released or activated through the reaction, were sufficient to annihilate such cells, there would fail to be established a permanent line of cells that possessed the specific information necessary for antibody formation during the time when undegraded, antigenically potent antigen was still present in the rabbit. Direct evidence is already at hand that the addition of antigen to tissue breis or to sera that contain specific antibody results in the activation of proteases¹³⁻¹⁵. It is anticipated that a similar activation will follow the addition of antibody to sera, to homogenates of tissue, or to subcellular fractions that contain specific antigen. Damage by proteases that are activated by immunological reactions has been suggested repeatedly over the years^{14,16} as a reasonable basis for pathological changes at the tissue-level that occur in states of hypersensitivity. The present suggestion is that under certain conditions such damage would not extend beyond individual cells in which antibody formation had been initiated. The fact that induced immunological unresponsiveness is not permanent, unless antigen is continually administered⁴, is attributed to the gradual loss (by degradation or by dilution) of haptene residues from the potential antibody-forming cells, or to a fortuitous asymmetric distribution to daughter cells of the discrete granules that contain the antigen.

Many more data are required before it will be possible to decide whether a number of phenomena already recorded in the literature are manifestations of some of the cellular events postulated here. Insurmountable difficulties may confront attempts to assign microscopically visible effects unequivocally to macroscopically imposed causes, particularly when the effects that are judged as pertinent to the argument could be exceedingly rare events. Nevertheless, it may be significant that degenerating, fragmented nuclei are found beside viable, primitive cells in the germinal centres of the lymphoid follicles, particularly during the natural immunization that accompanies bacterial infections¹⁷. This paradoxical phenomenon

is enhanced by immunization with antigens ordinarily regarded as innocuous. Since a few molecules of antigen may be adequate to initiate antibody formation, while a relatively large amount of antigen may be required to ensure complete annihilation of antibody-forming cells, it is possible that the remarkable action of adjuvants (see ref. 18) is to minimize the flood of antigen into the cytoplasmic granules of potential antibody-forming cells so that survival is more probable if the improbable events occur that culminate in antibody formation.

It is noteworthy that application of the fluorescent antibody techniques of Coons to adult rabbits has shown that antibody is rarely detectable in cells that take up antigen, where devastating intracellular antigen-antibody reactions would be possible¹⁸. Moreover, the antibody within germinal centres of stimulated lymph nodes is limited not only to individual cells, as in the medullary area, but occurs also "over an area of the follicle involving a number of cells in an indistinct way, often with a particulate distribution between the cells as well"¹⁹. Antibody distributed in this manner may correspond to debris from cells which undertook antibody production while excessive amounts of antigen were still present in cytoplasmic particles. On the other hand, antibody, but rarely antigen, is easily detected in members of the plasma cell series^{19,20}. The superficial injury that plasma cells are liable to suffer as a result of an extracellular antigen-antibody reaction, rather than causing cell death, may form what is frequently overlooked by many theorists, a concrete basis for the specific proliferative stimulus that must underlie the secondary response. The mechanism which must be modified (or selected) in order for appreciable amounts of antibody to be formed appears to reside in cells that are highly sensitive to X-irradiation. Once it is established, however, the antibody-forming mechanism is remarkably radioresistant²¹. Although cells with different morphological properties appear to be involved at the beginning and at the end of the overall process of antibody formation, the striking qualitative differences of these cells with respect to radioresistance might depend upon the cellular locus of antigen-antibody reactions, rather than a fundamental change in cell type. Perhaps death is an inevitable sequel to X-ray damage in cells that are also damaged by intracellular antigen-antibody reactions, while antibody-forming cells may survive X-irradiation in the absence of additional intracellular damage from antigen-antibody reactions. Very recently, it was suggested²² that X-irradiation destroys within minutes the ability of cells in lymphatic tissues to derive energy from nuclear phosphorylation reactions. The intracellular antigen-antibody reactions postulated here might be expected in addition to derange alternative, cytoplasmic reactions that otherwise could have produced energy utilizable for survival and for eventual repair of the X-ray damage.

Many previous theories of antibody formation have failed to provide adequate explanations for the fact that the secondary response is more intense than the primary response (for a discussion, see ref. 19). On the other hand, certain versions of the 'selection theory', which currently enjoys much favour²³, appear to neglect the same fact viewed from the other direction, that the primary response is much less intense than the secondary response. In the outline of the proposals presented here, the secondary response is assumed to depend upon a stimulation to

proliferate that is selective for lines of cells that have inherited, or otherwise acquired, the specific information needed to synthesize antibody, which information was initially established in the few surviving cells that were modified as a result of the primary encounter with antigen. The absence of a 'suitable environment' that was postulated to account for the failure of appreciable formation of antibody in new born rabbits, even when competent cells were transferred from normal adult donors, may depend upon a possible deficiency of metabolites essential for survival and necessary to repair the intracellular damage caused by antigen-antibody reactions in individual cells where antibody formation was initiated.

That transfer to new born rabbits of lymphatic tissue from immunized donors is followed by formation of antibody¹¹ would depend upon the existence in the transferred tissue of cells in which the antibody forming mechanism is free from potentially lethal intracellular antigen. Natural tolerance towards self materials and experimentally induced tolerance towards homografts, where many of the antigenic determinants that are involved still await chemical characterization, may also depend upon the selective destruction of cells in which auto-antibody formation is initiated. The accidental survival of a few such cells if followed by the passage of the antibody forming mechanism into cells that are impervious to 'antigen', would explain the development of conditions of auto immunization.

The finding that isodoproteins appear to undergo the same fate in unresponsive rabbits as in normal rabbits has suggested simple mechanisms which might account for specific unresponsiveness and for a number of other immunological phenomena. However, it is clear that the experiments have not clarified the ultimate problems of where and how the information necessary for the synthesis of a specific combining site is materialized or whether this information exists in cells prior to a primary injection of the antigen.

A complete and more critical account of the experimental studies which form the basis of this discussion is being prepared for publication. This work was supported by the United States Public Health Research Grants E 1290 and E 1296(7). We are indebted to Dr Joshua L. Edwards for many informative and stimulating discussions, and for making available the opportunities and facilities that made the studies possible. One of us (F. R. F.) has received support from US Public Health Service RG 4801 (C251) (May 13).

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HYDROGENATION OF LIPIDS BY RUMEN PROTOZOA

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IT has been observed by several workers that dietary unsaturated fats are modified in the rumen by hydrogenation. Shorland, Woonink and Johns¹ found that the fatty acid composition of ingested plant material was considerably changed by rumen contents. In particular the high content of linolenic acid was markedly reduced, being converted mainly to stearic acid. This work was confirmed by Shorland, Woonink, Johns and McDonald² when they demonstrated that rumen contents *in vitro* could hydrogenate oleic, linoleic and linolenic acids. Other studies on hydrogenation include those by Hofflund, Holmberg and Sellmann³ using cows fed linolenic acid, Reiser and Reddy⁴ with goats fed on a diet supplemented with unsaturated oils, and more recently Garton, Hobson and Lough⁵ with sheep. The type of micro-organism responsible for the hydrogenating activity has not been determined in these studies.

It has been observed that some species of protozoa are able to ingest chloroplasts.⁶ Since chloroplasts are rich in lipid material, particularly unsaturated

fatty acids, it was thought likely that these ciliates may be responsible for at least some of the hydrogenation occurring in the rumen.

Rumen contents were collected from a rumen fistulated cow fed on fresh red clover (*Trifolium pratense*) and the protozoa allowed to settle by gravity. Microscopic examination of the protozoa showed a mixed population of holotrichs and oligotrichs the latter group being mainly Epidinia. Washed suspensions of the ciliates were prepared by the procedure described by Oxford⁷ using an acetate-bicarbonate-phosphate buffer containing penicillin and neomycin. After washing to free them of bacteria, the protozoa were suspended in the buffer with antibiotics to which the substrate and clover starch were added. The flasks were incubated under carbon dioxide at 38° or 4°. After overnight incubation the lipid material was extracted from the solution by acidifying with hydrochloric acid and extracting with petroleum ether. The fatty acids were isolated by the usual methods and their iodine numbers calculated by the Hanus procedure. Under three

Table 1 HYDROGENATION OF SODIUM LINOLEATE AND LINSEED OIL BY A SUSPENSION OF RUMEN PROTOZOA

| Incubation temperature | Substrate | Iodine number |
|------------------------|------------------|---------------|
| 4° | Sodium linoleate | 162.0 |
| 38° | Sodium linoleate | 101.2 |
| 4° | Linseed oil | 160.0 |
| 38° | Linseed oil | 120.0 |

conditions, hydrogenation of both linoleic acid and linseed oil was found (Table 1)

The hydrogenation of chloroplast fat was next examined by incubating protozoa with chloroplasts. A suspension of chloroplasts was prepared by grinding freshly picked red clover leaves in an end-runner mill with a sucrose-phosphate buffer solution⁷. After removing the fibrous material by filtration through muslin, the filtrate was centrifuged at 100*g* for 10 min to remove large plant particles and the supernatant centrifuged at 1,500*g* for 20 min to sediment chloroplasts. The chloroplasts were suspended in the acetate-bicarbonate-phosphate buffer plus antibiotics and equal volumes added to two 100-ml conical flasks containing washed protozoa suspensions, one of which had been placed in a boiling water-bath to destroy enzyme activity. The flasks were flushed with carbon dioxide and then incubated at 38° C, provision being made for the release of gas from the flasks.

After incubating overnight, the boiled control sample was still green in colour, but the test sample was coloured yellow, indicating breakdown of chlorophyll. The samples were freeze-dried and the lipids extracted by boiling with diethyl ether. The ether solutions were evaporated to dryness, taken up in petroleum ether and the solvent removed *in vacuo*. The lipids were saponified and fractionated into water-soluble, non-saponifiable and fatty acid fractions. The fatty acids were converted to the methyl esters and analysed by gas-liquid chromatography. Considerable differences were noted between the test and control sample fatty acids (Table 2).

The composition of the C¹⁸ acids in the boiled control sample is typical of red clover chloroplast lipid (Weenink, R. O., personal communication).

Table 2 COMPARISONS BETWEEN C¹⁸ FATTY ACID COMPOSITION OF CHLOROPLAST LIPIDS INCUBATED WITH LIVE OR DEAD RUMEN PROTOZOA

Fatty acids weight per cent

| Sample + Chloroplasts | Saturated | Unsaturated | | |
|-----------------------|-----------|-------------|-------|---------|
| | | mon- | di- | tri-ene |
| Live protozoa | 17.5 | 10.6 | 27.6 | 44.3 |
| Boiled protozoa | 10.7 | 16.2 | 2.8 | 70.3 |
| Difference | +6.8 | -5.6 | +24.8 | -26.0 |

There has been considerable conversion of trienoic acid to dienoic acid and monoenoic to stearic acid. Only a slight conversion of diene to monoenoic seems to have occurred. This is rather surprising since it was shown above that protozoa could hydrogenate linoleic acid. Reiser⁸ suggested that rumen contents convert linolenic acid merely to linoleic acid although Shorland *et al.*¹ showed further hydrogenation of linoleic acid to monoenoic and saturated acids. Since a considerable amount of linolenic acid still remained in these protozoa experiments, there must have been an excess of unsaturated lipid present and it may be possible that the enzyme or enzymes responsible for hydrogenation show some degree of specificity and attack the trienoic and monoenoic acids preferentially. Since little is known about the mechanisms of enzymic hydrogenation, this must remain speculative at the moment.

The non-saponifiable material from both samples was yellow in colour, had similar intensities and spectra typical of a carotene-xanthophyll mixture. In spite of the carotene being highly unsaturated, little hydrogenation of the pigment has occurred. This is in agreement with the observations made by Shorland, Weenink, Johns and McDonald².

In spite of attempts to wash the protozoa clean of oxalate bacteria, some bacteria were undoubtedly present inside the ciliates. Their role in hydrogenation is difficult to assess, but it seems likely that they were not present in great enough numbers to have much effect. Preliminary experiments using washed suspensions of rumen bacteria suggest that bacteria do not contribute a great deal to the hydrogenation occurring in the rumen. It is interesting to speculate whether fluctuations in the population of protozoa could be correlated with the seasonal variation in iodine numbers of milk fat noted in New Zealand⁹.

Further studies on the role of bacteria and individual species of protozoa in lipid metabolism are in progress. I would like to thank Miss J. Michael for technical assistance, and Dr J. C. Hawke and Miss J. Cook, of the Fat Research Laboratory, Wollington, for the gas-liquid chromatography data.

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FORMATION OF THE PORPHYRIN RING

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IT is generally agreed that the naturally occurring porphyrins arise through the condensation of four molecules of porphobilinogen (I). However, it has proved very difficult to formulate a sequence of reactions leading uniquely from porphobilinogen to the type III and type I porphyrins. Several years before any of the reactions leading to porphyrin

formation were recognized, Turner¹ had realized that the essential clue to the understanding of the cyclization of the porphyrin ring was to be found in the behaviour of tripyrrylmethanes, established by Corwin *et al.*^{2,3} Shemin, Russell and Abramsky⁴ and Bogorad and Granick⁵ have elaborated these ideas. In the course of the isolation of isotopically labelled haem from duck red blood cells⁶, Shemin

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of 0.1 M ammonium acetate solution was added and the resulting solution (pH 7.1) was incubated at 37° C for 24 hr. The incubated solution was freeze-dried, which removed most of the excess ammonium acetate. The product was dissolved in water (1 ml) and treated with ethanol (3 ml). The precipitate was recovered by centrifugation, dried and shaken with a small volume of 0.05 M calcium chloride solution. The insoluble fraction was recovered and dissolved in the minimum volume of hot water. On cooling, crystallization occurred. The insoluble material was recrystallized from hot water. The crystals were isolated and dried *in vacuo* at 60° C over phosphorus pentoxide. Yield approximately 6 mgm. Similar material was isolated from reaction mixtures containing cell extract. In both cases the product was calcium dipicolinate according to the following criteria: (1) appearance of the crystals, (2) extinction coefficients at 2700 and 2775 Å, (3) the infra-red spectra of both products which agreed exactly with that of natural calcium dipicolinate, (4) paper chromatography using Whatman paper (No 1 or 4) and butanol/acetic acid/water (4:1:5 v/v, upper phase) as solvent. The spots corresponding to the products and authentic calcium dipicolinate were visible when the dried paper was viewed with a source of ultra-violet light ('Chromalite' lamp) and had the same R_F value. When the paper was sprayed with a solution containing ferrous ammonium sulphate (0.1 per cent w/v) and ascorbic acid (0.1 per cent w/v) in 0.5 M acetate buffer, pH 5.5 (ref 8), the spots turned pink.

The formation of dipicolinate in the absence of oxygen uptake can only be explained in terms of an oxidation-reduction reaction occurring between the products of the reaction of diketopimelic acid with ammonia, and perhaps diketopimelic acid. Identification of products other than dipicolinate has not been attempted, but paper chromatography of reaction mixtures showed that a number of compounds is produced. When the effect of oxidizing agents on the reaction was studied it was found that quinone had an effect similar to that of cell extract on the rate of production and final yield of ultra-violet light absorbing product. Fig 2 shows the rate of production of material absorbing at 2700 Å in the presence and absence of quinone. The absorbency values were affected by the formation of hydroquinone, but increased formation of dipicolinate in the presence of quinone was confirmed by paper chromatography. It is possible that the oxidative system in bacterial cells acts in a similar way to quinone and the reduced system is then oxidized directly or indirectly by atmospheric oxygen.

Attempts to demonstrate diketopimelic acid as a constituent of sporulating cells of *Bacillus cereus* were unsuccessful. In these experiments, deproteinized cell extracts were treated with 2,4-dinitrophenylhydrazine and the keto-acid derivatives were extracted with ethyl acetate and chromatographed on paper⁹. Comparison spots of the 2,4-dinitrophenylhydrazones of α -ketoglutaric, oxaloacetic, pyruvic and α -diketopimelic acids and of acetone were run on the same paper. The chromatogram showed derivatives of pyruvic acid and acetone to be present but no diketopimelic acid could be detected in 120 mgm (dry weight) of cells. However, it was found that when diketopimelic acid was added to cell suspensions which were then disintegrated, treated with reagent and chromatographed, the dinitrophenylhydrazone of this keto acid could not be

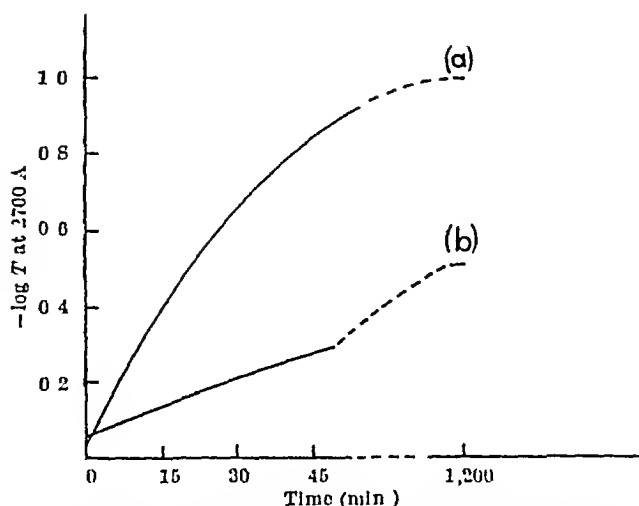


Fig 2. Effect of quinone on the formation of dipicolinic acid from diketopimelic acid and ammonium salt. (a) Reaction mixture (1 ml) contained diketo acid (2 mgm), calcium carbonate (1 mgm), ammonium acetate (4 mgm) and quinone (0.1 ml sat aq solution). Control solution contained no diketo acid. (b) As for (a) but without quinone. Solutions incubated at 37° C and samples treated as in Fig 1.

detected. A negative result was probably due to the rapid reaction of the keto acid with endogenous ammonia when the cells were disrupted.

Attempts to implicate α -diketopimelic acid as a precursor of α -diaminopimelic acid in bacterial cells were unsuccessful. Reaction mixtures after incubation of cell homogenate with keto acid and either ammonium chloride, glutamic acid, glutamine or aspartic acid were tested for the presence of diaminopimelic acid using the solvent system of Rhuland *et al*¹⁰. Unheated cell homogenates were tested in these experiments and pyridoxal phosphate was added. No diaminopimelic acid was detected in samples of reaction mixture initially containing 130 μ gm of the keto acid.

In an interesting article on the pyridine ring and the problem of its biosynthesis, Grimshaw and Marion¹¹ have suggested that the pyridine ring might be built directly from smaller units arising from alanine and glycine or possibly from non-nitrogenous precursors and ammonia. Martin and Foster¹² have reported two possible pathways of dipicolinate synthesis in *Bacillus megaterium* involving either pyruvate and aspartate or alanine and oxaloacetate. The experiments reported here are of interest in this connexion, and we consider that even though diketopimelic acid has not been demonstrated as a cell constituent, its reactions with ammonia in the presence and absence of cell extract suggest some interesting possibilities.

We wish to thank Mr S Lovett for synthesizing α -diketopimelic acid and Dr K P Norris for infra-red spectrophotometry. We are grateful to Dr D H Herbert, Mr E O Powell and Major L H Kent for useful suggestions and discussion.

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HIGH-RESOLUTION FIBRE OPTICS USING SUB-MICRON MULTIPLE FIBRES

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IN various image transmitting applications of fibre optics^{1,2} using the light conduction property of fibres because of total internal reflexions, it is desired that the fibres have a high light transmission, complete optical insulation and diameter as small as possible. The information density in a perfectly insulated fibre bundle is dependent only on the fibre diameter, which has been limited by mechanical properties of the fibres and the basic diffraction phenomenon. This latter limitation, due to diffraction, has not been investigated in the past^{3,4}, and it had been believed that only fibres larger than 10-20 wave lengths in diameter are capable of conducting energy. For smaller diameters, it was believed that the energy escapes from the fibre wall due to the diffracted wave striking at angles less than critical incidence.

This is found not to be true for circular cross-section straight fibres down to approximately two wave-lengths in diameter. Fibres as small as 0.75 μ in diameter have been drawn using the newly developed technique of 'multiple fibres', and found to give acceptable light transmission. Whereas diffraction effects occur for fibres of smaller diameter, it has been found that the effective numerical aperture of the emergent diffracted light cone from a straight fibre of diameter greater than two wave-lengths of light is not substantially in excess of the numerical aperture of the lens system required to resolve clearly the fibres at the image pickup end. On the other hand, all the emergent flux is received when a photodetector or photographic plate is placed in contact with the emergent end. Thus high resolution, as well as high light efficiency, is achievable using the more recent techniques in fibre optics.

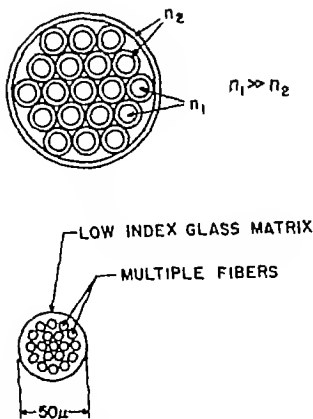


Fig. 1 Illustrating the method of drawing multiple fibres

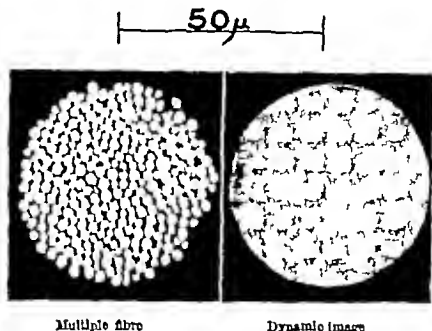


Fig. 2 Photomicrograph of grid object through a 50 μ overall diameter multiple fibre consisting of approximately 275 fibres of 2.5 μ average diameter

A method for drawing high refractive index fibres coated with a glass of low refractive index consists, essentially, of placing a high index rod in a low index tube and pulling the assembly down to a fibre on a continuously rotating drum⁵. Fibres down to 25 μ diameter with a coating thickness of 0.5-1 μ have been drawn in nominal infinite lengths. In addition to optically insulating the fibre, the coating, also eliminates surface absorption or scattering losses. A 7 ft long glass-coated glass fibre is found to transmit an average of 20 per cent in the visible spectrum and nearly 50 per cent in the yellow green region. However, such fibres become very difficult to handle mechanically in diameters much smaller than 25 μ .

A new type of 'multiple fibre' consisting of a large number of fibres of high refractive index in an insulating matrix of low refractive index has been developed. They have the mechanical strength of large fibres and resolution yield of much smaller fibres. Fig. 1 shows a method for drawing multiple fibres. A large number of high refractive index rods are inserted in low refractive index tubes and the entire bundle is placed in a larger tube of compatible glass. This unit is then drawn into a fibre on a continuously rotating drum. The cross-section of resultant fibres is also illustrated in Fig. 1. The ratio of the parent rod to tube thickness etc., is maintained in the fibre form. Multiple fibres down to 50 μ overall diameter, consisting of as many as 275 fibres of approximately 2.5 μ diameter, have been drawn by this method. A high information density is thus achievable. The mechanical advantages of manipulating and fusing fibres down to a few microns in diameter by this technique are obvious.

Fig. 2 shows a multiple fibre of overall diameter 50 μ , with average fibre diameter of 2.5 μ . A dynamic picture of a grid test object through this multiple fibre is also shown in Fig. 2. Limiting static resolution of up to 200 lines/mm has been measured in such an assembly of multiple fibres. As is indicated by further

diffraction studies, the resolution obtained thus far is not the upper limit for the fibre optical systems.

In order to study the optical properties and diffraction effects in smaller fibres, multiple fibres ranging between 0.75μ and 20μ in diameter have been drawn. This was achieved simply by choosing parent rods and tubes of different diameters. A multiple fibre was placed on a microscope in which both the numerical apertures of the condenser and the objective could be varied along with the wave-length of light. Fig. 3 illustrates this apparatus diagrammatically. The image of the multiple fibre is formed on a photodetector for the purposes of photometry of fibres of various diameters. Interference filters were introduced in the path, thus different ratios of wave-length of light to fibre diameter are obtained. From elementary considerations, it is clear that due to the diffraction by the fibres, as the objective N.A. is decreased, the photodetector would receive less flux per unit area from fibres of smaller diameters.

Multiple fibres ranging from 0.75μ to 8μ diameter, 0.2 in long, were thus studied on the above-mentioned system. Two wave-lengths peaked at $386\text{ m}\mu$ and $663\text{ m}\mu$ with half band-width of 125 \AA were used. The condenser numerical aperture was varied from 0.4 to 0.8 and the objective N.A. was varied from 0.3 to 1.33 . Within this range of N.A. and wave-lengths, for fibres above 0.75μ diameter, no measurable difference in flux density was observed. For smaller N.A. of the objective, however, one might expect the effects to show up. On the other hand, for such small objective N.A. the fibres fall close to the resolution limit of the system used for image pickup. Fig. 4 shows various diameter multiple fibres that were examined in this manner and a 0.75μ diameter fibre is indicated by an arrow. In Fig. 4a, it should be noticed that some fibre separations are of the order of one wave-length, which is the desired thickness, in order to prevent light leakage between neighbouring fibres ($d > \lambda$) due to frustrated total reflection⁵. Very small quantities of light were observed

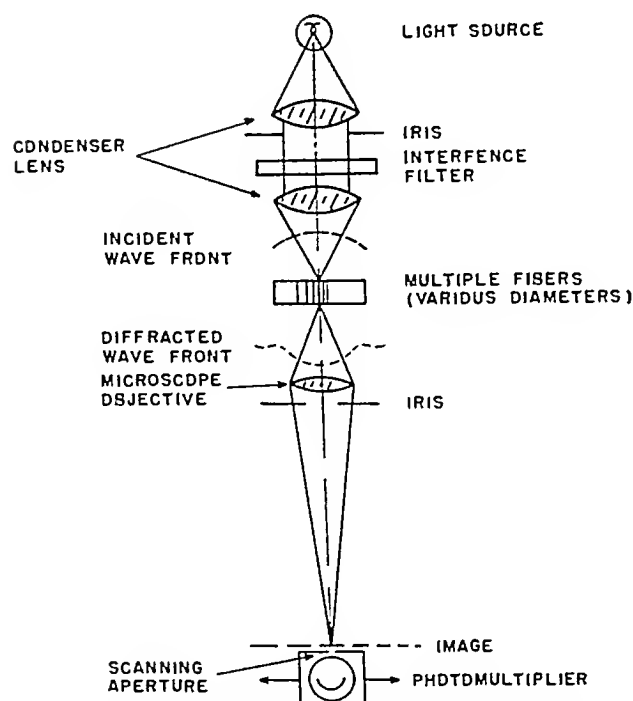


Fig. 3 Illustrating the optical system for studying the flux density in the diffracted wave by multiple fibres of various diameters

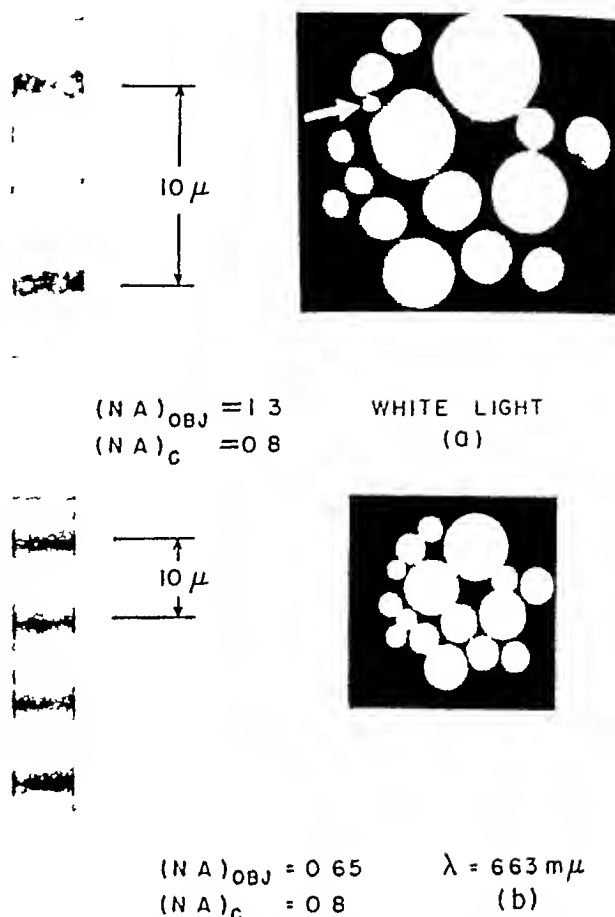


Fig. 4 Photomicrograph of variable diameter multiple fibres (0.75 – 8μ diameter) obtained on the optical arrangement in Fig. 3. A 0.75μ diameter fibre is pointed out by the arrow.

between adjacent fibres. This is attributable primarily to the diffraction effects in the microscope objective and perhaps to a lesser degree to light scattering by the low-index medium that may experience large amounts of stress. In Fig. 4b the fibre separation is not observable because the low-index coating falls near the threshold of limiting resolution of the 0.65 N.A. objective. The optical insulation of these fibres was also tested by forming the image of a knife edge and observing the intensity gradient in the transmitted image.

From the results of these experiments, and basic theoretical studies, the following conclusions are derived. To a first approximation, the diffraction in straight circular fibres above two wave-lengths in diameter occur primarily at the two ends. The incoherent wave incident on a fibre suffers diffraction at the entrance dielectric aperture. The diffracted wave then suffers total reflexions and phase changes along its passage in the fibre until it arrives at the emergent end, where it suffers diffraction again. Thus, of course, assumes that the refractive index of the fibre core and surround is such that the critical angle conditions for the wave in the fibre are satisfied. It is clear that for a plane monochromatic incident wave, as the diameter of the fibre decreases, so the emergent diffracted cone angle increases. On the other hand, as the fibre diameter goes down, so the required N.A. of the optical system receiving the image from the fibres goes up, in order that full use is made of the smaller diameter fibre resolution. For smaller fibres ($d > \lambda$) the limiting resolution of the optical system is set by the fibre coating ($\approx \lambda$). Thus,

most of the energy emerging from fibres down to 1μ in diameter is received by the appropriate N.A. optical system. These conclusions are also substantiated by a parallel study using microwave analogues of fibre optics at 1.25 cm wave-length and polystyrene cylinders. Theoretical and experimental studies of diffraction by fibres smaller than the wave-length and the boundary wave skin effect are now in progress.

From the foregoing it is evident that the optical performance of fibres down to a few microns in diameter do not suffer due to diffraction effects. An appropriate assembly of 1μ diameter fibres is capable of a static resolution of 500 lines/mm and dynamic resolution of nearly 1,000 lines/mm. Fibre optics in the ultra-violet region are capable of even higher

resolution. Multiple fibres have rendered such fibre optical systems practical. The impact of these investigations on such applications of fibre optics as flexible endoscopes, field flattener and image transfer from Lambertian emitters is evident. These results are also relevant to some basic studies of the visual mechanism in the retinal rods and cones.

Acknowledgment is due to A. Brushenko and D. F. Capellaro for valuable assistance.

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PALAEOMAGNETIC STUDIES OF CENOZOIC VOLCANIC ROCKS IN NEW ZEALAND

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POSTULATED reversals of the geomagnetic field offer a potential tool for the chronological subdivision and correlation of lavas within a restricted volcanic province¹⁻⁴. On a broader scale they provide potential world wide datum planes of virtually instantaneous time significance so far as most geological processes are concerned. For reversals to be useful for long range correlations, not only must their reality be established, but also the length of time between reversals must not be too small in comparison with the time duration of stratigraphically separable stages. An early Pleistocene reversal as postulated by Roche⁵, Hoopers⁶, Ennasson⁴ and others should prove to be of considerable importance in Pleistocene chronology if it is established that only one such simultaneous reversal occurred during Pleistocene time. On the other hand, it may be much more difficult to establish contemporaneity of early- or pre-Tertiary reversals. Detailed study of many well-dated suites will be required to demonstrate whether long range correlation of reversals can be effected, and if so, to determine the date at which each reversal occurred. Data from some New Zealand rocks are here recorded as a contribution towards the solution of these problems. Correlations of New Zealand stages follow the table of Hornbrouk⁷.

1 *Pleistocene*. Ignimbrite sheets of the Whakamaru district, North Island, New Zealand, are normally magnetized⁸. According to J. Healy (personal communication), they probably belong to the Haveria or late Castledillonian stage (Upper Pleistocene). Tholeiitic basalt at Timaru overlying gravels of the Waitotaran (Upper Pliocene) to Nukumaruan (Lower Pleistocene) and possibly itself of Nukumaruan age (Gair, H. S., personal communication) is found to have reverse magnetization (north pole directed downwards dip 75° , declination 228°).

2 *Late Middle to Upper Miocene*. The directions of magnetization have been measured of more than fifty suites of rocks from the Dunedin Volcanic Complex, which has been divided⁹ into an Initial, and First, Second and Third Major Eruptive Phases. Each suite consisted of 3-8 (usually 5-6) specimens collected where possible over some tens of yards of

exposures in road cuts, quarries and cliff sides. Results from exposed, craggy outcrops are not here considered. Collections were made from sequences of flows in localities scattered over an area of about 12×15 miles. The results from each suite have been treated by Fisher's method to obtain the mean directions which are shown in the figures.

Basalts, trachyte, phonolites, and trachyandesites from the First and earlier parts of the Second Major Eruptive Phase all indicate essentially normal magnetization (Fig. 1). In contrast, all flows sampled from the upper part of the middle sub phase (2M) and the late sub phase (2L) of the Second Major Eruptive Phase (above flow 21 of the North Head sequence¹⁰) show reverse or anomalous directions of magnetization (Fig. 2). Basalts, trachyandesites and phonolites are plotted the basalts being the most consistent. Dotted lines join points representing mean directions of magnetization calculated from two localities in the one

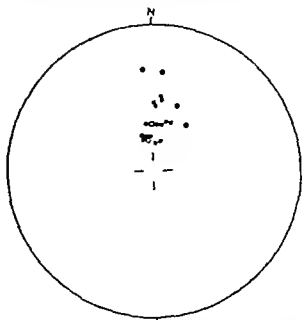


Fig. 1. Directions of magnetization for lavas of First and earlier parts of Second Major Eruptive Phase. Dunedin district plotted on equal area projection. ● North pole directed upwards on equal area of confidence 50 per cent (level $< 75^\circ$). ○ North pole directed upwards radius of circle of confidence, 60 per cent (level 12-15). □ direction for asymmetrical axial dipole field latitude 45° .

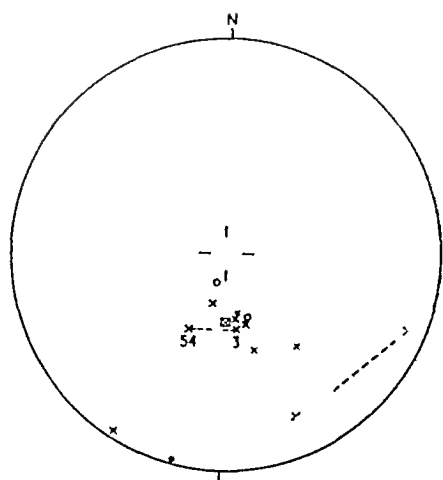


Fig 2 Directions of magnetization for lavas of the upper-middle and late sub phases of the Second Major Eruptive Phase, Dunedin district. X, North pole directed downwards, radius of circle of confidence, 5 per cent level, $< 12^\circ$; x, north pole directed downwards, radius of circle of confidence, 5 per cent level, $12-20^\circ$; X, north pole directed downwards, radius of circle of confidence, 5 per cent level, $> 20^\circ$; O, north pole directed upwards, radius of circle of confidence, 5 per cent level, $< 12^\circ$; O, north pole directed upwards, radius of circle of confidence, 5 per cent level, $12-20^\circ$; □, direction for reversed symmetrical axial dipole field, latitude 46° S

flow (for example, Roslyn doleritic basalt, 3 and 54) The Leth Valley trachyandesite and some similar flows of this period are weakly and erratically magnetized in directions which are consistent only in that they are abnormal. These have not been plotted. We can detect no consistent trend with time for these abnormal directions, and instability is possible, although 'magnetic cleaning' experiments of several types have failed to make them significantly more consistent. Three basalts and two weakly magnetized phonolites of the Third Major Eruptive Phase give normal directions while two other weakly magnetized phonolites correlated with the same period show anomalous declinations (Fig 3).

There is thus a fairly clear sequence normal—reverse (plus anomalous)—normal in this petrographically diverse volcanic complex. The age of the earlier First Phase volcanics has been established¹¹ as later Waiuan (latest Middle Miocene) or possibly early Tongaporutuan (earliest Upper Miocene). The upper age limit is not clear although activity probably did not extend far into the Pliocene. If the hypothesis of world-wide contemporaneity of reversals is accepted, a plausible correlation of the reverse period

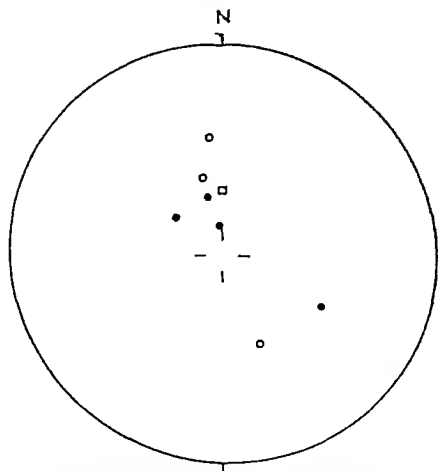


Fig 3 Directions of magnetization for lavas of the Third Major Eruptive Phase, Dunedin district. Symbols as for Fig 1

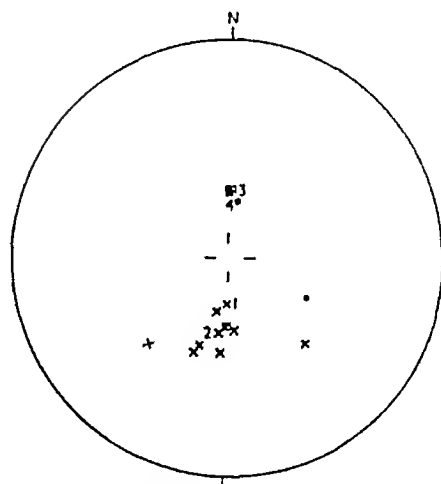


Fig 4 Directions of magnetization for Upper Eocene-Lower Oligocene volcanics of north-east Otago. Symbols as for Figs. 1 and 2

would be with the Upper Miocene-Lower Pliocene (Pontian-basal Plaisancian) reversal reported in France^{3,5}, but the possibility that it represents an earlier reversal within Upper Miocene time cannot at present be eliminated.

3 *Eocene-Lowermost Oligocene* Pillow lava (1), and a dolerite sheet (2) at Oamaru, North Otago, together with a series of dykes and other intrusions of dolerite at Moeraki Peninsula, show reverse magnetization. The results plotted (Fig 4) have been corrected for post-consolidational tilting. The pillow lava occurs above tuffs correlated with the Kaikō stage and immediately below tuffs and tuffaceous limestone bands with microfaunas of Kaikō or Runangan age, that is, earlier or later Upper Eocene (Hornibrook, N de B, and Marwick, J, personal communication). The Moeraki rocks are also placed in the Kaikō or Runangan stages on microfaunal evidence (Scott, G H, personal communication), whereas the Oamaru sheet is Whangaroan (earlier Lower Oligocene)¹². A dyke (3) and sheet (4) at Enfield, North Otago, of approximately the same age have normal magnetization.

An Upper Eocene period of reversal is indicated. The evidence does not show whether this continued through to Lower Oligocene times, or whether one or more periods of normal magnetization intervened. The North Otago results are also of interest in that, together with the later Tertiary and Pleistocene results, they do not suggest any measurable polar wandering with respect to New Zealand since Late Eocene times.

We are grateful for the assistance of a number of colleagues. Dr A J R White has given much help in the field, and a grant to one of us (D S C) from the University of New Zealand Research Fund is gratefully acknowledged.

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LETTERS TO THE EDITORS

ASTROPHYSICS

Observations of the Fine Structure of Enhanced Solar Radio Radiation with a Narrow-Band Spectrum Analyser

THE different components of the solar radio emission at metre wavelengths were classified according to their spectral properties by Wild and McCready¹ in 1950. In this classification the noise storm or type 1 radiation is characterized by a relatively steady enhancement over a wide range of frequencies, usually with short-lived, narrow band bursts superposed (storm bursts type 1 bursts). With equipment of high resolving power, these bursts may be resolved into pips, each lasting for a fraction of a second only.

Observations on single or multiple closely spaced frequencies with high speed recording facilities have hitherto given valuable information about the pips. At the Solar Observatory at Harestua a double channel receiver was run during solar noise storms in 1957. The recordings revealed that the very short pips often occurred at slightly different times in neighbouring channels.² This was then interpreted as being due to a frequency-drift of the pips. Such time differences could not be detected by de Jager and van T Veer in the 200 Mc/s range or by de Groot around 400 Mc/s (ref. 3).

In order to obtain more complete information about the transients, a narrow band swept receiver has been set up at Harestua. In principle this receiver is a double conversion superheterodyne. The sweep is performed in the first local oscillator by variable permeability techniques. A frequency range of 25 Mc/s from 100 to 215 Mc/s is swept fifty times per second with a resolution of 0.3 Mc/s. The output is displayed on a cathode ray tube, with provisions for amplitude and intensity modulation. The screen is continuously recorded on film, and frequency and time marks are inserted at suitable intervals. The spectrometer is connected to the giant Würzburg aerial of the Observatory. The sensitivity is uniform over the entire frequency band.

Some very interesting results have now emerged from the observations. Many pips are found with frequency drifts, and it is important to note that drifts in both directions that is to lower or to higher frequencies are about equally likely. The drift rate commonly amounts to some 2-5 Mc/s per sec but may also well be higher. In some cases, very irregular frequency drifts exist whereas at the other extreme the pips may be quite stable. As a rule the half power band width of a pip is less than 5 Mc/s. The mean line profile of five radio pips was found to be symmetrical within the limits of error and was only slightly broader than a Gaussian distribution.

On August 18 a very remarkable fine structure was found in the 200 Mc/s radiation. This day was characterized by strong optical activity. Interferometer observations gave a position line for the radio source coinciding with a region 30°W on the northern hemisphere where several flares occurred.

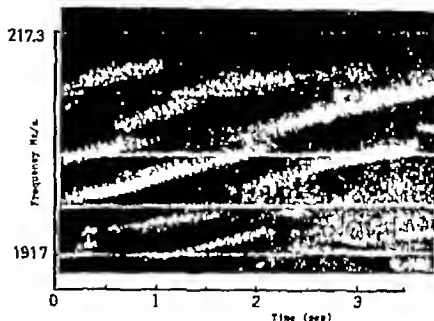


Fig. 1. Narrow band bursts with regular frequency drift from lower to higher frequencies (Distance between calibration marks 0.4 Mc/s).

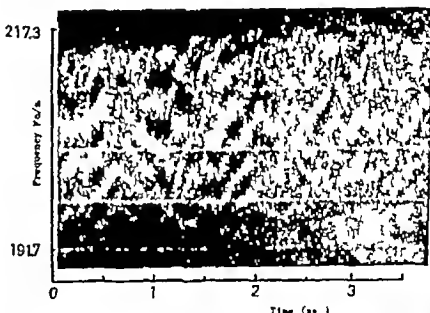


Fig. 2. (Complex pattern with drifts in all directions)

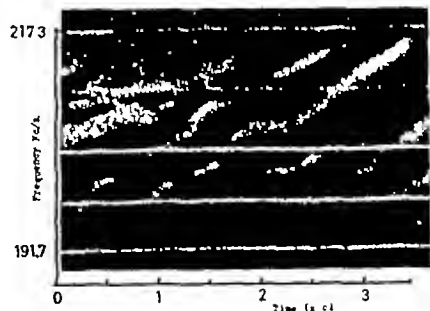


Fig. 3. Burst with possible echo

The radiation was nearly completely polarized. Between 14h 28m UT and 14h 36m UT typical storm bursts appeared on the total power record of the interferometer. On the radio spectrometer, however, these bursts were most interesting. Typical examples are shown in Figs 1, 2 and 3. On Aug. 18

bursts are seen which have a band-width of about 2 Mc/s and a sharp cut-off at the low-frequency side. The duration as measured on a single frequency is less than a second, whereas the total life time amounts to 2-3 sec. All bursts show a regular frequency drift from lower to higher frequencies at a rate of approximately 2-4 Mc/s per sec. In Fig 2 the general pattern is complicated, with a most irregular drift, but some kind of order exists, as simultaneous bursts on different frequencies appear to have similar frequency-time paths. Examples of probable echo effects were also recorded. One of them is reproduced in Fig 3.

There is good reason for believing that the recorded bursts are of solar origin. They are definitely not generated in the receiver, nor, at the present moment, can I see how such effects can be produced by terrestrial interference or exceptional ionospheric conditions.

These preliminary observations show that the phenomenon of frequency drift is not confined to the type 2 and type 3 emissions, but is also found in the fine structure of type 1 radiation, although here on a smaller scale. The storm bursts are probably more complicated than has been supposed, but as the wide-band radio spectrographs have been powerful tools in the investigation of the large-scale structure of the solar radio emission, there is reason for believing that high-resolution spectrometry would give a most valuable insight into the fine structure of the storm phenomena.

The results of a more detailed investigation of the spectrograph records will be published elsewhere.

My thanks are due to Mr G. Eriksen for assistance with the equipment. The investigation is being sponsored in part by the U.S. Air Force (ARDC, European Office).

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¹ Wild, J. P., and McCready, L. L., *Aust. J. Sci. Res.*, A, 3, No. 3 (1950).

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Evidence for Cosmic Ray Energy Spectrum Changes During a Forbush Decrease

THE multiplicity of neutron production in a conventional neutron monitor, though not a rapidly varying function of incident particle energy, might be expected to be determined by the spectrum of incident particles. During the Forbush decrease which started on May 10, and for a considerable period previously, one half of the Sydney neutron monitor was connected to a scaler with a paralysis time of 500 μ sec as well as to the conventional recorder. The purpose of the second scaler is to study changes in multiplicity, and its operation is as follows.

A single interaction in the lead of the monitor structure often produces more than one neutron, so that the normal recording system, which has a resolving time of a few μ sec, can record several counts for a single incident particle. The lifetime of the neutrons in the structure is about 150 μ sec, so the long paralysis time of the second scaler effectively ensures that it will record only one count per incident particle. Thus the difference between the readings of the two scalers for the same time-interval gives a measure of the number of 'multiple' neutrons produced, and the ratio

of this quantity to the rate of the scaler with the long paralysis time is related to the average multiplicity.

In particular, let N_1 be the daily count of the scaler with short paralysis time, and N_2 that of the other. To search for multiplicity effects we have examined the variation of the quantity

$$m = \frac{N_1 - N_2}{N_2}$$

The values of N_1 and N_2 on a typical day are 300,000 counts and 250,000 counts, and the value of m is 0.2.

Taking the period April 1-May 6, 1959, and deriving the standard deviation from the actual scatter in values

$$m_1 = 0.1980 \pm 0.001$$

During the period of the decrease, that is to say from May 7 to approximately May 31

$$m_2 = 0.2085 \pm 0.0006$$

and even from June 1 to July 5,

$$m_3 = 0.2013 \pm 0.0007$$

The daily values and the monitor counting rate are shown in Fig 1. Corrections to these values of m for the dead times of the scalers, and the detection of multiple neutrons after 500 μ sec are small and relatively constant. It seems likely that the interactions in the monitor during the period of the decrease in rate were of higher than average multiplicity, which corresponds to an increased proportion of incident particles of high energy.

The Sydney group is operating an underground spectrometer, located in a tunnel under about 60 m water equivalent of rock. Statistics are not good, but no change in rate greater than a few per cent occurred during this period. The spectrometer was operating at zero field at the time, and the minimum energy detected was about 13 GeV.

We are thus drawn to conclude that the mechanism of this decrease was such that the rate was lowered by removing particles from the low-energy end of the cosmic-ray spectrum, which agrees with work on the dependence on latitude of Forbush decreases. In view of the interest shown in the mechanism of the Forbush decrease it would seem to be worth while to attach a second scaler with a long paralysis time to

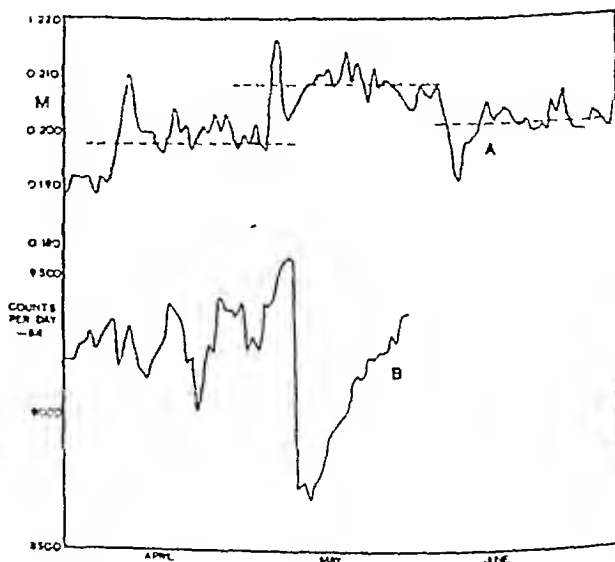


Fig 1

other monitors to confirm this observation. A circuit responding only to events with recorded multiplicity greater than two or three could be used also, and might give a larger effect. One cannot however expect a rapid variation of m with energy, especially since the monitor is designed to maximize the rate by the use of a thick lead neutron producer.

K. W. OGILVIE
M. M. WINN

The F.B.S. Falkner Nuclear Research Laboratory,
School of Physics,
University of Sydney
July 15

GEOPHYSICS

Diurnal Variation of Aurora and Geomagnetic Disturbance at New Zealand Antarctic Stations

THE diurnal variation of auroral incidence for Scott Base (New Zealand) and Hallett Station (United States-New Zealand) during the International Geophysical Year is shown in Fig. 1A. Curves derived from analyses of concurrent visual and all-sky camera observations are shown separately. The visual curves are based on observations during all hours which have $\frac{1}{2}$ or less cloud cover and the all-sky camera curves on photographs in which the Southern Cross is visible (exposures Scott Base 20 sec., Hallett Station 15 sec., on Tri X film). The auroral frequencies were computed from quarter hourly data except Hallett Station visual for which virtually continuous observations were used. Thus higher density and also the greater sensitivity of the visual observations at Hallett Station for displays near the horizon and in the presence of moonlight, twilight and thin cloud lift the Hallett visual frequencies well above the photographic frequencies. The Scott Base visual curve is indistinguishable from the one obtained at Cape Evans during 1911, a period of sunspot minimum by the British (*Terra Nova*) Antarctic Expedition.¹

The diurnal variations of auroral frequency for the two stations are very similar in form and characterized by primary morning and secondary evening maxima. Such bi-modal frequency curves have been derived before and have been the subject of comment by Hulbert² who however, failed to ascribe any significance to them. Obvious considerations make it impossible to obtain full diurnal curves except at very high latitudes and this has retarded the study of the diurnal variation of auroral incidence, a subject which must have considerable bearing on the theories of aurora.

On the other hand geomagnetic disturbance can be studied for the full day at all latitudes. Following the 1932-33 International Polar Year, an analysis of the irregular magnetic disturbance D at ten high latitude stations led Stagg³ to postulate three zones with different characteristics in the diurnal variation of D . The outer zone ($\phi_m < 70^\circ$) is primarily governed by a 24 hr wave with the maximum in the evening, the maximum occurring at midnight at $\phi_m = 70^\circ$. For $\phi_m > 78^\circ$ the diurnal variation in D has again one dominant maximum but this is invariably in the forenoon. The transitional zone ($\phi_m = 70^\circ$ to $\phi_m = 78^\circ$) has a daily variation in D marked by two maxima, one in the morning and the other in the evening.

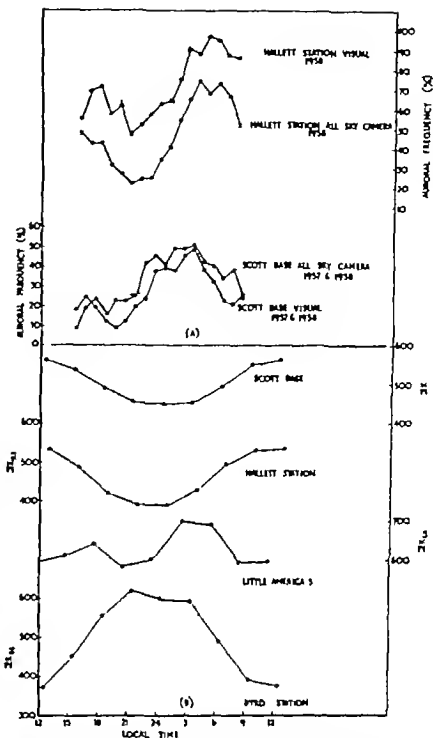


Fig. 1. A. Diurnal variation of auroral frequency Scott Base (mean of 1957 and 1958) and Hallett Station 1958. Visual and photographic data shown separately. X indicates sample less than 30. B. Diurnal variation of magnetic disturbance at several Antarctic stations for months March to September 1958 inclusive.

K indices measured during the International Geophysical Year have been used to derive the daily variations of magnetic disturbance at Scott Base and Hallett Station and at two other stations, Byrd Station and Little America 5. The co-ordinates of the stations are shown in Table 1.

Table 1 CO-ORDINATES OF ANTARCTIC STATIONS USED IN MAGNETIC DISTURBANCE ANALYSIS

| Station | Latitude | | Magnetic |
|------------------|--------------|-------------|-------------|
| | Geographical | Geomagnetic | Dip |
| Byrd Station | 80° 0' S | -70° 6' | Approx -75° |
| Little America 5 | 78° 2' S | -74° 0' | -79° 0' |
| Hallett Station | 76° 3' S | -74° 7' | -84° 8' |
| Scott Base | 77° 9' S | -79° 0' | -82° 0' |

K indices from these Stations for each 3 hr period have been summed for the auroral months March-September 1958 inclusive. The diurnal variation of EK for each station is shown in Fig. 1B. According to Stagg's classification, Byrd Station is in the outer zone, Little America 5 is in the transition zone, and Scott Base and Hallett Station are in the inner zone although Hallett Station and Little America are of similar geomagnetic latitude. Their dips, however, are dissimilar.

The diurnal variations of auroral incidence and local geomagnetic disturbance at Scott Base and

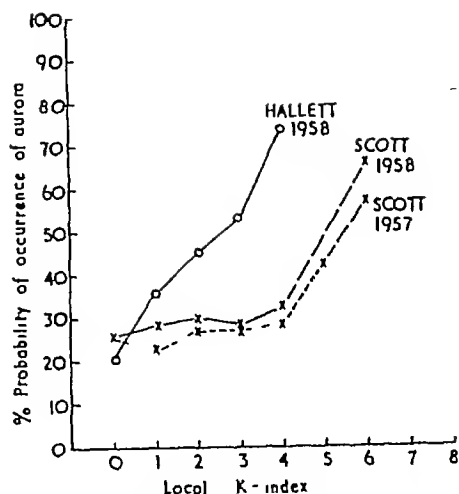


Fig 2 Change in auroral probability with increase in local geomagnetic disturbance Scott Base and Hallett Station. The last point on each of the Scott Base curves (joined by the longer dashed line) has a sample of less than 30.

Hallett Station appear to have no simple relationship. The probability of occurrence of aurora during an hour which is part of a three hourly interval of any K index is shown for Scott Base and Hallett Station in Fig 2. At Scott Base auroral probability increases only slightly with K index until conditions become stormy, whereas at Hallett Station there is a marked increase in auroral probability with increase in geomagnetic disturbance. A computation of diurnal auroral occurrence from Fig 2 and the frequency spectrum of K indices at each 3-hr interval gives single maximum curves with less than 10 per cent diurnal variation in probability. Thus, although there is a relationship between aurora and geomagnetic disturbance the main features of the diurnal variation curves are caused by events unrelated to local geomagnetic disturbance. On the other hand the principal maximum, secondary maximum and the minimum of geomagnetic disturbance at Little America 5 appear to be almost coincident with similar auroral events at Scott Base and Hallett Station.

An interesting difference occurs between the diurnal character of magnetic disturbance at Little America 1 (1929-30) and that reported above for Little America 5 from recent K indices. Davies⁴ found that at all seasons during 1929-30 the magnetic disturbance curve was of the single-maximum outer zone type, the maximum being at 03.5 hr local time. This is approximately the time of the primary maximum in the 1958 observations but the quite well developed secondary maximum of 1958 is absent from the earlier observations. It should be stated that Little America 5 (Kainan Bay) is about 50 miles east of Little America 1 (Bay of Whales) and the geomagnetic latitude of Little America 5 is less than that of Little America 1. It should also be noted that the magnetic dip has decreased from $-82^{\circ} 20'$ at Little America 1 in 1929 to $-79^{\circ} 56'$ at Little America 5 in 1958. Sunspot numbers in 1929 were lower than 1958 although 1928 was the maximum year of the cycle.

Comparison of auroral incidence obtained by visual and photographic methods is of some interest apart from the main themes discussed in this letter for it is highly probable that most future auroral studies will be made photographically and it is necessary to decide whether the large body of visual data gathered in the past can be used together with that derived

by photographic techniques. The intensive observations made at Scott Base and Hallett Station during the International Geophysical Year enable the methods to be compared for frequency studies and Fig 1A shows clearly that visual methods provide results comparable in this respect with photographic studies.

We are indebted to the Director, U.S. Coast and Geodetic Survey for providing K indices for Little America and Byrd Stations.

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² Hulbert L. O. *Terr. Mag.*, 36, 23 (1931)

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Exchange Interaction as a Cause of Reverse Thermo-Remanent Magnetism

We reported, in 1952, the occurrence of self-reversing thermo-remanent magnetism of the ferromagnetic minerals contained in the hypersthene hornblende dacite pumice of Mount Hama, Japan¹. The physical mechanism producing this particular phenomenon was at first considered to be one postulated by Neel², that is, a magneto static interaction during field-cooling, between two ferromagnetic phases (A and B) with different Curie points (T_{cA} and T_{cB}). We ascertained that the ferromagnetic minerals consist of two distinct phases, A being a cubic titanium-poor titanomagnetite ($T_{cA} \sim 500^{\circ}\text{C}$) and B a rhombohedral solid solution between ilmenite and hematite ($0.55\text{ FeTiO}_3 \cdot 0.45\text{ Fe}_2\text{O}_3$ ($T_{cB} \sim 200^{\circ}\text{C}$))³. The abundance ratio of A and B was found to be A/B about 0.02. Subsequent investigations have revealed that the ilmenite-hematite phase is the only constituent responsible for our reverse thermo remanent magnetism, the titanomagnetite phase, although more abundant, is irrelevant to the phenomenon⁴.

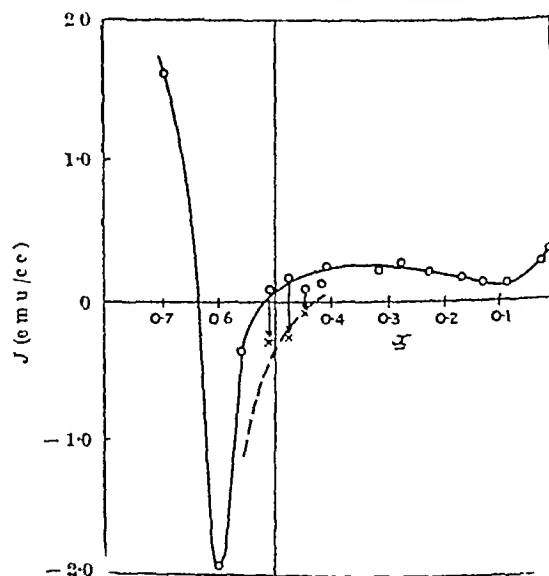


Fig 1 Intensity of thermo remanent magnetism of synthetic ilmenite-hematite $x\text{FeTiO}_3 \cdot (1-x)\text{Fe}_2\text{O}_3$ series as dependent on x . O—O, Just after synthesis at 1200°C and quenching; x—x, after heat treatment.

Recently, evidence has been obtained showing that this property of reverse thermo remanent magnetism is intrinsic to the ilmenite hematite series and that the mechanism causing it should be of the nature of the exchange interaction. Fig 1 shows the intensity of the total thermo remanent magnetism produced by cooling from above the Curie point in a magnetic field of 20 oersteds, of a series of synthetic ilmenite hematite solutions, $x\text{FeTiO}_3$ ($1-x$) Fe_2O_3 , the abscissa denoting the value of x in the chemical formula. It is observed that the reversal of the polarity takes place within a restricted range of x , namely, $0.45 \leq x \leq 0.6$. The members having $0.45 \leq x \leq 0.5$ show only normal thermo remanent magnetism just after the synthesis at 1200°C followed by quenching but can acquire the reverse thermo remanent magnetism property after an appropriate heat-treatment.

The magnetic properties of the ilmenite hematite series are known to be complex⁵. At room temperature the series is divided into the following three regions, namely, the paramagnetic region for $1 \geq x \geq 0.8$, the ferrimagnetic region for $0.8 \geq x \geq 0.45$ and the anti ferromagnetic region for $0.45 \geq x \geq 0$. In the last region, so-called paramagnetic ferromagnetism of the hematite type is superimposed. This complicated nature of the magnetic property of the $x\text{FeTiO}_3$ ($1-x$) Fe_2O_3 series has been interpreted in terms of an order-disorder phenomenon among the iron and titanium ions in the lattice⁶, an ordered state of $R3$ symmetry is realized in the ferrimagnetic region whereas the disordered state of $R3C$ symmetry prevails in the antiferromagnetic region. In support of this, it was also shown that the magnetic properties are extremely sensitive to heat-treatment for the members with x about 0.5, that is, near the border between ferrimagnetic and antiferromagnetic regions⁷. Taking the above quoted general magnetic properties of the series into consideration, it may safely be said that the results in Fig 1 show that the ability to produce the reverse thermo remanent magnetism is peculiar to those members of the ilmenite hematite series which belong to the border region between the ferrimagnetic and the antiferromagnetic regions and the true mechanism of the reverse thermo remanent magnetism should be closely related to the same order disorder phenomenon as that which causes the ferrimagnetic \leftrightarrow antiferromagnetic transformation.

Whatever the detailed mechanism may be it is possible to express the effective magnetic field that should be responsible for the production of the reverse thermo remanent magnetism as $H_{\text{eff}} = H_{\text{ex}} - H_{\text{int}}$, where the suffixes stand for effective, external and interaction respectively. $H_{\text{eff}} > 0$ and $H_{\text{eff}} < 0$ correspond to the cases of normal and reverse thermo remanent magnetism. Therefore, the dependence of the intensity of thermo remanent magnetism on H_{ex} will give a lower limit value of the interaction field H_{int} at the value of H_{ex} where the thermo remanent magnetism becomes zero. The reason for the lower limit is that the other ferromagnetic constituents, like the A component in the Haruna specimen, will favour the normal thermo remanent magnetism. In Fig 2, the curves (a), (b) and (c) show the intensity of thermo remanent magnetism versus H_{ex} for the original Haruna ferromagnetic minerals (A + B), the Haruna ferromagnetic ilmenite hematite (B) minerals after separation from titanomagnetite (A) and the synthetic specimen 0.48FeTiO_3 $0.52\text{Fe}_2\text{O}_3$, respectively. In the former two cases, the condition $H_{\text{eff}} = 0$ gives the magnitude of the apparent H_{int} as

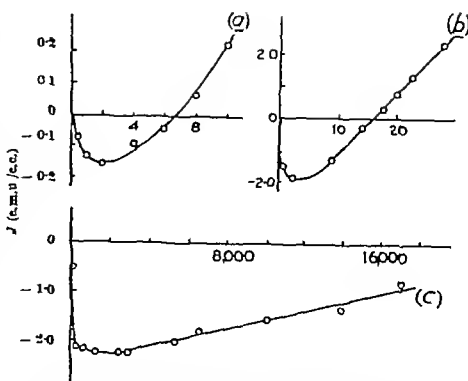


Fig 2 (a) Partial thermo-remnant magnetism J ($250^\circ\text{--}350^\circ$) versus H_{ex} (oersteds) of Haruna ferromagnetic minerals (A + B). (b) Total thermo-remnant magnetism J ($20^\circ\text{--}350^\circ$) versus H_{ex} (oersteds) of Haruna ilmenite-hematite B. (c) Total thermo-remnant magnetism J ($20^\circ\text{--}400^\circ$) versus H_{ex} (oersteds) of synthetic ilmenite-hematite 0.48FeTiO_3 , $0.52\text{Fe}_2\text{O}_3$.

about 7 and 15 oersteds and in the last case it gives a value greater than 1.6×10^4 oersteds. Although the former two values can be explained in terms of magneto static interaction⁴ it would be evident that the last figure can never be accounted for by any magneto static interaction.

It may well be mentioned that the careful study of the thermal variation of the saturation magnetization gave no indication that the specimen concerned had Néel's N type characteristics⁸. Excluding the possibility of the N type ferromagnetics, the only possible source of such an intense interaction seems to be the exchange interaction across the boundary between two connected phases. This possibility has been mentioned by Néel⁹ and Gorter¹⁰ recently. Actual examples of the exchange interaction across the boundary between separate phases have been reported by Moulejohn and Bean as a cause of the extremely strong magnetic anisotropy of Co CoO , Fe FeO and $\text{Fe Fe}_2\text{O}_4$ systems¹¹. In our case the participating phases are both considered to be in the ilmenite hematite series and the order-disorder phenomenon is the possible source for the distinction of the two phases. A fuller account of the present study will be seen elsewhere¹¹. The detailed nature of the exchange interaction concerned is under investigation.

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PHYSICS

A Comparison of the Charges of the Electron, Proton and Neutron

It has recently been suggested by Bondi and Lyttleton^{1,2} that the magnitudes of the electric charges on the proton and electron may differ by a little more than one part in 10^{18} , in which case electrostatic forces would cause the universe to expand. In fact, Piccard and Kessler³ attempted to detect such a difference in 1925, and found that a molecule of carbon dioxide did not have an electric charge greater than $2 \times 10^{-19}e$, where $-e$ is the electronic charge, from which they concluded that the magnitudes of the proton and electron charges were the same to within 5 parts in 10^{21} , assuming that matter was built entirely of protons and electrons. Since matter also contains neutrons, they have assumed in effect that the neutron has a charge equal to that of a hydrogen atom, but the neutron might equally well have a charge opposite to that of a hydrogen atom, in which case their experiment does not settle the point at issue, since carbon dioxide contains equal numbers of protons and neutrons (to within 0.1 per cent). It therefore seemed desirable to find whether matter in which there is an excess of neutrons is electrically neutral. We have found that the charge on an argon atom (18 protons, 18 electrons and 22 neutrons) is not greater than $8 \times 10^{-20}e$ and that on a nitrogen molecule (14 protons, 14 electrons and 14 neutrons) is not greater than $12 \times 10^{-20}e$. Treating the charges on nitrogen and argon as the sums of charges on protons, electrons and neutrons, it is deduced that the proton charge is $(1 \pm 4 \times 10^{-20})e$ and the charge on the neutron is less than $4 \times 10^{-20}e$.

As in the earlier experiment, the method used was to attempt to detect a charge on a large volume of de-ionized gas by detecting a change of potential of a vessel from which the gas was allowed to escape. Fig. 1 is a diagram of the apparatus. A cylinder of compressed gas was placed inside an aluminium box *A* which was itself placed inside, but well insulated from, a larger aluminium box, *B*. A vibrating-reed electrometer (type 1086C) was used to observe changes in potential of box *A* relative to *B* when gas was transferred from inside the inner box to a gasometer outside the system, the gas flow being controlled by a clip on the gasometer inlet tube. Before leaving the inner box, the gas passed through the 1.2-mm gap between two coaxial cylinders held at 45 V potential difference to remove ions from the gas. (The time taken for an ion of normal molecular mobility to drift across the gap would be 1.2×10^{-6} sec, whereas the gas spends at least 5×10^{-3} sec in the ion trap at the rates of flow used.) Care was taken that although the copper outlet tube (*H*) was well insulated from the inner box, the gas did not flow directly over any insulators after leaving the ion trap, before passing out of the system.

The large ionization current in the air between the boxes was backed off by applying a potential of about 0.25 V between them before making the measurements, but convection currents which started when the expanding gas cooled the tubes caused fluctuations in the current. These effects were considerably reduced by using double-walled tubes containing thermal insulation.

On starting and stopping the flow of gas, there were sudden changes of potential, which depended only

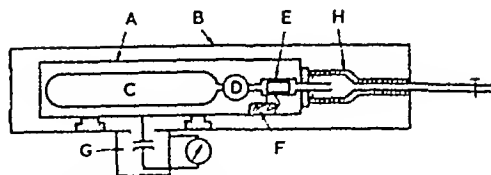
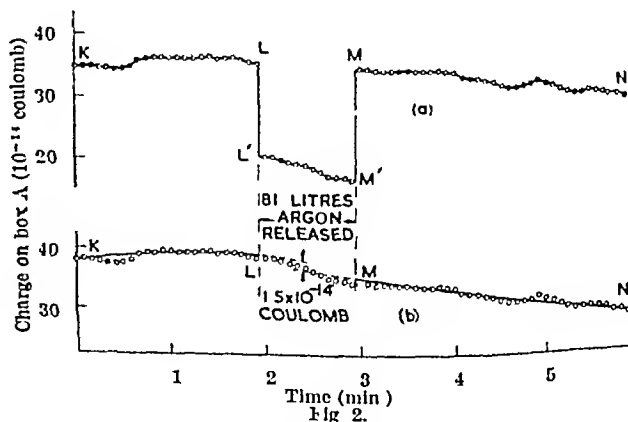


Fig. 1 *C*, Gas cylinder *D*, reducing valve *E*, Ion trap, *F*, battery *G*, electrometer, *H*, double-walled outlet tube containing thermal insulation, hatched areas, polystyrene insulators

on the rate of flow, and not on the duration. These were presumably due to mechanical movements when the pressure changed, through capacitative effect of the applied potential differences and contact potential differences.

Fig. 2a shows the mean of 19 sets of observation with argon, with the potential changes converted into charge on the inner box. The charge on the box is plotted at 5 sec intervals from *K* to *L*, when the gas flow was started. The readings were continued during a steady release of gas (*L'* to *M'*) and after the flow of gas was stopped (*M* to *N*). Since the potential jumps on starting and stopping the flow of gas were unequal (due to a charge apparently carried by the first 30 cc of gas) the results are replotted (Fig. 2b) with the jumps *LL'* and *MM'* subtracted. As the trend of the points from *L* to *M* is not significantly different from the rest, the gas can have carried no significant amount of charge. To obtain a quantitative result, an attempt is made to extrapolate the readings *KL* and *NM* (dashed lines), with the result that the charge carried away by 81 litres of argon (at N.T.P.) is estimated as $(+1.5 \pm 1.5) \times 10^{-14}$ coulomb, corresponding to a charge of $(4 \pm 4) \times 10^{-20}e$ per atom of argon. When no field was applied in the ion trap, a charge of $(+5.5 \pm 2) \times 10^{-16}$ coulomb per litre was carried away under the same conditions, corresponding to an excess of 3 positive ions per cm³, but this varied considerably with gas pressure and rate of flow. (This result is not unreasonable, taking account of initial recombination in the high-pressure gas, and removal of ions by thermal diffusion in the trap.) With nitrogen the mean result of 5 runs was that 58 litres carried $(+1.5 \pm 1.5) \times 10^{-14}$ coulomb, corresponding to $(6 \pm 6) \times 10^{-20}e$ per molecule. It is hence deduced that the neutron charge is $(-1 \pm 3) \times 10^{-20}e$ and the hydrogen-atom charge is $(1 \pm 3) \times 10^{-20}e$.

The ion trap would not remove charges carried by sufficiently large particles, but it is unlikely that such charges have neutralized a bulk charge of the gas, as any space charge equilibrium set up in the cylinder would be governed by thermal diffusion and



drift of the small ions, which are later removed by the ion trap. The same results were obtained with several different gas cylinders and also with 300 V applied in the ion trap. The charge calibration was checked using a 10^{12} -ohm resistor connected to box A.

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Proc Roy Soc. (in the press)

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Decay of a Tau-Meson Underground

THE decay of heavy cosmic ray particles underground has been reported by Higashi *et al*¹, and L. and M. Avan². Higashi found a neutral V particle in a multiplate cloud chamber at a depth of 40 metres water equivalent underground. The V particle was produced by a shower secondary from a large interaction in the chamber. Avan, using glass backed emulsions at a depth of 800 metres water equivalent, reported the decay of two K mesons, one of which was produced in the glass backing of an emulsion.

Support of an unambiguous nature is given here to the foregoing evidence on K meson decay underground in that the easily recognizable tau mode of decay has been observed in favourable conditions. The tau meson decayed at rest in Ilford $G5$ emulsions of thickness 400 microns. The emulsions formed part of a stack of 24 strips of major dimensions 10×10 cm. which were manufactured, exposed, and developed at a depth of 57 metres water equivalent underground in Holborn tube station (London). During the exposure of 97 days the emulsion strips were interleaved with thin sheets of tissue paper with their planes vertical, and were packed in an air tight container surrounded by 15 cm. of lead.

The tau meson was found among 134 μ mesons, 97 p mesons, 17 c mesons, 5 π^+ mesons, 10 neutron stars and 9 stars with charged primaries, in a scan covering 38 cc of emulsion. Of the c mesons two were associated with more than one interaction proton of residual range greater than 10μ , and seven had only one or more short interaction tracks, of residual range less than 5μ , such as are characteristic of slow μ -meson interactions. Two of the π^+ mesons were decay particles of the tau meson. All the stars included above had three or more heavily ionizing tracks of which at least one had a residual range greater than 100μ . There were 12 other stars in the scanned volume which did not satisfy the above criteria. Four of these were of the $1+1P$ type which have been interpreted as due to giant resonance interactions of μ mesons³.

The tau meson entered the stack moving down wards at an angle of 80° to the vertical and stopped in the stack after covering a range of 4.7 mm. According to the range-energy tables of the Göttingen group⁴, which were also used in calculating energies in Table 1 this corresponds to a kinetic energy on entry of 25.0 ± 0.3 MeV. The tau meson was identified by its characteristic decay scheme and by the results of gap counting which indicated a singly charged particle of mass $1000 \pm 200 m_e$. Decay at rest was confirmed by observations on the decay π mesons (see Table 1) which were coplanar to within 2° , and showed momentum balance at the point of decay

Table 1 THE DECAY PARTICLES

| Particle No. | Nature | General | Residual range (mm.) | Energy at decay point (MeV) | Q value of decay (MeV.) |
|--------------|---------|---|----------------------|-----------------------------|-------------------------|
| 1 | π^+ | Decay at end of range $\pi^+ \rightarrow \mu^+ + \nu$ | 29.0 | 43.0 ± 0.1 | |
| 2 | π^+ | Interaction at end of range. Single (0.5 ± 0.4) MeV proton emitted | 4.4 | 14.5 ± 0.3 | 70.6 ± 0.7 |
| 3 | π^- | | 3.7 | 13.1 ± 0.3 | |

Of the decay particles, only No. 3 stops outside the scanned volume

within 5 per cent along and perpendicular to the direction of decay particle No. 1

Errors in the energies given are based on the statistical distribution of mean ranges⁴. They do not allow for systematic errors due to such factors as track losses in the interleaving tissue paper between emulsion strips, in erosion and anomalous development at emulsion surfaces, or any difference in density which may exist between the emulsions used here and those on which the Göttingen tables are based. However, from observations on the five μ^+ mesons from the decay of π^+ mesons in the stack, two of which passed from one emulsion strip to another it would appear that any systematic errors included in the results are small and may lead at most to an underestimation of the Q value of about 2 or 3 per cent. Hence the best mass value for the tau meson based on the Q value and the masses of the decay particles is $(958 \pm 2)m_e$, and agrees with the accepted value of $(966.8 \pm 0.4)m_e$ ⁵. In view of the above observations it may be taken that the decay of a heavy meson has been established.

The tau mode of decay is rare and occurs with a frequency of about 1/14 among K^+ meson decays. This ratio appears to apply whether production is by charged particles or by photons⁶. Hence where the tau mode is observed, it is likely that the other modes also occur. Of the other decay modes the $K\mu$, $K\pi$, and $K\pi$, which together account for some 86 per cent of K^+ meson decays⁷ resemble μ meson decay, or $1+0p$ stars in that they are associated with a relativistic decay particle whose ionization is near the plateau value. These would be difficult to identify without extensive measurements in emulsions exposed underground as the rates of particles stopping are small even for long exposures, fading of the latent track image occurs and a high background density has to be overcome⁸. Further, all the extensive emulsion exposures underground by other workers have so far been made with emulsions mounted on glass plates. As the glass plates restrict measurements on any event to the narrow emulsion strip in which it is found, it is not surprising that only two K^+ mesons have been reported hitherto.

If direct production of K mesons by μ mesons is assumed, then the cross section for the process should be given by the Williams Weissaker method as used by George⁹. The method associates a virtual photon spectrum with relativistic μ mesons and their cross section for nuclear interactions is given by the product of the virtual photon spectrum and the cross section of real photons for the process considered. There are two major obstacles which prevent such a calculation here. The first of these involves uncertainties in the validity of the method for energy transfers greater than 500 MeV at μ meson energies above 10 GeV¹.

while the second concerns the paucity of the data on heavy meson production by real photons. However, the limited data which are available on the interactions of 1 GeV photons are encouraging in that heavy mesons¹⁰ and multiple π -mesons^{11,12} are produced. This would seem to indicate that the W - W method may be used to interpret the showers induced underground by μ -mesons. If this is the case, then photon interaction processes such as the production of K -mesons and hyperons should occur.

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Ratio of Nucleon Mass and Electron Mass

In classical physics, the value of the fine structure constant $\epsilon^2/\hbar c$ is $1/137$. The value of the pion-nucleon interaction constant $g^2/\hbar c$ is about 14.

The mass of the electron is given by $m_e = \epsilon^2/2r_0c^2$. The fundamental length r_0 appearing in this formula is also equal to the Compton wave-length of the pion.

Let us assume that the mass of the nucleon is given by a formula strictly similar to that for the electronic mass, in particular with the same value of r_0 . Then

$$\frac{m_n}{m_e} = \frac{g^2/2r_0c^2}{\epsilon^2/2r_0c^2} = \frac{g^2}{\epsilon^2} = \frac{g^2/\hbar c}{\epsilon^2/\hbar c} = \frac{14}{1/137} = 1920$$

which is not too far from the experimental value 1840.

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Analysis of Permanent Gases by Gas Chromatography Using a Radioactive Ionization Type Detector

BECAUSE of its high sensitivity, simplicity of operation and stability under changing operating conditions, the radioactive ionization-type detector for gas chromatography is one of the most useful so far developed. This detector is, however, relatively insensitive to the permanent gases. From preliminary experiments it has been found possible to increase this sensitivity greatly by introducing a small continuous bleed of organic vapour into the argon carrier stream.

Without the organic vapour bleed into the detector, the mechanism of detection is as described by Lovelock¹ the argon forms metastable atoms capable of ionizing atoms of any eluted component having a lower ionization potential than argon, and resulting in

very high sensitivity to them. The permanent gases, however, have ionization potentials greater than that of metastable argon and hence are not ionized by the argon, thus sensitivity to them is low. Used in this way, the detector current is quite small when the carrier only is passing.

With an organic vapour bleed into the system, the organic vapour is ionized by the metastable argon and produces a relatively high standing ionization current, this is, however, kept below the saturation current of the detector. Permanent gas components entering the detector reduce this higher ionization current to a greater extent than the alteration in current they produce with argon alone. The mechanism of this process may be expected to be complex but can be qualitatively explained from a consideration of energy levels and collision processes.

Using a Pye argon chromatograph with argon carrier gas and a Linde 5A molecular sieve column, it has been found possible to detect permanent gases in the range 0-50 p.p.m. by bleeding ethylene into the carrier stream between the column and detector. With a concentration of ethylene in the detector of the order of 1 p.p.m., the minimum detectable concentrations of hydrogen, oxygen and methane were 0.5 p.p.m. and for nitrogen 1.0 p.p.m. (Similar results were obtained using an acetylene bleed into the detector). Sensitivity is further increased by a factor of about seven when the ethylene concentration is at its optimum value which would appear to be about 100 p.p.m. In cases where the organic vapour has no adverse effect on the column, it was found possible to include it in the carrier gas supply in the required concentration.

A patent application on this work has been made.

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¹ *J. Chromatography*, 1, 1 (1959)

Etching of Calcite

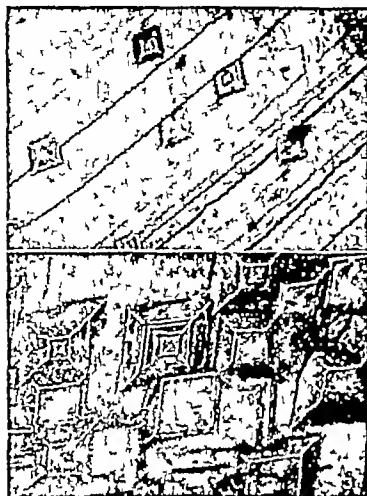
EXPERIMENTS on etching of calcite have been carried out earlier by a number of workers¹ and etch pits on calcite have been reported recently by H. Watts² and R. C. Stanley³. We have been carrying out experiments on etching of mineral crystals with different etching reagents for some time and have investigated calcite very thoroughly. Some typical results are reported here.

On etching cleavage faces of calcite with a strong solution of sodium hydroxide for one hour, perfectly boat-shaped figures are obtained. A light profile photomicrograph is shown in Fig. 1. The depth of this particular etch pit is 1μ at the centre and 0.8μ at the ends.

The etch figures produced by ammonium chloride solution on a freshly cleaved surface of calcite are parallelograms, and these are oriented with their sides parallel to the edges; their depths vary from a few hundred angstroms to 2 microns, according to the etching time. Figs. 2 and 3 show photomicrographs for the two stages of etching for fifteen minutes and one hour respectively. In Fig. 2 the pits are more scattered and cleavage lines are found to be moving as reported earlier by Patel and



Fig 1 (x500)



Figs. 2 and 3 (x56)

Tolansky⁴ in the case of the etching of mica. Multiple beam interference pictures have also been taken over these etch pits for measuring their depths.

Detailed results will be published elsewhere.

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Field Effects on Chemisorbed Films in Electron Emission Microscopy

The migration of surface atoms of tungsten under the influence of a high electric field is a well-established phenomenon¹⁻³. In addition the migration of multi-layers of adsorbed most gases in the applied field necessary for field emission has been observed⁴. Strangely enough the effect of the field on the gases commonly used as adsorbates, namely oxygen, nitrogen, hydrogen, carbon monoxide, etc., does not seem to have been investigated although field desorption⁵ and the migration of barium⁶ have been studied.

We have found that when oxygen is adsorbed by a tungsten emitter at pressures of about 3×10^{-6} mm. in the presence of the applied field adsorption first occurs around the 011 and 112 planes and particularly on the stopped region joining them, and that only after these appear to be saturated does substantial darkening of the 001 region occur. (A preliminary statement of the effect of the field on carbon monoxide was made at the Fourth International Congress on Electron Microscopy at Berlin in September, 1958 but at that time it was believed that field effects did not occur with oxygen.) This darkening occurs after about 5 min. at the pressure stated. In contrast if the cleaned emitter is exposed to oxygen at the same pressure for more than 30 min. in the absence of the field the characteristic black regions around the 001 planes do not form. On applying the field, the 001 regions commence to darken immediately and the process is complete within 3 min.

A similar phenomenon occurs with carbon monoxide although with this gas the initial adsorption is less specific, a rather granular pattern being obtained without the specific adsorption on the 011-112 'bridge' which is so characteristic of oxygen. Dark circles which engulf the 001 planes are apparent after 12 min. (Fig. 1). If adsorption is allowed to occur for as long as 30 min. at the same pressure without the applied field the pattern shown in Fig. 2 is obtained. (Incidentally this is a convincing illustration of the absence of oxygen contamination.) When the field is now applied rapid darkening of the 001 region occurs (Fig. 3). The process is apparently irreversible, for 16 min. with the field reversed fails to have any effect (Fig. 4) on the 001 region.

There appear to be two main reasons why the observed changes could occur at a faster rate in the presence of the field. These are: (i) The production of positive ions in the gas phase which bombard the emitter and so increase the rate of arrival of adsorbate above the value predicted by kinetic theory, (ii) The

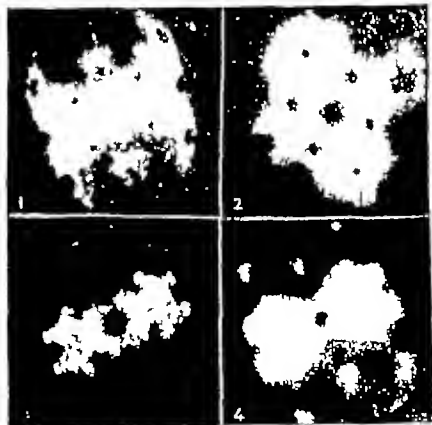


Fig. 1. Emission pattern obtained after adsorption of carbon monoxide for 12 min., at a pressure of 3×10^{-6} mm., in the presence of the field (12 kV).

Fig. 2. Emission pattern obtained after 30 min. exposure in the absence of the field (11.6 kV).

Fig. 3. Pattern of Fig. 2 after applying the field (11.4 kV).

Fig. 4. Pattern of Fig. 3 after 20 min. further exposure in the presence of the field and 15 min. with the field reversed (12.2 kV). Reversal of the field produced no detectable changes.

roughness of the emitter surface leads to the field being inhomogeneous, polarized adatoms or admoles will thus tend to move to positions where their free energy is a minimum, that is, to where the field is highest. If in the course of such diffusion, the migrating adsorbate meets hole sites such as occur in the 023 planes of tungsten for example, it will tend to be trapped there. We believe that the effects observed with oxygen and carbon monoxide can be accounted for in this manner, rather than by bombardment with ions which would be expected to penetrate well below the surface layers because of their high energies. A fuller account of this and related work will be published in due course.

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METALLURGY

Fatigue-Induced After-Effect in Zinc Single Crystals

BOLTZMANN proposed his theory of superposition in 1874 to account for the memory effects in deformed materials¹. Since then the after-effect, namely the tendency of plastically strained materials to return to their original dimensions when the external stress is removed, has received only occasional attention, possibly due to the fact that, in itself, it is not of direct technological importance. When observed in conjunction with forward creep the effect has been called creep-recovery and most of the published work deals with this expression of the phenomenon.

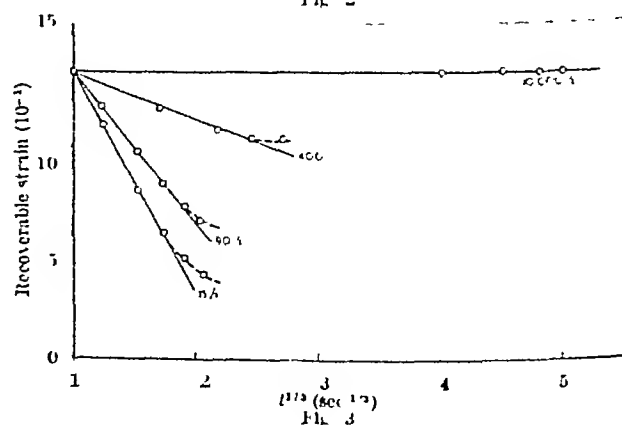
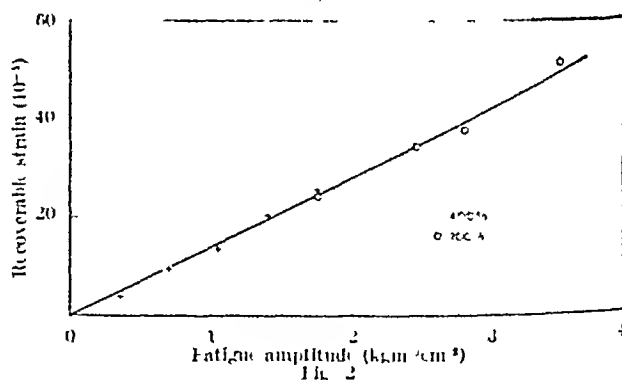
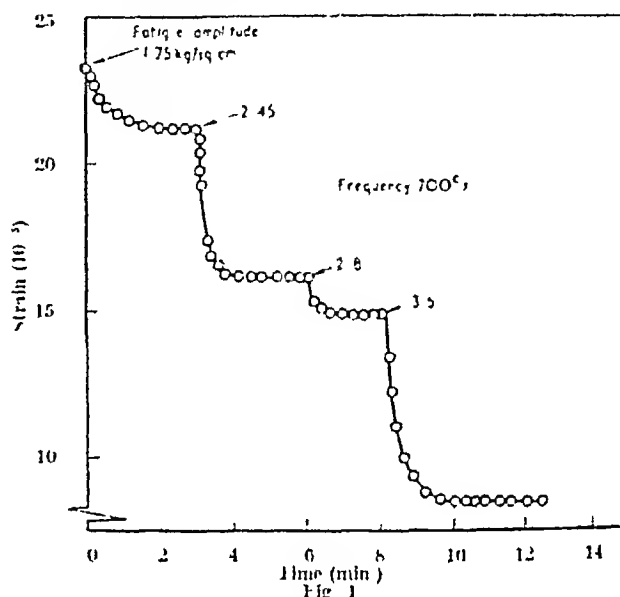
The laws governing the after-effect have been investigated using polycrystalline metal specimens and various attempts have been made to reproduce the phenomenon in single crystals without success²⁻⁵. This has formed the basis for the theories put forward to explain the after-effect. We have observed large recoverable strains in zinc single crystals originally deformed by creep, a fatigue stress was found necessary to promote the process.

Zinc single crystals, 99.995 per cent purity, were grown from the melt in evacuated capsules in a gradient furnace. The crystals, 7 cm long and 5 mm in diameter were annealed at room temperature for several weeks and etched in 20 per cent hydrochloric acid to remove any surface oxide. The straining grips were soldered to the ends of the crystals so as to produce the minimum of end deformation during straining. The orientation λ of the crystals used, which varied between 20° and 22°, was determined by the X-ray back-reflexion Laue method (λ is the angle between the crystal axis and the glide plane). The experiments were carried out at room temperature.

A static resolved shear stress of 24.8 kgm/sq cm was applied to the crystal resulting in a steady-state creep strain rate of 1.4×10^{-4} /min. After the deformation had passed well into this region the stress was reduced to 4.9 kgm/sq cm and the fatigue stress was then introduced. This produced an immediate negative strain-rate which gradually decreased to a vanishing small value. However, by increasing the fatigue stress amplitude further recovery was produced and the effect could be repeated many times as shown in the typical example in Fig. 1.

It was observed that the total recoverable strain increased linearly with fatigue stress amplitude and that the transient part of the recovery curve followed a $(\text{time})^{1/3}$ law, as shown in Figs. 2 and 3 respectively. The magnitude of the effect was found to be dependent on the frequency of the fatigue stress, decreasing with increasing frequency. The frequency-range investigated in the present work was between 10 and 10,000 cycles per sec.

The present observations show that previous theories for the after-effect based on grain boundary behaviour or the uneven distribution of strain in a polycrystalline aggregate are not sufficient in accounting for all cases. The processes leading to the after-effect must have their origin inside the individual grain as well. The dislocation model proposed below appears to explain satisfactorily the observations made in the present work.



A proportion of the dislocations generated under the original static stress pile up beneath the free surface of the crystal or against obstacles in the slip plane. When the stress is substantially reduced these dislocations tend to move back towards the generating source under their mutual repulsive stresses. This process is resisted by minor 'frictional' obstacles in the slip plane but the application of a fatigue stress, which causes the dislocations to oscillate assists them to overcome these obstacles thus increasing their mobility. Larger fatigue stresses would result in more dislocation mobility leading to further strain recovery. It is not clear, however, why a dislocation oscillating at the frequencies used in the present work which are much lower than the 'resonance' frequency of a dislocation line, should become much more mobile than a static dislocation. It is possible that the low frequency oscillations of the large dislocation networks in the crystal may induce high frequency oscillations in the smaller elements. Alternatively the additional energy imparted to the dislocation line even at low frequencies, may be sufficient to assist it in overcoming the minor frictional obstacles in the slip plane. Experiments are being carried out to reveal which of the two mechanisms is in fact responsible for the effects observed.

Recent evidence in support of the concept of the increased mobility of an oscillating dislocation is given by Moleka and Evered⁶ where a fatigue stress was found to increase forward creep and by Bloha and Langecker⁷ who observed a decrease in the static stress required for continued glide when a fatigue stress was applied.

A full account of this work will be published elsewhere.

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Impact Ductile Molybdenum

It has recently been reported that unnotched single crystals of zone melted molybdenum are ductile in impact well below room temperature.¹ Although the impurity content of this material was very low it was felt that the improvement may be due to the single crystal structure and not the purity. Some crystals were therefore forged and recrystallized to give a polycrystalline material of grain size 4/cm. The specimens were turned to $\frac{1}{2}$ in diameter and electro-polished to produce a surface similar to that of the zone melted crystals. Tested in a 10 ft/lb Charpy impact machine these gave a 5 ft/lb transition temperature of -80°C compared with -140°C for similar purity single crystals. A graph of the two sets of results is shown in Fig. 1, the points and full line refer to polycrystals and the broken line to single crystals.

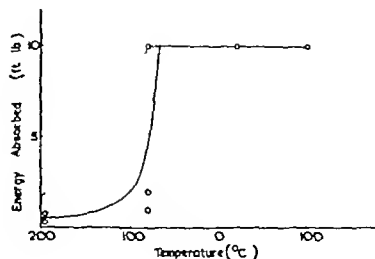


Fig. 1

The increase in transition temperature may be due to the effect of the grain boundaries or a slightly worked surface layer. No grain boundary facets are apparent in the fracture surface. The transition temperature of recrystallized vacuum arc melted molybdenum is about 350°C under similar conditions. A comparison of the impurity contents in weight per cent of the arc-cast and zone melted material is given below.

| Impurity | Arc-cast | Zone-melted |
|----------|----------|-------------|
| Carbon | 0.01 | 0.002 |
| Silicon | 0.002 | 0.002 |
| Iron | 0.004 | 0.0001 |
| Copper | 0.004 | 0.001 |
| Chromium | 0.001 | 0.001 |
| Nickel | 0.007 | 0.0001 |
| Cobalt | 0.010 | 0.0002 |

The oxygen content of both materials is about at the limit of detection of the available vacuum fusion apparatus, approximately 1 part per million.

The surface condition of the recrystallized zone melted metal was important. Electropolishing improved the impact ductility. Further experiments are in hand to assess to what extent carbon is the impurity responsible for the poor impact properties of arc cast molybdenum.

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Belk J. A., *J. Less Common Metals* 1 59 (1959)

ENGINEERING

Strength of a Grooved Stud

It is commonly accepted that an abrupt change of section (such as a circumferential groove in a bar under the action of tension) will lead to a stress concentration at the root of the groove, and hence to a weakening of the bar in excess of that resulting from reduction in sectional area. That the bar is not necessarily weaker but may be very much stronger is now well established but is not generally recognized.

I recently needed to design safety studs which would fracture at a load of 29,300 lb with a maximum coefficient of variation of 1.3 per cent. The studs were 7 in long and $1\frac{1}{2}$ in diameter with a circumferential groove of semi-circular section turned on it with a parting tool. It was found that the studs broke at loads which were 60 per cent greater than those calculated from the tensile strength (28/33 tons/sq in) of the material (which was structural steel) and the cross-sectional area. The test results are shown in Table 1.

Table 1 RESULTS OF GROOVE TEST

| Diam at Groove d (in) | Ratio D/d | Limit of Proportionality | | Yield Point | | Tensile Strength | | Remarks |
|----------------------------|----------------|--------------------------|------------|-------------|------------|------------------|------------|---------------------------------|
| | | 1,000 lb | tons/sq in | 1,000 lb | tons/sq in | 1,000 lb | tons/sq in | |
| 0.778 | 1.93 | no | no | no | no | 51.2 | 48.1 | Trial stud (scrap material) |
| 0.591 | 2.54 | no | no | no | no | 30.8 | 50.1 | Bar 1 |
| 0.5703 | 2.60 | no | no | no | no | 20.0 | 10.7 | Bar 1 |
| 0.5809 | 2.59 | no | no | no | no | 20.2 | 49.3 | Bar 1 |
| 0.5805 | 2.58 | no | no | no | no | 20.4 | 49.6 | Bar 1 |
| 0.577 | 2.60 | 11.4 | 24.0 | 17.8 | 30.3 | 23.0 | 40.2 | Bar 1 |
| 0.531 | 2.82 | no | no | 15.2 | 30.0 | 24.2 | 48.0 | Bar 1 |
| 0.520 | 2.88 | no | no | 14.8 | 31.1 | 23.2 | 48.8 | Bar 1 |
| 0.518 | 2.90 | no | no | 14.4 | 30.4 | 23.0 | 48.0 | Bar 1 |
| — | 1.00 | no | no | 8.4 | 16.1 | 142.5 | 30.7 | Bar 1 Full section test results |
| 1.005 | 1.40 | 20.0 | 10.4 | 48.3 | 27.3 | 76.4 | 43.0 | Bar 2 |
| 1.202 | 1.25 | 44.0 | 17.3 | 55.5 | 21.8 | 100.5 | 39.7 | Bar 2 |
| 0.421 | 3.56 | 4.1 | 13.2 | 7.3 | 23.4 | 13.4 | 43.0 | Bar 2 |
| 0.551 | 2.53 | 8.3 | 14.0 | 15.0 | 25.1 | 26.0 | 43.0 | Bar 2 |
| — | 1.00 | — | 9.0 | — | 15.2 | — | 27.1 | Bar 2 Assumed figures |

D (full diameter of stud) 1.5 in

no no attempt made to observe this property

Bar 2, no test data available on full section quoted figures obtained by comparison of studs of 0.58 in diameter

From the point of view of stress concentration, the stress condition, according to Petersen¹, is one of bi-axial tension, that is, axial tension together with circumferential tension. Yielding should then depend upon the axial stress value only, since the lowest principal stress remains zero. Assuming an elastic condition, Petersen calculated that the axial stress was 1.7 times that in a plain bar of the same diameter. Allowing for the fact that yielding depends on the Mises criterion, the stress concentration was calculated to be 1.6 at the yield point.

Orowan² has pointed out that the stress system at the root of a groove of this type very rapidly becomes tri-axial tension because of the constraining effect of the groove in preventing the development of yielding. This fundamentally alters the picture, because the two smaller principal stresses become equal to each other and rise with the axial stress. Under this condition, yielding cannot proceed any further, and the material will stand very high stresses until it breaks in a brittle fashion at the value of maximum principal (axial) stress which is the limit for the material. Orowan postulates that this limit is such that the studs could not have their apparent tensile strengths increased by more than 3.3 times by an infinitely sharp groove.

With this background most of the experimental results could be explained. The 'plastic constraint factor' (to use Orowan's term) was about 1.6, but his theory did not explain the observed increase in yield point and limit of proportionality. These were measured by Martens-type extensometers indicating axial extension across the grooves. In each case the increase was almost as great as the 'plastic constraint factor'. It seems that a very small plastic flow was sufficient to produce the tri-axial condition, and that the shear stress did increase somewhat so that yielding still occurred generally across the sections.

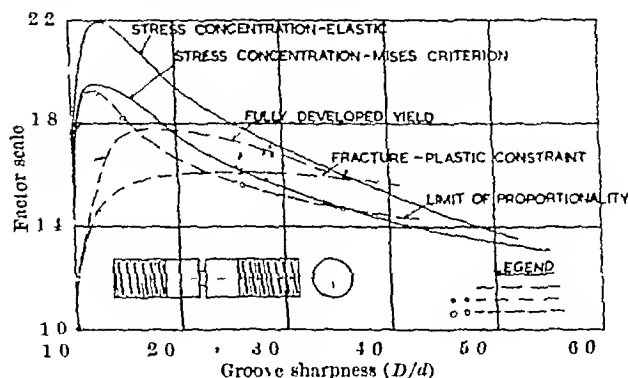


Fig. 1 shows the various factors plotted against a groove sharpness parameter D/d , with further factors comprising the ratios of yield strength and limit of proportionality. It is interesting to note the close resemblance of the Petersen (Mises criterion) stress concentration curve with the experimental curve for limit of proportionality. The discrepancy between the shape of both the Petersen curves and the experimental curve for fracture is very great.

The fractured specimens showed mainly brittle failure except for narrow bands of ductile failure around the edge.

In view of the evidence of reasonable ductility, and the fact that the desired coefficient of variation was easily obtained, manufacture of the safety studs was continued and they have, in fact, given perfectly satisfactory service.

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CHEMISTRY

Dielectric Absorption in Dispersed Systems

If a high-frequency alternating field is applied to a system containing mobile ions or movable dipoles, the loss factor should increase when the applied frequency approaches the natural relaxation frequency of the system. In dilute aqueous solutions of simple electrolytes this frequency is of the order 100 Mc/s (Falkenhagen effect), in pure water it is 10,000 Mc/s (dipole oscillation effect). With polyelectrolytes the cylindrical symmetry of the ionic atmosphere results in a much slower relaxation ($0.1-1 \mu\text{sec}$)¹, and we have now found a similar effect but with a much higher loss factor for microscopic two-phase systems, such as fibres, suspensions and emulsions, with water as the continuous phase. It also occurs in disperse systems where the continuous phase is an insulator, and is indeed more easily verified than with aqueous systems, when the frequency-independent conductance may mask the critical frequency effect.

We prefer to use bridge methods, on account of their high accuracy but it is very easy to be misled by spurious effects due to electrical 'strays' and

'residuals' in the megacycle frequency range. Even short leads are inadvisable above 5 Mc/s we use a micrometer cell sitting directly on the terminals of a product arm radio frequency bridge, which accepts its initial balance at zero resistance, with the cell electrodes in contact.

Work is proceeding with polyelectrolytes, where no dependence of critical frequency on degree of polymerization has yet been found. With emulsions and suspensions, on the other hand, particular size does have a specific effect, which is being examined.

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¹ Chadwick G S and Neale S M *Nature* 173 403 (1954)

'Thermal Regeneration' in the Nickel-Oxygen System

OBSERVATIONS of photo-electric activation¹ (lowering of the photo electric threshold energy) through the interaction of small quantities of oxygen with various metals are recorded in the literature². Such activation, for which no satisfactory theory has been advanced, is obtained without heat treatment and most of the metals concerned possess a low work function (below about 3 eV). Large admissions of oxygen always cause the reverse effect: the threshold is shifted to shorter wave lengths. The phenomenon of thermal regeneration, that is the removal of oxygen from the surface of certain metals and semiconductors by heating *in vacuo* is also well established. The oxygen which disappears from the surface in these cases is not desorbed: it is either incorporated by regions below the surface^{3,4} or it is effectively aggregated into islands on the surface as the result of recrystallization processes to leave bare areas⁵. We have observed photo electric activation in nickel films (work function about 5.1 eV) after interaction with oxygen followed by thermal regeneration of the surface. There appears, therefore to be a close parallel between thermal regeneration and photo-electric activation. Further we have found that regeneration of a nickel surface to which oxygen has been admitted at 20° C occurs spontaneously on standing *in vacuo* at that temperature.

Table 1 WORK FUNCTIONS OF EVAPORATED NICKEL FILMS UNDER GOING INTERACTION WITH OXYGEN

| Surface | Work function (eV) |
|--|--------------------|
| Freshly evaporated Film I | 5.15 |
| Throughout stepwise chemisorption of O ₂ at 20° C | 5.01 |
| Stood in 10 ⁻⁴ mm. O ₂ | 5.24 |
| Pumped and raised to 400° C in 1 hr. Cooled rapidly | 4.8* |
| Reactivated with O | 5.23 |
| Freshly evaporated Film II | 5.14 |
| Stood 14 hr. in 2 mm. O ₂ . Pumped and raised to 400° C in 1 hr. Cooled rapidly | 4.66 |
| Leaved O ₂ | 5.19 |
| Pumped. Stood 2 days <i>in vacuo</i> | 5.09 |
| Raised to 400° C in 1 hr. Cooled rapidly | 4.78 |
| Reactivated with O ₂ | 5.33 |
| Film III after oxidation followed by complete reduction with H ₂ and outgassing at 500° C | 5.09 |
| At once after admission of O ₂ at 20° C | 5.30 |
| Surface just saturated | 5.23 |
| After 15 hr. <i>in vacuo</i> at 20° C | 5.18 |
| After 42 hr. | 5.18 |
| After 66 hr. | 5.16 |
| After 125 hr. (An absorptive capacity was restored in this surface) | 5.15 |

Photo electric measurements were made at 20° C in an all glass photocell using evaporated nickel films as the photocathode. Photo-electric charges were recorded in a Compton quadrant electrometer using the method of charge up in an isolated circuit. Spectral sensitivity data were plotted as the square root of the photo-electric yield versus wave-numbers⁶. For all except clean films (which possessed unique work functions) the points corresponding to any one run could be fitted to two straight lines: double thresholds were inferred accordingly. The work functions presented in Table 1 correspond to the lower thresholds only.

These results indicate that in the case of the nickel-oxygen system regeneration occurs slowly at 20° C but only to a limited extent (the work function does not fall much below that of the clean metal surface). Thermal regeneration, however, causes a marked fall in the work function which may be as much as half a volt lower than that of the metal. It therefore appears unlikely that bare metal surface is responsible for the observations accompanying thermal regeneration. We tentatively suggest that both regeneration and photo-electric activation are the manifestations of a cation rich surface (positive surface potential) such as may result from a migration of cations through the thin oxide film. It is possible that these phenomena are general to all oxygenated surfaces. Thus the extent to which regeneration is observed appears to depend only on the surface concentration of oxygen and the extent of the electronic interaction with the metal or semiconductor involved.

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Polymerization of Phosphonitrilic Chlorides

It has been stated¹ that phosphonitrilic chlorides polymerize by a free radical mechanism. If this were so the reaction could be initiated by high-energy radiation.

Since the phosphonitrilic chlorides are solids at room temperature (the melting point of (PNCI₂)₃ is 114°C) this would provide a convenient method of polymerization².

Six specimens of a commercial mixture of phosphonitrilic chlorides [Albright and Wilson Ltd], enclosed in evacuated glass tubes, were exposed in the Spont. Fuel Irradiation Facility of the Atomic Energy Research Establishment to 0.6×10^6 rads/hr of gamma radiation. The total radiation received varied from 10^5 to 10^6 rads. Using the same rate of gamma radiation Chapiro³ and his colleagues obtained 0.5 per cent conversion per hour for styrene with higher conversions in the cases of non aromatic compounds⁴.

Two of the irradiated samples were heated at 90°C for 2 hr without significant change in the percentage of material which was soluble in benzene. When phosphonitrilic chloride is polymerized by heating to 250°C a long chain rubber is formed, no sign of this was seen in any of the irradiated specimens.

The specimens were extracted with benzene, in which the polymerized phosphonitrilic chloride is insoluble, in no case was the amount of insoluble matter significantly different from that of the starting material. This was approximately 3 per cent which presumably represents low molecular weight linear polymers in the commercial mixture.

Further specimens which were irradiated by means of a linear accelerator up to 10^6 rads, also showed no signs of polymerization. As this is three orders of magnitude greater than the dose³ required to initiate the polymerization of styrene it would appear that free radicals do not initiate the polymerization of phosphorus nitrilic chlorides.

For all these irradiations I am indebted to Dr R. Roberts and the Technological Irradiation Group of the Atomic Energy Research Establishment, Harwell.

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A Method for Determining Carbon-14 by Combustion using Calcium Carbonate

WHEN organic material is to be analysed quantitatively for the content of carbon-14 by combustion a standard method is to convert all the carbon into carbon dioxide which is then absorbed in a solution of sodium hydroxide¹. The carbonate thus formed is then precipitated by the addition of barium chloride and the total amount of carbon present determined by back titration with hydrochloric acid. The barium carbonate is collected in a manner suitable for counting.

Precipitation by barium chloride is convenient because accurate back titration is possible, and the precipitate can be collected fairly easily on a filter paper to give an even deposit suitable for counting. Where the total amount of carbon in the sample is small, the high atomic weight of barium is advantageous in bulking up the precipitate, but it also carries the disadvantage that there is high self absorption and consequently in comparison with lighter elements the sensitivity of counting is reduced.

Thus when there is adequate carbon available (in excess of 10 mgm for a 2.4 cm diameter end counting window) a carbonate formed from a lighter metal can give valuable extra sensitivity which may be especially needed when the material being assayed is of low activity.

Of the commoner metals with a low atomic weight only calcium carbonate gives a highly insoluble carbonate necessary for quantitative analysis. It has been found (Table 1) that when a comparison is made between precipitates of 'infinite thickness' of barium carbonate and calcium carbonate prepared from material of the same specific activity calcium carbonate gives an increased counting rate over barium carbonate by a factor of 1.85 ± 0.08 (cf. the molecular weight ratio of barium carbonate to calcium carbonate of 1.981).

Unfortunately precipitates of calcium carbonate formed by adding calcium chloride to mixtures of sodium hydroxide and sodium carbonate show a tendency to be gelatinous, and titration is made difficult and irreproducible by fading end points. The calcium carbonate crystals which form on standing may also be large and thus tend to form uneven preparations because filtration is too rapid.

It has been established that these difficulties can be avoided by adding magnesium chloride to the calcium chloride—a convenient proportion is one part magnesium chloride to two parts calcium chloride. With this mixture, back titration is consistent and reliable when thymol blue is employed as the indicator. The end point is not so readily recognized when the mixture of the calcium and magnesium chloride is substituted for barium chloride, but a warning of the approach of the end-point is given by a change in colour from blue to grey. Titration should not be carried out until sufficient time has elapsed for precipitation to be completed. About 1 hr has been found to be satisfactory for a wide range of conditions. The precipitates formed are not gelatinous, and the crystals are fine enough to give good filter preparations which can be dried without the cracking and distortions which may be produced by precipitates of barium carbonate. Moreover, the addition of magnesium chloride gives precipitates which show less tendency to stick to the flask.

These findings are based on a series of tests over a range of total alkalinities and ratios of sodium hydroxide to sodium carbonate (Table 1). Precipita-

| Alkali concentration (Normality) | Ratio NaOH Na ₂ CO ₃ | BaCl ₂ , CaCl ₂ , CaCl ₂ + MgCl ₂ | | | Counting Sensitivity Ratio | | |
|--|--|--|-------------------|--|-------------------------------|-------------------|--|
| | | BaCl ₂ | CaCl ₂ | CaCl ₂ + MgCl ₂ | BaCl ₂ | CaCl ₂ | CaCl ₂ + MgCl ₂ |
| High N = 0.4 | 1/1 | 97 | 85 | 95 | 1 | 1.83 | 1.77 |
| | 1/3 | 95 | 90 | 96 | 1 | — | 1.77 |
| Medium N = 0.2 | 1/1 | 100 | 92 | 100 | — | — | — |
| | 1/1 | 101 | 103 | 100 | 1 | 1.96 | 1.83 |
| | 1/3 | 100 | 106 | 101 | 1 | — | 1.75 |
| Low N = 0.1 | 1/1 | 100 | 99 | 100 | 1 | 1.87 | 1.88 |
| | 1/1 | 100 | 109 | 101 | 1 | 1.87 | 1.70 |
| | 1/3 | 100 | 107 | 102 | 1 | 1.96 | 1.93 |

Normal hydrochloric acid was used for titration throughout.

ting agents were all added in excess. All precipitates were prepared by filtration on to filter paper disks to 'infinite thickness' (more than 100 mgm) and replicated samples counted to 10,000 counts. From Table 1 it can be seen that calcium carbonate precipitates from calcium chloride alone as against the magnesium chloride mixture on average exhibit a slightly greater activity which is statistically significant ($P=0.01$). It is probable therefore that the precipitates from the mixed chlorides are slightly contaminated with magnesium hydroxide (not magnesium carbonate as this would tend to increase the sensitivity). Qualitative analysis shows magnesium to be present in the precipitates. The reason why magnesium chloride is effective is not understood.

I am indebted to Prof G. E. Blackman and members of his staff for their guidance and encouragement.

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Aromatic Ring Opening in the Presence of Oxygen in Irradiated Solutions

WHEN aqueous solutions of benzene are irradiated *in vacuo* with α rays or neutrons which produce oxygen, a dialdehyde, identified as muconodialdehyde, is produced¹. The same product was found also when solutions of benzene containing oxygen were irradiated with X rays². Thus ring opening appeared to be connected with the presence of oxygen, rather than with high radical concentrations and multiple reactions on the same benzene ring. The identification of the product as muconodialdehyde was confirmed³. Material balance cannot be obtained⁴ unless the formation of oxidation products other than phenol is assumed. The interesting possibility arises that aromatic ring opening in the presence of oxygen may occur as the result of a single primary radical reaction step and that muconodialdehyde is a primary product, being formed in direct competition with the formation of phenol. Analytical methods were used which enabled us to determine phenol, catechol and quinol^{1,2} in the presence of hydrogen peroxide⁵ and of muconodialdehyde, *o* and *p* quinone. These last three were determined after condensation with *p*-NO₂ phenylhydrazine in 2 *N* sulphuric acid, extraction into carbon tetrachloride re-extraction into 2 *N* sodium hydroxide and spectrophotometric measurement in 0.8 *N* sodium hydrate at 390 m μ (muconodialdehyde) 510 m μ (max) and 400 m μ (min) (*o* quinone) and 475 m μ (*p* quinone). Details of the analytical methods developed will be published separately.

We have found that muconodialdehyde is indeed formed simultaneously with phenol directly from benzene, without the previous formation of phenol, catechol, quinol or quinones. In Fig. 1 it is shown that in aqueous benzene solution irradiated with X rays at pH = 7.1 while phenol is formed with an initial yield of $G = 2.60$ muconodialdehyde is being formed with an initial yield of $G = 0.8$. Under the same conditions quinones are not formed in measurable quantities. The addition of phenol to the solution before irradiation does not increase the yield of muconodialdehyde. The ratio of G (phenol)/ G (muconodialdehyde) remains constant at ~ 3 in the range pH = 0.4–7.5. The absolute yield increases slightly at low pH values.

One possible explanation of the direct aromatic ring opening is that due to Weiss⁶ who assumes that the addition to benzene of one radical formed from water by the radiation leads to further addition of oxygen and formation of a hydroperoxide which, losing water, yields muconodialdehyde directly through ring opening. Alternative possibilities include the interaction of an excited benzene molecule with oxygen leading to direct ring opening and dialdehyde formation.

We have therefore investigated the photochemistry of aqueous benzene solutions containing oxygen, irradiated with ultra violet light of wave length above 2100 Å. Formation of phenol and muconodialdehyde was observed muconodialdehyde being once again a primary product formed in competition with the formation of phenol. The ratio of phenol/muconodialdehyde however changes with changing pH, the relative yield of muconodialdehyde decreasing strongly with decreasing pH. The different degrees of dependence on pH would indicate that the mechanisms involved in photochemistry and radiation chemistry are not wholly identical.

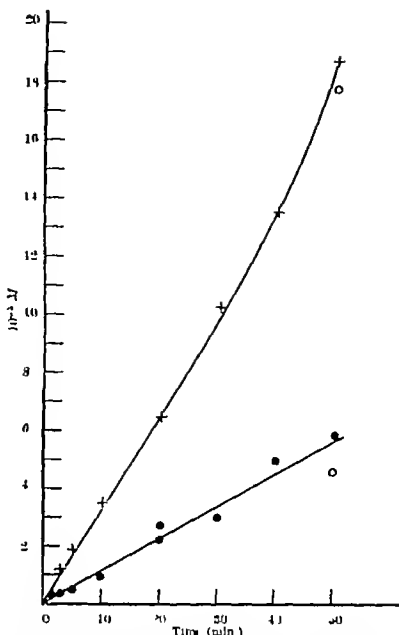


Fig. 1. Formation of phenol (+) and muconodialdehyde (●) in irradiated benzene solution at pH = 7.1. a, results in presence of initially added phenol (2×10^{-4} M, 200–450 Å). X rays 1540 r/min.

It appears therefore that the interaction with molecular oxygen of both an excited benzene molecule or of a radical formed from benzene may lead in aqueous solution directly to aromatic ring opening. We are investigating the possible connexion with the known effect of oxygen on the spectrum of benzene⁷.

Full details will be published separately.

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BIOCHEMISTRY

Isolation of 2-Aminoethane Phosphonic Acid from Rumen Protozoa

IN the course of experiments on the amino acid composition of rumen Protozoa an unknown nutrient positive substance was found by paper chromatography to be present in acid hydrolysates of the ether-ethanol soluble fraction of Protozoa. The substance was isolated in crystalline form and identified as 2-amino-ethane phosphonic acid.

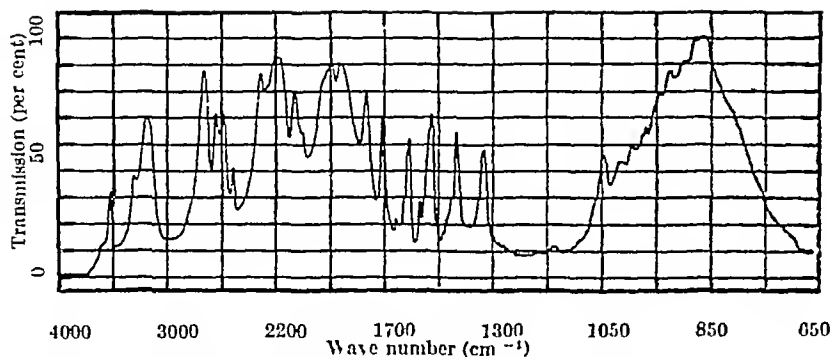


Fig 1 Infra red spectrum of isolated 2-aminoethane phosphonic acid ('Najol mull')

$\text{H}_2\text{NCH}_2\text{CH}_2\text{PO}(\text{OH})_2$, (synthesized by Finkelstein¹, Kosolapoff², Hackspill³ and Chavane⁴)

The isolation of this new amino-phosphonic acid was made possible by using paper chromatography for following the compound through each stage in the process

Protozoa were obtained by a modification of the method of McNaught *et al*⁵. Rumen contents were taken out through the rumen fistulas of two sheep maintained on daily rations consisting of 250 gm of concentrate mixture (equal parts of soybean cake and wheat bran) and 4 kgm of green grass or 1 kgm of dried grass. The contents were diluted with equal volumes of 0.5 per cent glucose and 0.5 per cent sodium chloride solution (39°C), and squeezed through 8-folded surgical gauze. The liquid was then poured into cylinders and allowed to stand in a warm water-bath (39°C). After a short time, the floating fibrous layer was removed by suction and the liquid was decanted, and the well-defined layer of larger Protozoa at the bottom was collected. The fibrous layer was well mixed with glucose-sodium chloride solution and allowed to settle once more to remove any Protozoa trapped in the fibrous materials. The liquid obtained by decantation was centrifuged (approximately 3,000 r.p.m.) and the smaller Protozoa were collected. The combined protozoal fractions were resuspended in glucose-sodium chloride solution and then treated in a manual centrifuge repeatedly until the supernatant layer was quite clear. The latter treatment is essential to obtain the Protozoa almost free from bacteria. Microscopic examination of the protozoal preparation showed that it contained no extracellular material, and its fibre content measured by the method of A.O.A.C. (1950) was 0.0 per cent. The Protozoa, which were still actively moving, were then preserved in acetone, filtered and air dried. In all, 50 kgm of rumen contents were treated in this way giving a total yield of 203 gm of Protozoa on a dry basis.

The fauna consisted of *Diplodinium* (mainly *D. magri* and *D. ecaudatum*), *Isotricha*, *Ophryoscolex*, *Dasytricha* and *Entodinium* (mainly *E. simplex*, *E. longinucleatum* and *E. caudatum*). *Entodinium*, *Ophryoscolex* and *Dasytricha* constituted a large portion of the whole.

The Protozoa were extracted with several portions of hot ether-ethanol (1:1). The extract was hydrolysed by refluxing for 13 hr with 100 ml constant-boiling hydrochloric acid. After extracting the resultant lipids with ether, the hydrolysate was taken to dryness and transferred with 4 ml of water to a bed (1.3 cm × 4 cm) of 'Dowex 50-X4' (hydrogen form). After washing the bed with water, the fraction containing acidic and neutral amino-acids was eluted with 5 per cent pyridine. The eluate was taken to dryness and transferred to a column (1.1 cm × 58 cm)

with 'Dowex 50-X4' (hydrogen form) a 1.2 ml of 0.6 N hydrochloric acid. Elution was carried out with 0.6 N hydrochloric acid. Under these conditions, the compound emerged from the column after about 150 ml as a single peak. The pooled effluent fractions containing the compound were concentrated to dryness, and the resultant liquid was transferred with 1-2 ml of 0.5 N acetic acid to a bed (1.1 cm × 4 cm) of 'Dowex 1 X8' (acetate form). The bed was washed with 0.5 N acetic acid until aliquots

from successive portions of the effluent were negative to ninhydrin. The first 7 ml of the effluent usually contained all this compound. The effluent was taken to dryness, dissolved in a small amount of 5 per cent acetic acid and treated with a small bed of decolourising carbon. Then the compound was obtained in crystalline form upon evaporation of the acetic acid, and recrystallization from water-ethanol gave 63 mgm of tiny rhombic crystals.

The compound had a melting point of 295-297° (decomp.), (found C, 19.57, H, 5.66, N, 11.34, P, 24.7; $\text{C}_2\text{H}_5\text{NPO}_3$ requires C, 19.20, H, 5.55, N, 11.20; P, 24.76 per cent), the nitrogen was present entirely as amino-nitrogen as shown by the Van Slyke amino-nitrogen method; the compound was soluble in water, less soluble in methanol, insoluble in ethanol, acetone, ether and benzene. It was optically inactive and had no unsaturated bond. Hydrolysis with 5 N sodium hydroxide at 120° for 8 hr did not liberate phosphoric acid. The infra-red spectrum (Fig 1) showed the absence of COO^- in the molecule. From the titration curve the molecular weight was estimated as 125.

From these results, the compound was assumed to be 2-aminoethane phosphonic acid, and this was synthesized by us by Chavane's method⁴. The isolated and synthetic compounds behaved identically on paper chromatograms developed in *n*-butanol-acetic acid-water, phenol-water, and lutidine-aniline-water solvents, and showed the same infra-red spectra.

Phosphorus is combined with other elements in organisms, as well as in their products, giving O-P, O=P and N-P, now the occurrence of the C-P bond has been demonstrated. It will be interesting to investigate whether this compound is widely distributed in Nature or occurs only in rumen Protozoa.

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Presence in Rose Hips of Substances Inhibiting the Oxidation of Ascorbic Acid

It has been demonstrated that even AnalaR grade chemicals may contain sufficient heavy-metal impurity to catalyse the oxidation of ascorbic acid¹, it was found that this oxidation was diminished by the addition of an aqueous extract of the flesh from hips of *Rosa canina*. The protective action of the hip extract was then tested in the presence of extracts of cauliflower ascorbic oxidase, apple polyphenolase and horseradish peroxidase. In each case reaction

Table 1 THE EFFECT OF AN AQUEOUS EXTRACT OF HIP FLESH ON THE OXIDATION OF ASCORBIC ACID BY DIFFERENT SYSTEMS

| Oxidizing system | Initial rate of oxidation of ascorbic acid (mgm/ml of reaction mixture/10 min.) | | Reduction in rate caused by hip extract (per cent) |
|---|---|--------------|--|
| | Control | +hip extract | |
| Cauliflower ascorbic oxidase | 0.093 | 0.090 | 39 |
| Apple polyphenolase | 0.112 | 0.077 | 22 |
| Hydroxylase peroxidase | 0.23 | 0.022 | 90 |
| $\times 10^{-3}M$ added copper sulphate | 0.085 | 0.003 | 96 |

mixtures were prepared containing the oxidase system, hip extract and added ascorbic acid (final concentration about 1.0 mgm/ml) buffered to pH 6.0, the mixtures were incubated at 25°C, aerated and samples taken at intervals for the assay of residual ascorbic acid. Controls were also run containing only the oxidase system, buffer and added ascorbic acid. To confirm the effect on metal catalysed oxidation a further mixture was made consisting of buffer ascorbic acid and copper sulphate (final concentration $2 \times 10^{-3}M$). Table 1 gives the average results for a number of replicate experiments.

The 'protective' substance or substances were thermostable and insoluble in ether but soluble in ethanol and acetone. An acetone extract was therefore reduced to dryness under vacuum and the residue in aqueous solution, was streaked on to Whatman No. 3 paper and run in butanol/acetone/water (4:1:5). The chromatogram was halved and one half was further cut into several longitudinal strips each strip was then sprayed with a different reagent. The other half was cut into ten transverse sections, each section was eluted with water and the eluates assayed for inhibitory activity as before, using cauliflower ascorbic oxidase. Controls were obtained from the eluates of the sections taken from before the starting line and from beyond the solvent front. Two inhibitory fractions appeared the first fraction giving the larger inhibition (83 per cent) remained on the starting line, had a brown colour, gave a darker brown colour with ammoniacal silver nitrate, a dark coloration with ferric chloride and reduced 2,6-dichlorophenolindophenol very slowly. The second fraction giving the smaller inhibition (30 per cent) was centred at R_F 0.5 and seemed to be associated with a band of yellow and blue fluorescence which appeared in ultra violet light after spraying with dilute ammonia. It also gave a pale greenish blue colour with ferric chloride.

The identities of the two fractions, and the effect of each of them on the other oxidases, have still to be worked out. In their combined effect on the three oxidases they resemble the inhibitor found in certain fruits and vegetables by Somogyi² so far as affinity to the tannins is concerned there is a similarity to the fraction isolated from the Indian gooseberry by Damodaran and Nair³. The function of these inhibitors *in vivo* is not known. It is perhaps significant however that (a) the flesh of rose hips possesses to a remarkable degree the ability to accumulate ascorbic acid and (b) the oxidation of ascorbic acid *in vitro* by the main soluble oxidase of the tissue (a peroxidase) is also inhibited by the protective substances described above.

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Dietary Protein and Serum Cholesterol in Rats

In order to study the influence of the diet on atherosclerotic changes in experimental animals diets have been developed which produce a high level of cholesterol in the blood. The degree of hypercholesterolemia is known to be dependent on several dietary factors, including the amount of protein.

In previous experiments with rats marked differences in the serum cholesterol level were observed if different protein concentrates were added to a hypercholesterolemic diet consisting of 15 per cent casein, 20 per cent hydrogenated coconut oil, 4 per cent minerals, 2.1 per cent vitamin mixture, 0.2 per cent choline chloride, 1 per cent cholesterol, 0.2 per cent choline acid and 67.5 per cent starch. The addition of 5 per cent wheat gluten resulted in a considerably lower cholesterol level than did the same amount of either gelatin or casein¹. Low serum cholesterol levels have also been observed in rats fed on diets containing wheat gluten as the only source of protein².

In order to obtain more information on the cholesterol lowering effect of various protein groups of 10–12 newly weaned male and female rats were fed the above hypercholesterolemic basal diet with supplements of different protein concentrates or amino acids. Additions were made at the expense of an equal amount of wheat starch. Growth and food consumption were recorded during 4 weeks. Thereafter the blood was analysed for total serum cholesterol content by the Liebermann-Burchard reaction. Results are presented in Table 1.

Each of the protein supplements added in a concentration of 5 per cent of the ration caused a decrease of the serum cholesterol level (experiment 1). The lowest levels were obtained with dried whole egg, wheat gluten, fish meal and meat meal. Supplements of casein, gelatin and soybean protein were less active in lowering serum cholesterol. The proteins with the higher activity supported faster weight gain.

In a subsequent experiment (experiment 2) the same low cholesterol level was obtained when a mixture of amino acids based on the composition of wheat gluten was substituted for the intact protein. Moreover it was observed that the addition of different combinations of each three essential amino acids (in concentrations of 0.2, 0.4 and 0.6 per cent respectively) lowered the cholesterol level if methionine was one of the three. This effect was paralleled by faster weight gain and increased food consumption.

Table 1 MEAN TOTAL SERUM CHOLESTEROL (MG/100 ML)

| Experiment | Addition to basal diet | Total serum cholesterol |
|------------|------------------------------------|-------------------------|
| 1 | None | 1021 |
| | Casein | 863 |
| | Gelatin | 780 |
| | Soybean protein | 762 |
| | Meat meal | 615 |
| | Fish meal | 610 |
| | Wheat gluten | 571 |
| | Dried whole egg | 555 |
| 2 | None | 177 |
| | Wheat gluten | 608 |
| | Amino acids of wheat gluten | 660 |
| | Methionine lysine isoleucine | 1076 |
| | Methionine threonine phenylalanine | 843 |
| | Tryptophan valine leucine | 1003 |
| | Histidine threonine leucine | 1239 |
| | Tryptophan lysine phenylalanine | 1739 |
| 3 | None | 1033 |
| | Wheat gluten | 464 |
| | Butanol extracted wheat gluten | 500 |
| | Butanol extract of wheat gluten | 59 |

¹ Respectively 0.4 and 0.6 per cent of the rat M.

These results suggest that the cholesterol-lowering effect of protein concentrates may be ascribed primarily to the amino-acids, especially methionine. This view is supported by the well-known hypercholesterolaemic effect of methionine, as observed in experiments with mice³, rats^{3,4} and chicks⁵⁻⁷. Moreover the basal diet used in our experiments is deficient in amino-acids containing sulphur, as it contains casein as the only source of protein in a suboptimal amount.

Recently, however, Nath and Harper⁸ arrived at the conclusion that the cholesterol lowering properties of wheat gluten are associated with the lipid fraction which may be removed by prolonged extraction with hot butanol. In our experimental design, however, wheat gluten extracted with butanol, showed nearly equal activity in lowering serum cholesterol as untreated wheat gluten, whereas the corresponding amount of butanol extract was less active (experiment 3).

Further experiments are necessary to evaluate the significance of amino-acids and accompanying lipids of protein-rich foods with respect to their cholesterol-lowering properties.

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Glutamic-Pyruvic Transaminase in Rabbit's Long Bones

THE finding that a transamination process is operative in metaphyseal cartilage of growing animals¹ led to drawn some relationship between protein metabolism and mineralization². Moreover, the observation that cortisone treatment which is known to inhibit skeletal development³ probably through a blocking activity on sulphate incorporation in the mucopolysaccharides⁴ of the organic matrix, also decreases the activity of glutamic-oxalacetic transaminase in metaphyseal cartilage⁵, suggests an active participation of transamination to osteogenesis, or at least in one of the metabolic processes leading to mineralization.

The relatively high level of pyruvate in pre-ossaceous cartilage⁶ prompted us to check the presence in this tissue of an enzyme involved in the utilization of this substrate, namely, glutamic pyruvic transaminase. This enzyme can be used as an indicator of amino-acid metabolism⁷. In order to connect the activity of this enzyme with mineral deposition, it was determined in three zones of the long bones of young rabbits in which mineralization (1) had not yet begun, (2) was proceeding, and (3) was already completed, namely, epiphyseal cartilage, the zone of the secondary spongiosa and cortical bone respectively.

The bones, which were obtained from 15 day-old rabbits, were quickly excised and chilled in ice. Glutamic-pyruvic transaminase was determined in the three zones mentioned above after careful homogenization of the tissues in a Waring blender. The reaction was followed for 30 min. at 37° C, following the method of Caldwell⁸.

Table 1. GLUTAMIC-PYRUVIC TRANSAMINASE IN THREE ZONES OF YOUNG RABBIT'S BONE (AVERAGE VALUES OF NINE DETERMINATIONS)

| | Metaphyseal cartilage | Secondary spongiosa | Epiphyseal bone |
|--|-----------------------|---------------------|-----------------|
| μmole pyruvate utilized/mg. bone (dry weight) /30 min. | 0.110 ± 0.038 | 0.209 ± 0.040 | 0.028 ± 0.003 |

The results show that besides aspartic-α-keto glutaric¹ glutamic pyruvic transaminase, is present in ossifiable cartilage. The comparison of the activities in the three zones shows a close relationship between the amount of the transamination and the degree of mineral deposition. The results obtained here do not show whether this fact is in some way related to an essential step in the bone-forming process, or whether it is only the expression of the local proteolysis which takes place during the osteoclastic resorption and reconstruction to which the zone of the secondary spongiosa is subjected⁹. However, the finding that testosterone treatment, which has a favourable influence on bone formation¹⁰, increases transamination in metaphyseal cartilage⁵ while corticoids, which are known to inhibit skeletal development¹¹, decrease transamination activity⁶, and the results reported here are consistent with an involvement of glutamic pyruvic transaminase in osteogenesis.

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Formation of Leucrose in Dextran-Producing Cultures of *Streptococcus bovis*

IN addition to dextran and fructose a mixture of reducing disaccharides, containing glucose and fructose, is formed when *Leuconostoc mesenteroides* strains are grown in sucrose media¹. The same disaccharides are produced when cell-free dextranase, obtained from a sucrose culture of *L. mesenteroides*, is incubated with sucrose². From this disaccharide mixture Stodola, Sharpe and Koepsell³ isolated one of the components as a crystalline compound. The pure sugar, named leucrose, was markedly resistant to acid hydrolysis and was shown to have the structure 5-O-α-D-glucopyranosyl-D-fructose². In recent studies on the production of dextran from sucrose by rumen strains of *Streptococcus bovis*^{3,4} it was noted that similar acid-resistant reducing disaccharides were formed in good yield when dextran was being produced. The exact nature of the sugars was not determined at the time. An examination of the disaccharide fraction has now been made.

Culture fluid (200 ml, freed from dextran) obtained from a 48 hr culture of *S. bovis* (strain 1)⁴ was fractionated with aqueous ethanol on a charcoal-celite column. The syrupy disaccharide fraction obtained (0.5 gm) was crystallized by the method of Stodola, Sharpe and Koepsell³ to yield, finally, 0.15 gm of twice recrystallized sugar. The sugar was shown to

be identical with authentic leucrose by the following evidence

After acid hydrolysis under conditions giving minimum fructose destruction (5 mgm in 1 ml of 0.25 *N* hydrochloric acid for 3 hr at 95°C)² approximately equal amounts of glucose and fructose together with some unhydrolysed disaccharide were detected on paper chromatograms. When the acid solution was heated for only 16 min., conditions which completely cleave furanoses, no detectable hydrolysis occurred. On paper chromatograms developed severally with the organic layers of mixtures of *n*-butanol, ethanol, water (40:11:10) pyridine, ethyl acetate water (1:2:2) and ethyl acetate acetic acid, water (8:2:2) the sugar was chromatographically identical to authentic leucrose. This identity was maintained on ionophore tograms run in borate buffer. The sugar was reducing to silver nitrate spray³ and gave a positive test for ketose with *p*-anisidine⁴. With urea phosphoric acid spray⁵ it gave the grey brown colour which is typical of leucrose⁶ but in marked contrast to the bright-lilac colour given by free fructose and acid labile fructose containing oligosaccharides. Similarly a positive ketose test was obtained with naphthoresorcinol and resorcinol sprays only when they were strongly acid⁴. With aniline diphenylamine spray⁷ both the sugar and authentic leucrose gave a greenish blue colour compared with a yellow-orange colour for free fructose. The colour reaction obtained with this spray is to be expected if leucrose has the structure assigned to it with the glycosyl linkage joined to the fourth carbon from the reducing carbon of the molecule⁸ (that is carbon 5 of fructopyranose).

By the Shaffer and Hartmann¹⁰ cuprimetric method the sugar had a reducing value of 46 per cent of that of fructose. This reducing value was unchanged after treatment with alkaline hypodite¹¹, showing that the reducing moiety of the sugar was fructose. Finally the infra red spectrum of the sugar was identical to that of leucrose and its m.p. (156–167°C) was not depressed by authentic leucrose (156–158°C)⁸.

The motile liquors from the crystallization contained in addition to leucrose, a second disaccharide which gave a blue ketose colour with urea phosphoric acid. This sugar appeared to be chromatographically similar to the second disaccharide which is present in *Leuconostoc* cultures. Attempts are being made to isolate and identify it.

It has been suggested that leucrose formation represents some intermediate step in dextran synthesis¹. This has been queried by Barker and Bourne¹ who suggest that leucrose synthesis if due to dextran sucrose activity is the result of a side reaction. Such a reaction could arise from the ability of fructose to

act as an alternative glucosyl acceptor in dextran synthesis. Although leucrose has been produced by the action of dextranase, the preparations used have been neither highly purified nor necessarily free from other carbohydrate synthesizing enzymes. The isolation of leucrose from *S. boydii* does offer further, indirect, evidence that its formation is due to dextran sucrose activity. First, with *S. boydii*, dextran is only produced from sucrose in the presence of abundant carbon dioxide^{3,4} although the organisms grow vigorously in sucrose in an atmosphere almost free of carbon dioxide. The reducing disaccharides were only detected in the cultures when they were producing dextran. Secondly, the rate of dextran formation can be controlled to some extent by buffering the culture when the disaccharide concentration increases as the rate of dextran production rises⁵.

The specimen of leucrose was kindly supplied by Dr F. H. Stodola, U.S. Dept. of Agriculture and the infra red spectra were prepared by Dr S. A. Barker of the University of Birmingham. This work was initiated (R. W. B.) at the Plant Chemistry Laboratory, Palmerston North, New Zealand and completed as part of a programme supported by the Department of Scientific and Industrial Research.

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PHYSIOLOGY

Neuromuscular Blocking Action of some Antibiotics

CURARE LIKE effects due to streptomycin and neomycin have been reported¹⁻³. These two antibiotics have been shown to be capable of exerting a curariform block of the neuromuscular transmission^{1,4}. One of us (G. B.) observed that some patients under heavy antitubercular treatment were more sensitive to

Table 1. PARALYSING ACTIVITY OF D-TUBOCURARINE CHLORIDE AND DECAMETHONIUM BROMIDE IN RABBIT¹ TREATED WITH ANTIBIOTICS

| Antibiotic | Dose mgm./kgm. | Curarizing drug | Dose μ gm./kgm. | Interval between the two treatments (min.) | Animals with partial paralysis/ treated animals | Animals with total paralysis/ treated animals ² | Dead animals/ treated animals |
|---------------------------|----------------|-----------------------|---------------------|--|---|--|-------------------------------|
| Control | — | d-tubocurarine | 120 | — | 14/21 | 0/21 | 0/21 |
| Streptomycin | 50 | " | 120 | 7-11 | 5/5 | 3/5 | 0/5 |
| Streptomycin | 20 | " | 120 | 10 | 1/2 | 0/2 | 0/2 |
| Chloramphenicol succinate | 100 | " | 120 | 8 | 5/9 | 1/9 | 0/9 |
| Control | — | " | 125 | — | 18/20 | 3/20 | 0/20 |
| Tetracycline | 25 | " | 125 | 7 | 7/7 | 6/7 | 2/7 |
| Penicillin .. | 100 | " | 125 | 3 | 0/9 | 1/9 | 0/9 |
| Control | — | Decamethonium bromide | 100 | — | 3/5 | 0/5 | 0/5 |
| Streptomycin | 50 | " | 100 | 5 | 0/5 | 0/5 | 0/5 |

¹ Partial paralysis means neuromuscular insufficiency which however allows the animals to resume quickly the normal standing position after they have been put in the lateral position.

² Total paralysis is a severe neuromuscular insufficiency in which the animals are unable to resume the normal position.

the muscular relaxant action of *d*-tubocurarine. We have therefore begun to study the influence exerted by the most widely used antibiotics on the sensitivity of rabbits to the paralyzing activity of curarizing drugs.

The antibiotic drugs so far tested include streptomycin sulphate, tetracycline, chloramphenicol succinate and benzyl sodium penicillin. The curarizing drugs were *d*-tubocurarine chloride and decamethonium bromide (C_{10}). All drugs were rapidly injected into the marginal vein of the rabbit's ear. The results obtained are shown in Table 1.

Streptomycin and tetracycline increase the curarizing effect of *d*-tubocurarine while the other two do not. Streptomycin did not affect the activity of decamethonium bromide under the experimental conditions we employed. However, if streptomycin is administered to rabbits which have just recovered from paralysis induced by decamethonium bromide it re-induces the muscular paralysis. A similar experiment was tried with *d*-tubocurarine and chloramphenicol succinate, but the results were negative.

This work is now being extended to other antibiotics and paralyzing drugs. The results will be published in detail elsewhere.

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Inositol Concentration in the Cerebrospinal and Ocular Fluids and Tissues of the Foetal and Adult Sheep

In the adult ewe the concentrations of free meso-inositol in the cerebrospinal fluid and aqueous humour are similar and exceed several-fold the concentration present in the plasma of the same animal¹. It was of interest to examine this relationship in the foetus since characteristically the concentration of inositol in foetal plasma is greater than in that of the mother².

Welsh mountain sheep of known conceptual age were used, in this breed, term is at the 145-147th day. In all cases the cerebrospinal fluid was obtained from the cisterna magna. Determination of the vitreous humour concentration was carried out after filtration through glass wool. The fluids and tissues were removed as rapidly as possible after death and estimated for inositol by the microbiological assay method³.

Krause and Weekers⁴, and later Van Heyningen⁵ showed that the lens was a tissue comparatively rich in inositol. In this series of observations the values obtained by Van Heyningen in adult sheep lens were confirmed and extended to include data on the foetal and neonatal lens. It will be seen from Table 1 that

Table 1 INOSITOL CONCENTRATION IN SHEEP LENSES (MG/100 GR MOIST TISSUE)

| | Free | | Total | |
|--------|---------|---------|---------|---------|
| | Mean | Range | Mean | Range |
| Foetal | — | — | 57 (6) | 50-60 |
| Adult | 487 (5) | 360-740 | 500 (6) | 340-940 |

Figures in parentheses refer to number of observations

free inositol forms a major part of the total inositol present in the adult lens, the total inositol concentration in the foetal lens is considerably less than that present in the adult. In the foetus no correlation of concentration with foetal age was apparent. By the 2nd and 10th day of neonatal life the free inositol in the lens had risen to 93 and 146 mgm/100 gm moist tissue, representing 99 and 79 per cent of the total inositol respectively. In contrast to the lens, the disparity between the total inositol in the optic nerve of the adult and foetus is not so great, the mean concentrations were 335 mgm/100 gm moist tissue (range, 280-440, six observations) and 245 mgm/100 gm moist tissue (range, 170-290, five observations) respectively.

It will be seen from Table 2 that in spite of the high concentration of inositol present in the foetal plasma, the concentration in the cerebrospinal fluid is correspondingly elevated, such that the cerebrospinal fluid/plasma ratio of the foetus and the lamb resembles that of the adult. The concentrations in the foetal aqueous humour, however, are similar to those of the plasma and only attain an aqueous humour/plasma ratio comparable to the adult in late foetal life or shortly after birth.

Table 2 FREE INOSITOL CONCENTRATION IN PLASMA, CEREBROSPINAL FLUID (CSF) AND OCULAR FLUIDS OF THE SHEEP (MG/100 ML)

| | Foetal or neonatal age (days) | Plasma | CSF | AH | VH |
|--------|-------------------------------|-----------|-----------|------------|------------|
| Foetus | 94 | 20.4 | 166.0 | 27.8 | — |
| | 113 | 23.4 | 83.0 | — | — |
| | 127 | 22.4 | 78.3 | 24.5 | 27.5 |
| | 141 | 14.1 | 71.1 | 17.7 | 20.2 |
| | 152 | 13.3 | 68.1 | 24.3 | 13.4 |
| | 158 | 11.2 | 70.1 | 22.3 | 14.2 |
| | 142 | 11.0 | 52.0 | 13.3 | 13.1 |
| | 145 | 4.1 | 41.0 | 10.4 | 10.4 |
| | 2 | 4.0 | 38.0 | 8.8 | 16.7 |
| | 2 | 2.4 | 40.6 | 11.2 | 24.3 |
| Lamb | 3 | 2.5 | 21.4 | 6.2 | — |
| | 5 | 3.8 | 22.8 | 18.7 | — |
| | 10 | 2.5 | 16.0 | 17.1 | 15.2 |
| | 15 | 1.6 | — | 7.7 | — |
| | Range | 0.44-5.8 | 5.3-21.5 | 6.4-20.6 | 7.7-19.0 |
| Adult | Mean | 1.28 (20) | 9.11 (20) | 10.07 (29) | 10.74 (81) |

Figures in parentheses refer to number of observations

The concentration in the vitreous humour, in both the adult and the foetus, is similar to the concentration present in the respective samples of aqueous humour. In the adult, the combined inositol in the vitreous humour amounted to a mean of 13.8 per cent of the total inositol present (seven observations).

A possible interpretation of these results is that the secretory processes responsible for the formation of cerebrospinal fluid and aqueous humour have a different developmental time course. Flexner⁶, in studies on the formation of cerebrospinal fluid in the foetal pig, concluded that up to the first third of gestation the formation was one of diffusion and thereafter one of secretion. A difference in the degree of development of the blood-cerebrospinal fluid and blood-aqueous humour barriers towards *p*-amino-hippurate was observed by Davson⁷ in the rabbit six weeks after birth. It is suggested, in view of the inositol concentrations, that an analogous development of the secretory processes responsible for the formation of these two extracellular fluids takes place. Thus, in the sheep foetus, a secretory process for the formation of cerebrospinal fluid would appear to be established by 94 days, whereas in the aqueous humour the change over from a plasma diffusate to a secretion is either delayed until birth or that the rate of turnover, due to a less efficient

blood aqueous barrier, is so fast as to mask the secretory activity

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Influence of Dietary Protein Percentage on Growth of Wool

As with other forms of animal production, it is a common experience that growth of wool is affected by nutrition and the quantitative relation between such growth and intake of food has been studied experimentally.^{1,2}

Early investigators stressed the high cystine content of wool, and suggested that the nutritive value of pastures for growth of wool depended on their ability to supply this amino acid.^{3,4} Marston⁵ elaborated the theory that the rate of growth of wool is determined principally by the dietary supply of essential amino acids, subject to competing demands on this supply. This view of the mechanism by which nutrition influences the rate of growth of wool has been widely accepted despite some earlier evidence to the contrary.^{6,7}

Results of recent experiments at this Laboratory indicate that growth of wool is independent of the dietary protein percentage over a wide range for diets fed both at maintenance and *ad libitum* levels of intake. Pelleted diets ranging from 7.5 to 20 per cent crude protein were prepared by varying the proportions of peanut meal and maize in the concentrate and the proportions of lucerne and wheat chaff in the roughage. An additional diet was used in which the concentrate comprised a mixture of wheat, oats, linseed meal and coconut meal. The diets all contained 50 per cent roughage and 50 per cent concentrate and were approximately equal in net energy content as judged by published starch equivalent values for the constituent feed stuffs.

Growth of wool was measured at 4 weekly intervals by clipping 10 x 10 cm midside sample areas defined by tattoo lines. The relation between the sample and total growth was determined for each sheep over a 12 week period during the experiment (period 2). It has been found that the ratio of total to midside growth is not affected by the level of feeding.⁸ The wool samples were extracted successively with ether and water to remove wool wax and suint and the oven dry weights obtained. The crude protein content (N x 6.25) of the diets was determined by Kjeldahl's method on aliquot samples of feed.

Thirty six 2 year old medium wool Merino ewes housed in individual pens were fed 500 gm daily of one diet prior to being divided at random into 4 groups and fed *ad libitum* diets of different protein percentage. Intakes of the same diets were reduced again to 500 gm per day for a further period. Afterwards the sheep were all again fed one diet prior to being divided into four different groups and fed another series of diets. The sequence of experimental treatments and results are shown in Table 1. The intake and growth data for periods 2 and 3 are for

Table 1. WOOL GROWTH, FEED INTAKE, CRUDE PROTEIN (PER CENT) OF DIET AND EFFICIENCY OF PROTEIN CONVERSION INTO WOOL

| Period | Days (week) | Group | Ration | Feed intake (gm/day) | Crude protein (per cent) | Wool growth (gm/day) | Efficiency (per cent) |
|--------|-------------|-------|--------|----------------------|--------------------------|----------------------|-----------------------|
| 1 | 8 | I | F0 | 500 | 16.9 | 4.00 | 5.7 |
| | | II | F0 | 517 | 16.0 | 4.40 | 5.0 |
| | | III | F0 | 507 | 16.0 | 4.21 | 5.6 |
| | | IV | F0 | 508 | 16.0 | 4.38 | 5.3 |
| 2 | 12 | I | F0 | 1,535 | 18.6 | 12.16 | 4.4 |
| | | II | F11 | 1,380 | 18.5 | 11.4 | 4.9 |
| | | III | F12 | 1,382 | 24.0 | 12.54 | 3.8 |
| | | IV | F13 | 1,359 | 29.3 | 12.27 | 3.2 |
| 3 | 12 | I | F10 | 400 | 18.3 | 6.38 | 6.0 |
| | | II | F11 | 500 | 18.3 | 6.45 | 7.0 |
| | | III | F12 | 500 | 21.5 | 6.80 | 5.7 |
| | | IV | F13 | 500 | 20.5 | 7.33 | 5.0 |
| 4 | 4 | I | F11 | 500 | 18.1 | 5.70 | 6.4 |
| | | II | F11 | 500 | 18.1 | 5.53 | 6.1 |
| | | III | F11 | 500 | 18.1 | 6.89 | 6.6 |
| | | IV | F11 | 500 | 18.1 | 6.02 | 6.7 |
| 5 | 12 | I | F10 | 447 | 7.5 | 5.10 | 16.8 |
| | | II | F15 | 401 | 11.2 | 4.6 | 8.4 |
| | | III | F14 | 500 | 13.6 | 4.88 | 7.7 |
| | | IV | F11 | 405 | 1.2 | 4.93 | 5.6 |

Efficiency is expressed as (gm. clean dry wool)/(gm. crude protein intake) x 100

the latter 8 weeks of these periods to allow some adjustment to occur to the changes in feed intake at the beginning of these periods. Intakes of 500 gm per day were sufficient to maintain the sheep in average body condition. No differences in body weight change were observed between the groups on diets of different protein content at this feed intake. On *ad libitum* intakes only slight differences were observed in the rates of body weight increase between the different diets. This suggests that diets were in fact approximately isocaloric in net energy.

The effect of increasing the intake of food of the sheep is shown by a comparison of the growth of wool in period 2 with that for the other periods. Comparison between periods also shows the existence of a seasonal trend in growth of wool.⁹ The experiment commenced on August 2, 1957 and finished a year later midsummer occurring in period 2.

Within any period there were no statistically significant differences in growth of wool between the groups fed diets of different protein content. The commonly observed growth response to increasing intake of food cannot therefore be attributed to an increasing dietary supply of amino acids and must be wholly due to an increased energy supply when diets containing more than 8 per cent crude protein (on a dry matter basis) are fed. It must be expected that with diets of lower protein content a point must be reached when the supply of amino acids is not sufficient for wool synthesis. However it is not known whether this point is reached before protein deficiency interferes with the digestive function of the rumen and thereby with the availability of energy from the diet.

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A New Trichothecin-like Antifungal Antibiotic

In a screening programme for antibiotic effects of Basidiomycetes we found a strain which inhibited *Candida albicans*. The antifungal substance was produced by this strain in surface and submerged culture in a medium containing peptone, glucose, inorganic salts and aneurin. The substance for which we provisionally propose the name 'antibiotic-T' was easily extracted from the fermentation liquor by most of the usual solvents. After extraction with benzene and evaporation of the solvent the residue became crystalline within a few days. Recrystallization twice from methyl alcohol gave pure crystals (prisms), melting point 126°C , $[\alpha]_D^{20} +13.5^{\circ}$, c 1 in chloroform. No ultra-violet absorption characteristic of antifungal antibiotics of the polyene type was found. The antibiotic contains no halogen, sulphur or nitrogen. Micro-analyses found (per cent): carbon, 68.51, hydrogen, 7.6, and oxygen, 25.0. The substance is very slightly soluble in hot water and gives a neutral solution; it is soluble in alcohols and sunflower oil and readily soluble in non-polar solvents. Its solution in water is stable for two months, is thermo-stable at its boiling point, but is inactivated at pH 12 within a few hours.

From the chemical and biological data available antibiotic-T seems to be very similar to the antifungal antibiotic trichothecin^{1,2}. The two materials have however different R_F values in paper chromatography tests. A further difference between the two antibiotics is the negative 2,4-dinitrophenylhydrazine test of the new antibiotic. The infra-red absorption spectra of the two substances (Fig. 1) are very similar; antibiotic-T however has no band at 1636 cm^{-1} and therefore presumably contains no ketone group.

Freeman *et al.*¹ found trichothecin to be an ester, the components of which are isocrotonic acid and a ketonic alcohol, trichothecolone. The structure of the latter was given by Freeman recently². The new antibiotic was hydrolysed with a cold methanolic solution of potassium hydroxide. The acid component obtained seems to be identical with the acid component of trichothecin by the paper chromatography test.

The new alcohol component of hydrolysis has a m.p. 152°C on recrystallization from a mixture of

TABLE 1

| | Days of incubation | | | | |
|------------------------------------|--------------------|-------|------|------|------|
| | 1 | 2 | 5 | 8 | 14 |
| <i>Candida albicans</i> | 4.0 | 11.0 | 45.0 | 90.0 | |
| <i>Saccharomyces cerevisiae</i> | 5.0 | 10.0 | 20.0 | 37.0 | |
| <i>Cryptococcus neoformans</i> | | 2.5 | 10.0 | 15.5 | 40.0 |
| <i>Aspergillus niger</i> | | 100.0 | | | |
| <i>Trichophyton mentagrophytes</i> | | 2.5 | 40.0 | 90.0 | |
| <i>Fulcrumophyton inguinale</i> | | | | 4.0 | 20.0 |
| <i>Microsporum audouinii</i> | | | 1.2 | 2.5 | 5.0 |

The fungi were seeded on the surface of agar slants containing various antibiotic concentrations. The tubes were incubated at 25°C . The figures indicate mean total inhibition on a given day of incubation.

benzene and light petroleum. The hydroxyl content was 6.82 per cent which corresponds to a molecular weight of 250, if one OH group is present per molecule.

The antifungal effects of antibiotic T (Table 1) are similar to those of trichothecin², though somewhat weaker in the case of most of the fungi examined. The effect is fungistatic. Bacteria are not inhibited at a concentration of less than $500\text{ }\mu\text{g}/\text{ml}$. The LD_{50} in mice after intraperitoneal administration in a gum arabic suspension is $810\text{ mg}/\text{kg}$ and after administration *per os* more than $1000\text{ mg}/\text{kg}$. Doses smaller than the LD_{50} produce transient collapse, ataxia, paralysis of the hind legs and some times convulsions, symptoms which are analogous to those observed by Freeman with trichothecin². No antibiotic was found in the blood after administration by various routes of 50 – $200\text{ mg}/\text{kg}$ to mice and rats. The antibiotic is inactivated when incubated with blood at 37°C for 24–48 hr. It is effective in reducing the yeast cells found in faeces of mice fed a standard diet containing terramycin, after the administration of $250\text{ mg}/\text{kg}$ by mouth with a sonde. Reddening and irritation is caused when the antibiotics applied to the skin of guinea pigs, rabbits and human beings; the alcohol component of the new antibiotic does not have this effect.

The antibiotic isolated seems to differ from those mentioned in the literature but is very similar to trichothecin. The antifungal antibiotic cephalothecin³, perhaps similar to trichothecin, contains carbon, hydrogen and oxygen and decomposes at 124 – 26°C . Antibiotic-T melts without decomposition at this temperature.

We wish to thank S. Holly for the infra-red absorption data.

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Phenazine Di-N-Oxide as a Carcinostatic Agent

PHENAZINE di-N-oxide has been found to be a carcinostatic agent for the Ehrlich ascites tumour. More than 90 per cent of tumour-bearing animals treated with this compound intraperitoneally survived 30 days or more, and were then free of tumours as

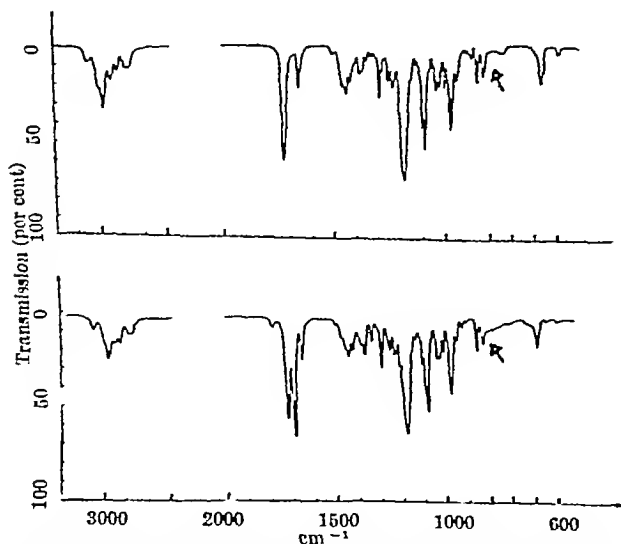


Fig. 1. Infra-red absorption spectra 1.6 per cent solutions of (top) antibiotic-T and (bottom) trichothecin in carbon tetrachloride. The region of solvent absorption is marked with an arrow.

compared with an average 13 day survival of the untreated control group. A comparison of this agent with other drugs active against this tumour reveals that 6 mercaptopurine administered intraperitoneally¹ or *N*-methylformamide given orally², extended mean survival time by 25-100 per cent but that all animals died with ascites tumour. Other phenazine compounds, like the dye janus green B⁴ have been reported to have activity against a transplanted mouse tumour but only at toxic levels.

The compound was made by oxidation of phenazine⁴ Swiss Webster mice were inoculated with 0.1 ml

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Table 1 EFFECT OF PHENAZINE DI-N-OXIDE ON SURVIVAL TIME OF MICE WITH EMBLICH ASCITES TUMOUR

| Drug | Number of Animals | Weight at day | | | Mean survival time | Range (days) | Number of survivors after 30 days |
|--|-------------------|---------------|------|------|------------------------------------|--------------|-----------------------------------|
| | | 7 | 14 | 21 | | | |
| Controls | 20 | 20.1 | 22.2 | 24.0 | 13.3 ± 2.0 | 10-17 | 0 |
| Phenazine-di-N-oxide intraperitoneally 50-75 mgm./kgm. | 50 | 10.5 | 10.2 | 10.0 | One animal dead on day 16 10 21 23 | — | 46 |
| Phenazine-di-N-oxide subcutaneously 50 mgm./kgm. | 10 | 20.1 | 21.7 | 25.0 | 22.6 ± 2.7 | 19-23 | 2 |
| Phenazine intraperitoneally 75 mgm./kgm. | 10 | 10.0 | 21.1 | 23.9 | 15.3 ± 1.8 | 12-17 | — |
| 2,3-dimethyl quinoxaline di-N-oxide intraperitoneally 50 mgm./kgm. | 10 | 18.1 | 22.2 | 30.2 | 12.4 ± 3.8 | 8-17 | 1 |

* Mean survival time calculated exclusive of 30 day survivors

$$SD = \frac{1}{\sqrt{n-1}} \sqrt{\frac{\sum (x-\bar{x})^2}{n-1}}$$

(10-16 × 10⁶ cells) of undiluted ascitic fluid from a donor mouse bearing a 7 day-old ascites tumour 24-48 hr later the drug was administered intraperitoneally or subcutaneously as a suspension in 1 per cent carboxymethylcellulose at a dose of 50-75 mgm./kgm. The drugs were given once daily for five consecutive days. Control animals were similarly treated with the exception that only the suspending agent without drug was injected. At the end of thirty days all surviving animals were killed and examined for tumours.

The results for the several agents are shown in Table 1. After intraperitoneal treatment 46 out of 50 mice survived 30 days and were then grossly free of tumours except in 2 cases where there were subcutaneous solid tumours. When the drug was administered subcutaneously the average survival was 22 days as compared with 13 days for the controls and only 2 of the animals survived to 30 days without the appearance of tumour. This suggests that the intraperitoneal effect was in part local. Phenazine itself and 2, 3-dimethylquinoxaline di-N-oxide a compound with structure similar to the active phenazine-di-N-oxide, were devoid of activity. In other experiments with the di-N-oxide now in progress a few subcutaneous solid tumours have been noted in animals surviving over 40 days. As a result the compound is being tested for carcinogenic activity also.

Phenazine-di-N-oxide is a simple compound it is apparently not an anti-metabolite and it is not a chelating agent. The nature of the inhibition is being investigated, but the presence of the potentially reducible N=O groups in the 9,10 positions of the molecule suggests that respiration may be depressed through interference with electron transfer.

Thiamine-sparing Action of Sorbitol in Rats and Mice

DEFICIENCY of thiamine may be prevented in rats if they are given sorbitol. Administration of sorbitol to deficient rats cures the deficiency. Withdrawal of the sorbitol leads to deficiency¹. All these results have now been found also in mice (Fig. 1). Mice like rats, also showed an enlarged caecum when they were fed diets with sorbitol (Table 1).

About 1 in 8 of the mice did not respond to sorbitol in these ways. On diets deficient in thiamine they lost weight and ultimately died even though sorbitol was present in their diets. We found that these mice which did not respond showed no enlargement of the caecum and developed bradycardia. This is a characteristic feature of thiamine deficiency in rats, although so far as we know it has not been described in mice.

With rats we have attempted to assess the thiamine equivalent² of sorbitol. First we compared the growth of rats receiving 15 per cent sorbitol in their diets and no thiamine with that of rats receiving 15 per cent glucose and graded doses of thiamine. The rats receiving 8 µgm thiamine daily grew rather more slowly than those receiving sorbitol, whereas those receiving 12 µgm daily grew faster. We can say then that 15 per cent sorbitol in the conditions of our experiments is equivalent to the administration of something like 10 µgm thiamine daily.

Secondly, we have compared the stores of thiamine in the tissues of rats fed sorbitol and no thiamine with those of rats fed glucose and graded doses of thiamine. We determined the thiamine by the thiochrome method in brain, liver and gastrocnemius muscle. By interpolation we calculated that the rats receiving sorbitol had stores of thiamine as large

Table 1 EFFECT OF SORBITOL ON WEIGHT OF ALIMENTARY CANAL IN MICE

| Organ | Wet weight (gm) | | |
|---|---------------------------|------------------------|-----------|
| | Diet without sorbitol (A) | Diet with sorbitol (B) | Ratio B/A |
| Small intestine | 1.18 | 1.55 | 1.3 |
| Small intestine with contents | 1.57 | 1.77 | 1.1 |
| Cæcum | 0.03 | 0.28 | 3.5 |
| Cæcum with contents | 0.24 | 0.99 | 4.1 |
| Average weight of mice (number of mice) | 29 (4) | 27.2 (9) | |

as they would have obtained from ingesting about 9 μ gm thiamine daily

Thirdly, we have roughly determined the thiamine equivalent of a single dose of sorbitol given to thiamine-deficient rats. The heart-rate of the rats was measured daily. When it had fallen from the normal 450 beats a minute to less than 300, we gave one dose of 1 gm. of sorbitol. This restored the heart-rate to normal for 12 days. A dose of 10 μ gm thiamine restored the heart-rate for 10 days.

In our earlier communication, we gave reasons for believing that the thiamine sparing action of sorbitol was brought about by a synthesis of thiamine in the gut. The question then arises whether the vitamin was absorbed in the gut, immediately after synthesis, or whether it was excreted in the faeces and was available only after the animal had eaten its faeces.

As is well known, coprophagy in rats is not prevented by simple means such as housing the animals on grids, as we have done in all our experiments. We therefore attempted to devise a procedure which

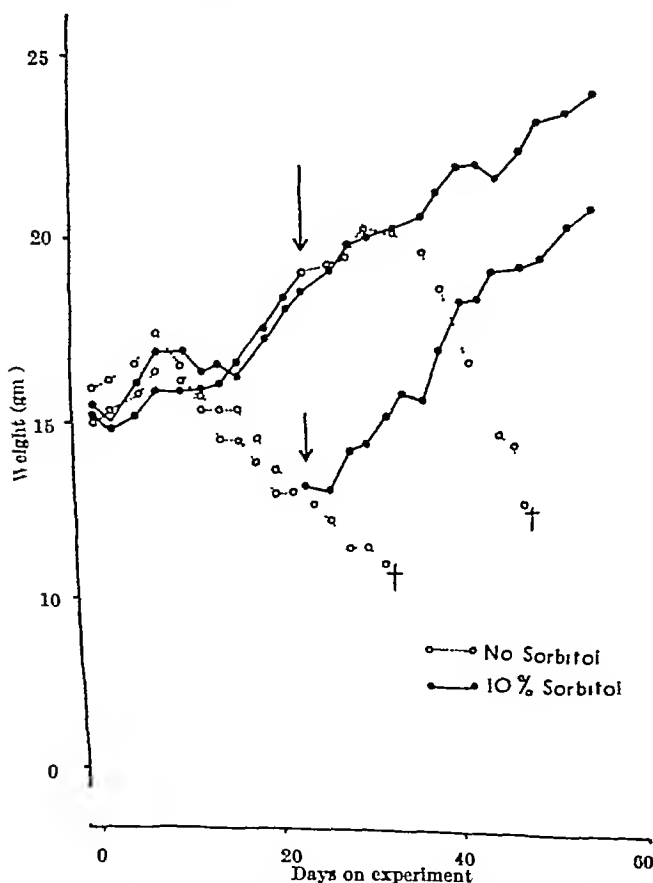


Fig. 1. Effect of change-over of diet. Growth of 4 mice on diets deficient in thiamine: one pair was initially given no sorbitol and one pair given 10 per cent sorbitol. At the times indicated the diet of one mouse of each pair was changed to that of the other pair. \circ , Diet with 60 per cent sucrose; \bullet , diet with 10 per cent sorbitol and 50 per cent sucrose.

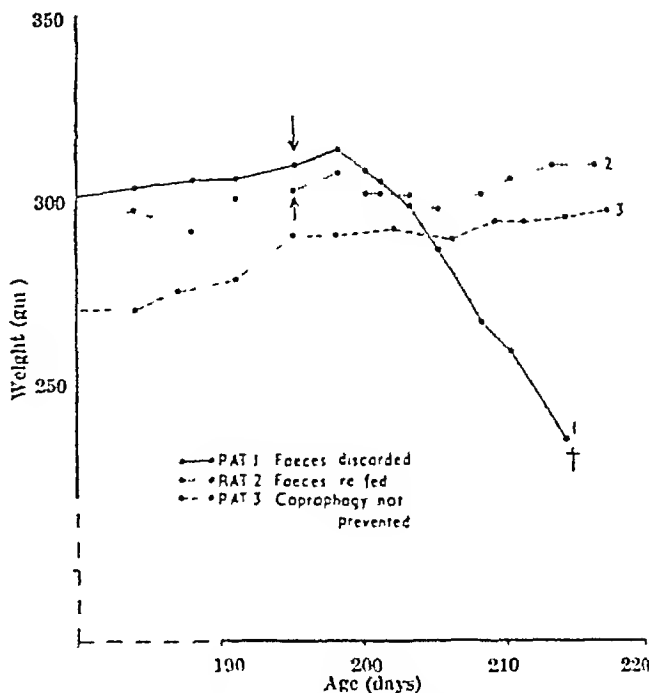


Fig. 2. Role of coprophagy in thiamine-sparing action of sorbitol. 3 rats fed thiamine free diet containing 10 per cent sorbitol and 50 per cent sucrose for about six months from weaning. At times indicated, devices to prevent coprophagy were fitted to rats 1 and 2. \bullet , Rat 1 faeces discarded; \circ , rat 2, faeces collected each day and fed to animal following day; \dots , rat 3 coprophagy not prevented.

would prevent coprophagy. In the first series of experiments when we thought we had achieved this sorbitol still showed its thiamine sparing action, and we reported that coprophagy was not a necessary feature of the action of sorbitol². Later, we were able quite definitely to prevent coprophagy by a recently published technique³. As a result, we can now say that most of the thiamine synthesized in the gut under the influence of sorbitol only becomes available to the rat after coprophagy. If coprophagy is prevented, rats fed sorbitol without thiamine lose weight and die of thiamine deficiency. If the faeces collected in these experiments are re fed to the rats, they grow in the usual way (Fig. 2). These faeces from sorbitol-fed rats also prevent the development of deficiency in rats fed on glucose.

By further experiments of this sort we found that the thiamine deficient rats fed on glucose also excrete a small amount of thiamine in the faeces. Though very little it is nevertheless enough to prolong the life of such rats for a short while. If coprophagy is prevented, death from thiamine deficiency is accelerated.

Measurement of the heart-rate confirmed that the effects of allowing or preventing coprophagy were due specifically to thiamine. The prevention of coprophagy in rats fed on sorbitol led not only to loss of weight but also to the development of bradycardia. Administration of thiamine, or removing the device which prevented coprophagy, led to a restoration of the heart rate.

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July 30

¹ Morgan T. B. and Yudkin J., *Nature*, 180, 543 (1957).

² Morgan T. B. and Yudkin J., *Chem. and Indust.* 37 (1959).

³ Barnes R. H., Flala G., McGhee, B. and Brown, A., *J. Natl.*, 63, 489 (1957).

Effect of Sorbitol on the Urinary Excretion of some B Vitamins in Man

THE inclusion of sorbitol in the diets of rats makes them able to survive and grow in the absence of dietary sources of B vitamins¹. It is likely that the sorbitol acts by increasing the synthesis of these vitamins in the alimentary canal. We have investigated the possibility that sorbitol similarly increases synthesis in man. We have done this by determining the urinary output of three vitamins in a male subject aged 27 (J.D.W.) before during and after the ingestion of sorbitol.

Urine was collected for exactly twelve hours daily, for four days a week, over a period of 26 weeks. From the beginning of the fifth week to the end of the thirteenth week sorbitol was taken. The intention was to begin with 20 gm daily for two or three days, and to increase it within two weeks to 50 gm daily. However, occasional mild diarrhoea led to reduction of the dose from time to time, so that the daily intake varied between 20 and 40 gm during the nine weeks of supplementation. The vitamins investigated were thiamine, riboflavin and nicotinic acid. We measured the excretion of the first two as such and of the major excretory product of the third, N¹ methyl nicotinamide. Fluorometric methods were used for all estimations, that of Mawson and Thompson for thiamine² of Slater and Morrell for riboflavin³ and of Carpenter and Kodicek for N¹ methyl nicotinamide⁴.

The subject kept a weighed record of all the food he ate during the 26 weeks of experiment; the nutrients therein were calculated from food tables. There was little variation in the intake of any nutrients including the three vitamins under study; in particular there was no significant difference in intake between the periods before, during and after the consumption of the sorbitol (Table 1).

The excretion of the vitamins fluctuated considerably (Fig. 1). The ingestion of sorbitol produced no effect during the first week or more, but then there was a distinct increase of excretion of all three vitamins. When the sorbitol was stopped there was again no change for a week or more. After this, the excretion of thiamine and riboflavin fell but the excretion of N¹ methyl nicotinamide remained at the level it had reached with sorbitol. It is possible that

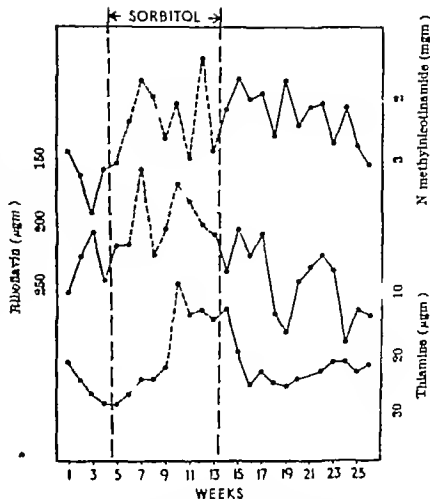


Fig. 1. Effect of sorbitol on urinary excretion of B vitamins. Urinary excretion of B vitamins before, during and after ingestion of 20-40 gm sorbitol daily. Values are mean 12-hourly excretions for 4 days weekly.

this might also have shown a fall if we had continued with the study for a longer period. For statistical calculation it seemed reasonable to omit a transition period of three weeks following the beginning or end of sorbitol administration (Table 2). We then find that the increases in excretion of all three vitamins with sorbitol and the decreases in excretion of thiamine and riboflavin after sorbitol are significant at levels of 1 per cent or less.

The effect of sorbitol on increasing the excretion of vitamins might be due either to increased synthesis with subsequent absorption, or to enhanced absorption of the vitamins already present in the diet. The latter mechanism it has been suggested occurs with vitamin B₁₂ (ref. 5). However, we already know from our animal experiments that sorbitol induces a synthesis of B vitamins. It is also known that vitamins synthesized in the human gut may be absorbed. We are inclined therefore to believe that our results are due to increased synthesis of three of the vitamins which are then absorbed. The delay in the effect of sorbitol on the excretion of these vitamins would support the suggestion that the effect is on microbial synthesis rather than on absorption. The final decision however must depend on further investigation.

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Table 1. AVERAGE DAILY INTAKE OF CALORIES AND NUTRIENTS

| | Weeks 1-4 (before sorbitol) | Weeks 5-13 (during sorbitol) | Weeks 14-26 (after sorbitol) |
|-----------------------|-----------------------------------|------------------------------------|------------------------------------|
| Calories | 2120 | 2200 | 2270 |
| Carbohydrate (gm.) | 290 | 285 | 235 |
| Fat (gm.) | 108 | 97 | 94 |
| Thiamine (μgm.) | 1.1 | 1.1 | 1.0 |
| Riboflavin (μgm.) | 2.1 | 2.0 | 2.0 |
| Nicotinic acid (mgm.) | 14.1 | 13.6 | 13.7 |

Table 2. VITAMIN EXCRETION IN URINE,
AVERAGE VALUES FOR 12 HR PERIODS

| Vitamin | Weeks 1-4 (before sorbitol) | Weeks 5-13 (during sorbitol) | Weeks 14-26 (after sorbitol) | Significance (P) |
|--|--------------------------------------|---------------------------------------|---------------------------------------|---------------------|
| Thiamine (μgm.) | 1.47 | 23.0 | 16.6 | 0.001 |
| Riboflavin (μgm.) | 172 | 200 | 147 | 0.01 |
| N ¹ methyl nicotinamide (mgm.) | 2.34 | 2.83 | 2.81 | 0.002 |

Sorbitol 20-40 gm daily was taken during 5th to 13th weeks of the experiment. Urine was collected for 12 hr each day from Monday to Thursday.

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PATHOLOGY

Tumourigenesis in Ovaries of Mice Transplanted to the Liver, Kidney and Adjacent Tissues

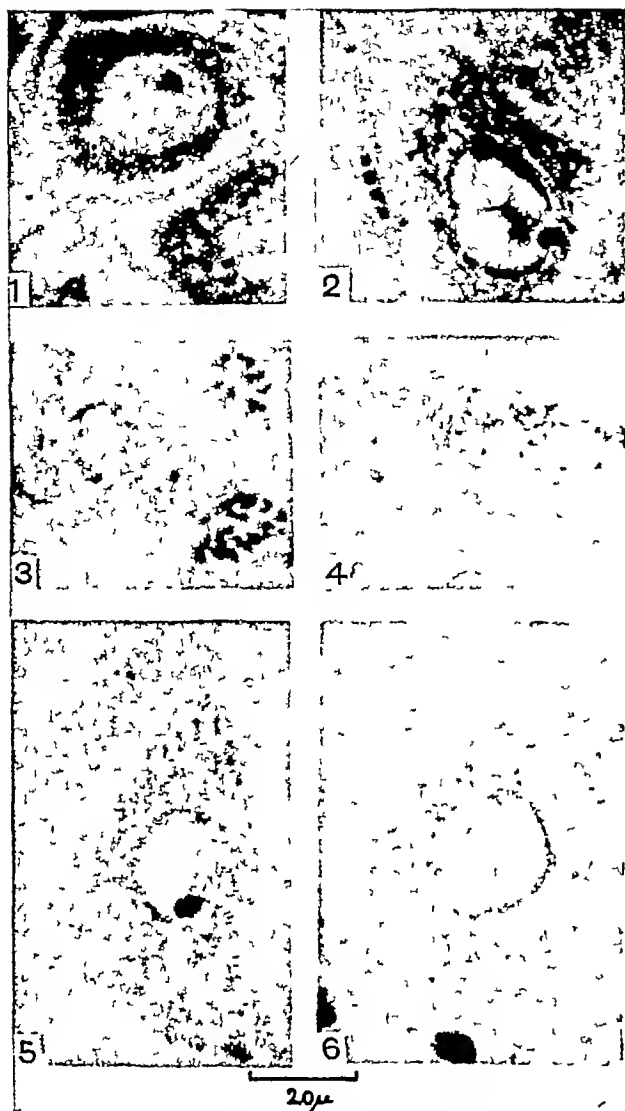
OVARIAN tumours, though rare in normal mice, occur with high frequency under a variety of experimental conditions: low doses of total body X-radiation¹, transplantation to the spleen², application of 9-10 dimethyl-1-2-benzanthracene to nearby skin³, return to normal site after a short sojourn in the spleen⁴, in mice hereditarily deficient with respect to reproductive function⁵, and in ovaries transplanted to the testes of intact mice⁶.

Study of the morphological sequences in tumourigenesis in ovaries of mice in the intrasplenic position⁷ and following low doses of total body X-radiation⁸ has shown precocious loss of ovarian follicles to be a conspicuous common feature. Drastic reduction of follicles has also been reported in ovaries of mice subjected to benzanthracene⁹ and in those genetically modified⁵. It is possible to refer the initiation of tumourigenesis in these ovaries to the local cellular imbalance. After reduction of the primary targets (granulosa cells) for gonadotropic hormone, latent growth potential is released in the interstitial cells. The tumour originates in an ovary that exists in an adult hormonal environment but is prematurely aged in so far as its content of follicles is concerned. Induced ovarian tumours in mice have been explained in terms of increased and prolonged gonadotropic stimulation⁹.

In order to explore more fully the relationship between disruption of cellular organization and tumour formation in the ovary of the mouse, auto-transplantations were made to the liver and kidney. These were made to render unlikely any modification of the hormonal balance in the animal and, also, to produce loss of the germinal epithelium in order to speed reduction in number of follicles and obviate confusion concerning the source of the tumour cells. The formation of intrahepatic and intrarenal ovarian tumours in the rat has been reported¹⁰.

Ovaries of recently born mice of the inbred strain *MAJ/Sp* (a milk-agent-free strain of Marsh albino) were removed under cold anaesthesia, and one of each pair was thrust into either the liver or the left kidney. Recoveries were made at intervals of 4-6 weeks for 18 months, some ovaries were found in adipose tissue and in the body wall near the liver or kidney. The report is based on serial sections of 119 ovaries.

Although encapsulation did not occur regularly at any of these sites, as it does in the spleen, the germinal epithelium was absent. Reduction in number of follicles was slower in ovaries resident in the liver, kidney, and adjacent tissues than in the spleen, this may be referred to the degree of vascularization. After the time of appearance of the first areas of disorganized growth during the 20th week after transplantation, 56 per cent of the ovaries recovered contained tumours. During the last 6 months of the experiment tumours were found in 65 per cent of the ovaries. In no instance did disorganized growth begin until the follicles were conspicuously reduced in number, ovaries characterized by marked loss of follicles always contained tumour areas. Luteinization of interstitial cells and granulosa cells of regressing follicles was common from an early period as in intrasplenic and X-irradiated ovaries. The pattern of tumour formation by the interstitial (stromal) cells of



Figs 1-6

Figs 1-6 Photomicrographs showing the effect of insecticides on Nissl bodies of locust (all taken from the fourth nymphal instars). Materials fixed in Carnoy's fluid and stained in Borret's methylene blue. Fig 1 Normal condition. Fig 2 BHC-treated specimen showing the reduction in number of Nissl bodies and their tendency to accumulate. Figs 3-4 BHC-treated specimens showing the reduced number of Nissl bodies and their migration towards the cell periphery. Fig 5 Large neurone from BHC-treated nymph showing that Nissl bodies are greatly reduced in number. Fig 6 Nymph treated with sodium arsenate in which very few Nissl bodies are found in the cytoplasm.

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³ Young, J. Z., *Quart. J. micr. Sci.*, 75 (1932).

oxygen which brought about the migration of the Nissl bodies along the axon of the cell after its death. Other pathological effects were reported by Young following axon sectioning. He noted that the Nissl substance began to disappear from the central part of the cell, and this continued until only a few granules, together with a few separate masses at the peripheral region of the cytoplasm, were left. Young noticed that the Nissl's bodies were reformed after fifteen days.

In the nerve cells of normal locusts the neurofibrillae appear as threads surrounding the nucleus and passing into the axon¹. The insecticides used exhibit no effect on the morphology or topography of the neurofibrils.

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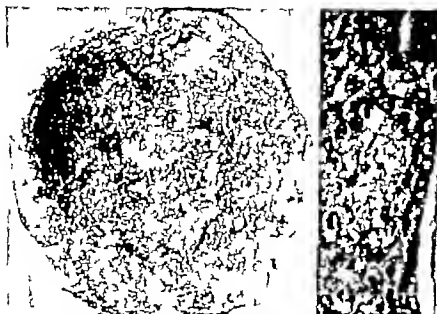


Fig 1 Tumour in ovary of mouse after 77 weeks in subcutaneous site. Left: entire section; right: cellular detail

the ovaries reported here was much like that of the intrasplenic ovary (Fig 1). It may be noted that control ovaries from *Ma/JSp* mice 18 months old contain normal follicles and corpora lutea and none of the atypical structures found in the transplanted ovaries.

A portion of uterine horn from each mouse was examined to determine the hormonal output of the transplanted ovaries. Although there was variation in the level of response among mice of a given lot, especially in the earlier stages, the horns were oestrogen stimulated¹¹. The matrix of the stroma was abundant mitotic figures occurred in the glandular and surface epithelium, and secretion was present in the glands. As tumourigenesis began, cystic hyperplasia was common and leucocytes were present in the stroma. Metaplasia was observed in a few horns.

The observations support the view⁶ that local factors play an important part in tumourigenesis in the ovary of the mouse. The primary lesion is found to be a profound disturbance of cellular balance by loss of the dominant structures of the organ. Under such conditions, the growth potential of cells ordinarily relatively quiescent is released in response to what can be presumed to be the normal flow of hypophyseal gonadotropins. The importance of cellular balance in biological controls has been discussed by Little¹².

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AGRICULTURE

Routine Methods for Determining Quality in Merino Wool

USUALLY two distinct definitions are given of the term 'quality'.^{1,2} First, there is the technical definition which is usually employed by the wool textile trade and which refers to the diameter of wool fibres. Secondly, there is the relative or primary definition which expresses an ideal so that a wool is said to be of good quality if it possesses to a marked extent the desirable features of its type. The term 'quality', as employed in this note, refers to the second definition and has no connexion with fibre diameter.

According to South African woolmen quality implies softness and kindness of handle and a well defined even crimp. Similarly wool textile experts with long industrial experience are able to predict the behaviour of a wool during processing from its appearance and feel. These subtle properties associated with wool quality have so far proved to be incapable of exact measurement by routine methods.

Samples of 50 Merino wools were submitted to four wool experts for the appraisal of quality in three degrees, namely good, fair and poor. From the 50 samples only 12 wools in which there was good agreement between the experts in the appraisal of quality, were selected for this study. Only root portions of these wool samples were used for the following determinations: plasticity³, total sulphur⁴, tyrosine⁵, solubility of wool in alkali⁶ and urea bisulphite⁷ solutions. The averages of these determinations together with their standard errors are given in Table 1.

TABLE 1

| Qual of ity | No. of samples ($\times 10^{-6}$) | Plasticity per cent | Sulphur per cent | Tyrosine mgm. per gm. | Alkali solubility per cent | Urea bisulphite solubility per cent |
|----------------|---|------------------------|---------------------|-----------------------------|----------------------------------|--|
| Good | 4 | 89.7 \pm 8.4 | 5.43 \pm 0.07 | 70.1 \pm 0.8 | 11.4 \pm 0.3 | 50.0 \pm 1.7 |
| Fair | 4 | 74.3 \pm 8.4 | 5.5 \pm 0.05 | 65.3 \pm 0.9 | 9.0 \pm 0.4 | 45.0 \pm 4.2 |
| Poor | 4 | 60.0 \pm 8.3 | 5.0 \pm 0.05 | 58.7 \pm 1.4 | 7.2 \pm 1.0 | 44.2 \pm 2.9 |

The results indicate that all these methods may be used to characterize wool quality. Of special interest are the solubilities of wool in alkali and urea bisulphite solutions as these determinations are of a routine nature. The relationship between these solubilities and wool quality has also been established in two other sets of wool samples as will be reported elsewhere.

Recently Dusenbury⁸ has shown that the urea bisulphite solubility measurement is a useful way of characterizing the cortical structures. The lowest solubility is exhibited by the paracortical fibre (for example human hair), the highest solubility by the orthocortical fibre (for example kid mohair) and intermediate solubilities are exhibited by the ortho para fibres. These results for the solubility in urea bisulphite, therefore, show that good quality wool contains a greater proportion of ortho-cortex than the inferior qualities.

The solubility of wool in alkali and urea bisulphite solutions is also used to determine damage in wools.⁹ In order to establish the effect of photochemical decomposition on the relationship between quality and solubility in alkali, wool samples were taken from 173 sheep of different qualities and the solubility

NATURE AND THE RECENT PRINTING DISPUTE

THE printing dispute which for about six weeks held up much printing and publishing in Britain is now happily over. Unfortunately, during that period it was not possible to publish *Nature*, nevertheless, contributions continued to be submitted from all parts of the world at the usual rate and volume. This meant that the Editors were able to function and face their normal duties during the dispute, but abnormal problems arose afterwards.

Now that the dispute has been resolved, type setters, block makers, printers and publishers throughout the country are finding themselves tied by commitments and inundated with requests. *Nature's* problem is not only to catch up as quickly as possible but also to accommodate the many contributions which have been accepted before, during and since the strike. Goodwill is prevailing among all those concerned with producing the journal and a spirit of understanding emanates from the scientists themselves. These the Editors gratefully acknowledge.

However, in spite of all efforts being made by the printers, who have been so completely and competently in charge of the production of *Nature* for the past well nigh thirty years, it has proved desirable to invoke the aid of other type setters and printers especially if the immediate aim is to be dual purpose—that is, come up to date quickly but not at the cost of volume of work published. Again we are happy to record that everyone connected with this move and the extension of activities is co-operating closely. Nevertheless, such a project involving as it does the transfer of some manuscripts not set some type of those partially or completely set and the selecting of when and where those are to be sent for finishing and collating is proving to be a heavy burden especially on the Editors. Yet this work is being carried out successfully and in good heart, and it is to be hoped that full issues of *Nature* will soon be appearing on their appropriate dates.

Nevertheless so complicated is this work that whereas some communications are delayed, others are being published more quickly than is normal. No doubt the authors who are suffering the longest delay are those whose manuscripts were only partially ready for printing when the dispute began. The Editors regret that in such cases they had no choice in the matter, and nobody can be blamed for this temporary set-back.

As readers of *Nature* will have noted, the recent modifications of normal procedure have resulted in each issue being published in two parts—the "Letters to the Editors" appearing as a supplement.

Although this will help to expedite the publication of letters, and ease the strain on the rest of the journal, and although this will soon mean that even more communications than hitherto can be published, now is an appropriate time for onlisting the assistance of contributors and indicating how they

can help—though it should be stressed that the following comments apply to any journal at any time.

When referring to the preparation of manuscripts for press, in a lecture delivered before the Royal Society of Edinburgh some years ago Mr L. J. F. Brimble suggested that a would-be author should ask himself the three following questions before mailing his manuscript: (1) Have I said what I really mean? (2) Have I said it in the minimum number of words? (3) Is it necessary to say it at all? The fact that this was quoted in at least eight journals throughout the world and afterwards personally reiterated by other editors indicates that authors might well ponder such queries for the sake of themselves, their readers and their editors.

By and large, an editor reserves the right to assist an author in deciding the answer to the third question, at any rate so far as his own journal is concerned. Yet, even if acceptable articles and other communications could often be much improved before submission for publication, and for this the author and/or his advisers are entirely responsible. For example, corrections in proof are exacting for a typesetter, time consuming for him and the printer, costly to the publisher (and in the case of some journals to the author himself) and frequently irritating to the editor especially when the last named knows full well that more careful preparation of the manuscript in its initial stages would have rendered many such corrections unnecessary. In the case of *Nature* costs of corrections are borne by the publishers.

There are authors who still rush their manuscripts to an editor knowing that they have not yet said the last word on the subject, but who aim at correcting and improving (1) in proof. Recently, for example, the manuscript of a communication to *Nature* contained the following numerical values: 7.28 ± 0.82 , 8.92 ± 1.00 , these were changed to 11.15 ± 1.30 , 5.12 ± 0.85 in the proof.

Although in general authors are reasonable with their corrections there are those contributors whose corrections cost more than the original setting. Perhaps the most expensive author is he who does not hesitate to make changes on the proof of an illustration which he himself had originally prepared, apparently assuming that such changes are possible. Actually, except in the case of very minor alterations, a new block has to be made which may cost several pounds sterling.

Another problem which must now be facing all editors of scientific journals and certainly most readers of such journals is that of abbreviations. Obviously many of these, symbols, etc., are essential to such an exact discipline as science; but among a high percentage of scientists to-day the devising of abbreviations seems to have developed into a cult. Often the straightforward full word is all that is needed but

even more important in any journal which covers all branches of science, it must be borne in mind that an abbreviation often has more than one meaning, especially between one subject and another. For example, a geologist recently submitted a communication containing the letters BC to mean Boulder Clay. To most biochemists PAS means periodic acid-Schiff, but to others it may mean *para*-amino-salicylic acid. The symbol H has been adopted by some to indicate histamine, but for a very long time to all scientists it has been the symbol for hydrogen. One author expected the editors to use the expression cytidylic acid-U-C¹⁴ to mean "uniformly labelled cytidylic acid with respect to carbon atoms contained therein". To a few authors the letters DCL stand for Distillers Co., Ltd., whereas in the much wider field of academics these have a quite different connotation. Some physiologists indicate cardiac output by the abbreviation CO, which might well confuse others. One author who wrote MIT to mean moniodotyrosine had apparently not heard of the Massachusetts Institute of Technology.

There is no doubt that many abbreviations are essential, for they can be so exact, but there are certainly a number of authors who apparently imagine that their articles appear more 'scientific' if these are peppered with abbreviations. Although the Editors of *Nature* are now well versed in abbreviations adopted by scientific writers, such is the present height of this Tower of Babel that the former sometimes have to refer a communication back to an author asking what he means. This is, to say the least of it, a waste of time. Recently a communication received had anything from one to three abbreviations in each line (some obviously made up by the author himself). The communication defied interpretation, yet after the author had been shown the error of his ways, the revised manuscript, without a single abbreviation, revealed an elegant and interesting piece of research work. But before that communication could be published it had to pass backwards and forwards three times half-way around the world.

It is not irrelevant to point out now that, despite many efforts at achieving standardization in scientific presentation, journals vary considerably, though each one endeavours to be consistent within itself. It would save much time and, indeed, be a courtesy to any editor, if an author consulted beforehand the journal to which he proposes submitting his manuscript. He would certainly obviate the risk of errors. For example, *Nature* endeavours to be consistent in the way footnote references are inserted, yet frequently authors adopt their own methods (or those of other journals), and these, sometimes being quite different from *Nature's* custom, involve extra work on the part of the Editors and the risk of wrong quotations or citations.

Perhaps the most problematical of all authors is he who wishes to withdraw his communication after it has been submitted. The timing of such withdrawal is often very awkward. If the author with-

draws at about the same time as the editor decides to reject then little harm has been done. But if the author withdraws, as he sometimes does, after the communication has been set in type, then considerable costs have been incurred and the time of editors, type setters (and sometimes even block-makers and printers) has been wasted. Moreover, if the request to withdraw comes after the contribution has reached page-proof stage, then really difficult editorial and printing problems arise. An author is therefore well advised to ponder his communication after he has written it, and scrutinize fully the possible consequences to himself and the readers of his communication, before submitting it to any journal, for there is the ultimate risk, which sometimes occurs, that it is too late to withdraw the publication, anyhow.

The foregoing suggestions and observations should be considered carefully by all likely contributors to the columns of *Nature*, for they apply at any time, though never so urgently as at present. It is to be hoped that all authors and readers will recognize the inevitability of a certain amount of delay during this period of getting back to normal, though we have already reached the stage when genuinely urgent material can be dealt with promptly. The time is not far off now when *Nature* will again be on an even keel so far as date of publication is concerned, and equally as soon it is hoped that even more text than hitherto can be accommodated.

The Editors gratefully acknowledge the assistance given and co-operation shown by all type setters, block-makers, printers and publishers during what has turned out to be the most exacting period in *Nature's* history, and everyone concerned with the production of the journal has been encouraged by the sympathetic understanding shown by scientists the world over.

FORTY-SEVEN AUTHORS IN SEARCH OF A CONCLUSION

Virus Growth and Variation

Ninth Symposium of the Society for General Microbiology held at the Senate House, University of London, April 1959. Edited by A. Isaacs and B. W. Lacey. Pp viii+272 (Cambridge). At the University Press, 1959. Published for the Society for General Microbiology. 35s net.

Perspectives in Virology

A Symposium Edited by Morris Pollard. Pp xix+312+2 plates (New York: John Wiley and Sons, Inc.; London: Chapman and Hall, Ltd., 1959). Published for the Institute of Microbiology, Rutgers University. 56s net.

Advances in Virus Research

Vol. 6. Edited by Konnoth M. Smith and Max A. Lauffer. Pp viii+382 (New York: Academic Press, Inc.; London: Academic Books, Ltd., 1959). 10 dollars.

THE most integrated of these three volumes is the collection of essays on virus multiplication that the Society for General Microbiology expected

those attending the symposium, that it arranged in April, to have brought and read before the meeting.

There is now fairly general agreement with the opinion, stressed by some when the same symposium was held in 1952, that virus multiplication cannot usefully be compared to the growth of a micro-organism on an inert medium. Rather, it is the exploitation and diversion of the pre-existing synthetic capacities of the host cell. One product of this anomalous metabolism is material that resembles the intruder. It is, however, clear from the papers by Harrison and Hoskins that the host has definite synthetic preferences. Not only is there the well-known insusceptibility of most organisms to most viruses, but there are many examples of variation induced by the host. Virus infection is a general metabolic derangement, and the derangement often precedes any apparent virus multiplication.

Luria, Kellenberger and Hurst stress the analogy between genetic processes and virus multiplication. It may well be that this is more than an analogy and that there is substance in Muller's suggestion in 1933 that viruses could be likened to free genes. Some writers, though not those quoted, have followed the analogy blindly and made it seem ridiculous. Put in sober biochemical terms it amounts to the proposition that among the mechanisms deranged are those normally concerned with the production of whatever it is that genes are made of and of the nucleoproteins of chromosomes. Enthusiasts will find that a colourless way to put the matter but this may serve to bring out the diversity of the problem. There was a time when some biochemists announced resoundingly that they were studying oxidations or even 'enzyme actions', we now have the sense to state the substrate and tissue actually used. So too with viruses. Different viruses in the same host interfere with different processes and the normal processes most commonly deranged vary from host to host. This book makes it abundantly clear that there is no one answer to the question: How do viruses multiply?

'Perspectives in Virology' is less integrated. It contains a charming essay by Dubos on the breaking of tulips; he realizes that a perspective can point in any direction. On the historical framework of the part played by this virus infection in promoting the spread of tulips around the world he discusses the irrationality of the criteria by which we commonly distinguish symbionts from pathogens. The puzzling relations between pigs, earthworms, lungworms and the hog cholera virus are clearly and thoughtfully set out by Shoppe. Almost half the symposium is devoted to tumour causation. Kilham discusses transformations and points out that many effects are as likely to be the result of the failure of a restraint as of the appearance of a new capacity. Beard deals with current work on viruses as a cause of cancer. This is a sensible article marred by the isolationist syndrome that often makes American scientists concentrate on work done in their own country. Its historical perspective is also limited: thus Gyo does not appear among the 114 references. Fashions in science are cyclical, so that one advantage of a knowledge of the older literature is that it gives one an up-to-date or even advance, perspective on contemporary controversies. The names change but the issues remain much the same.

The papers making up this symposium were apparently presented in February 1958, and the discussion that followed is printed though some of it

is rather slight. Verbatim treatment has, however, the immense advantage that it preserves several of Peyton Rous's reminiscences and anecdotes, and these might well have been shorn from a strictly edited version.

'Advances in Virus Research' appears annually, and is, naturally, without unity. A third of this issue is devoted to a review by Sonnenschein on kappa and related factors in *Paramyxo*; it is comprehensive and includes a valuable survey of similar bodies found in other protozoa and in insects, and a discussion of the reasons for looking on a particle as large as kappa as a virus. In the course of this he discusses the limits of the category virus and this is probably the main reason for including the essay in the volume. But it would have made an excellent 127 page book on its own. Two articles deal with the purification procedures used for plant and polio myolitis viruses. It is useful to have all these methods collected together, but it may be that the authors under rate the extent to which differences in the precise state of the host tissue normally used in different laboratories, will affect the way in which these methods work in practice. Consideration is also given to the inactivation of polio virus for use as a vaccine, here it is puzzling to find attention concentrated on formaldehyde. There are many other potentially useful inactivating agents with more systematic and predictable behaviour. There are lucid articles by Brenner on phage genetics and by Broadbent and Martin on the spread of plant viruses. The latter give so many examples of transmission through seeds that we can no longer regard this as unusual.

A review of thirty-six articles is necessarily selective: a list of titles and authors alone would nearly have filled the space allowed. In general the standard is high and it is by no means a bad thing that widely different audiences are aimed at. One wonders, however, whether such ephemeral material needs to appear with so expensive a format. The total cost of these three volumes is £8. N. W. PEAR

FROM AXES TO ATOMS

Man the Maker

A History of Technology and Engineering. By Prof. R. J. Forbes. Pp. xii+365+41 plates. (London: Constable and Co., Ltd., 1958.) 30s. net.

"MAN the Maker" is certainly the most flattering image of him. For whatever else may be dubious in man's relatively brief history, there is no doubt that his capacity to make (or rather, construct for man creates nothing) has steadily increased. Beginning with no more than the power to chip and hack, endowed with an instinctive dexterity less than that of some insects, he has acquired tool after tool and mastered process after process, until he can rearrange to accord with (at least partially) predetermined patterns all the component parts of the universe within his range from the particles of the nucleus to millions of tons of rock and water. The growth of man's power, as Prof. Forbes tells it, is the strongest confirmation of progress that history can offer. It is a story without retrogressions without Dark Ages. Further he is right to insist that this growing power has been used for constructive purposes unless we would limit men to the status of feeble parasites. As the first men took flesh from animals and burnt

from trees, then successors have gone on to pillage the Earth and poison the air on a scale ever proportionate to their growing power, for they could not build without materials nor beautify without making ugliness. But build they did and as a result human life has become ever more secure and comfortable and its focus has moved from the stomach to the brain.

The history of technology divides into two essentially different overlapping phases. The first is the development of craftsmanship, the limit of which is whatever is best of its kind, though not necessarily for its function. Some stone axes are perfect examples of craftsmanship, but a Woolworth's one is a better tool. The second is the transfer of craftsmanship to the machine and the factory, the production of which has no limit in whatever is good or bad. Once man had learnt to hunt and grow, to carpenter, smelt, and weave, as he had by about 2,000 B.C., the early history of techniques is largely concerned with the development of the fine crafts of the potter, silver-smith, silk-weaver and dyer. Such artisans possessed the most advanced skills. Under successive empires from the Egyptian to the Holy Roman they supplied their masters with beauty and luxury while the life of the peasant masses continued essentially unchanged, equally ungraced by the pottery of Corinth or Deruta, by the steel of Noricum or Toledo, by the linen of Pharaohs or the scarlet of kings. So far as the majority of humanity was aware of the finest works of ingenuity in machines, in architecture, in weapons or in pageantry, it was aware of them as arousing superstitious wonder or deferential awe. Until some 500 years ago technological progress, the use of metals and of bright colours, the building of clean, solid houses, the availability of transport and of variety of food, diffused downwards to the masses of Europe and Asia with incredible slowness. Nor in the age of craftsmanship could it be otherwise. Beginning under the Romans, however, and gathering momentum during the Middle Ages in Europe, is a new trend that will break down such restrictions, the importance of which is fully recognized by Prof. Forbes. This is the use of powered machines. The most astonishing fact in his book is given on p. 328: half the available energy in the United States is consumed by its inhabitants for their private uses, the other half being nearly evenly divided between manufacture and conversion-losses. That is the true sign of the affluent society.

The author, whose association with Royal Dutch Shell and experience as a historian of science and technology give him unique authority, has devoted more than a third of his book to the earlier phase of man's career as a maker. This section of the book, though it can enter into little detail of how things were done by the laborious craftsman, gives a clear and balanced account of the origins of the chief manufactures, nor are their social effects ignored. The later and longer section on the last five hundred years has much detail of inventions and their development. Prof. Forbes shows a wise caution in appraising the contribution of pure science to invention and the revolution in technology: the importance of science in this respect is little more than a century old. The extension of the wind- or water-driven machine from corn-milling to fulling, smelting, pumping, spinning and weaving, the use of coal as a fuel and cast iron as an engineering material, the mastery of steam and the beginnings of industrial chemistry were all effected through craft empiricism. Changes in industrial organization were scarcely less productive

than the new techniques. The effects of science in the nineteenth century were wrought on a world already changed, crudely perhaps, yet reaching towards "a rational exploitation of the material world on behalf of the common good". Through machinery and power, through book-printing and cotton-manufacture, railways and precision lathes, sulphuric acid, soda and glass, quantity production was offering the earth-bound peasant more than the whole history of craftsmanship had ever provided for the few. That, one cannot deny, is progress in making.

The text of "Man the Maker", now re-issued, is identical (even to misprints) with that issued by Henry Schuman (New York) in 1950. The author has enlarged the epilogue by several pages and has revised the bibliography. Although historians of technology are not idle, the book is still the broadest, most readable and complete survey of the field. It is written with continuity, perspective and social sense. Some casual statements that will annoy specialists and a number of relatively trivial slips in date and name might have been corrected, but these are minor blemishes on a work that will open a new prospect of the past to many readers.

A. R. HALL

HEAVIER ELEMENTS

The Transuranium Elements

By Glenn T. Seaborg (Yale University—Mrs. Hepsa Ely Silliman Memorial Lectures) Pp. xx+328 (London: Methuen and Co., Ltd., 1958) 50s. net

THE material in this book was originally presented at Yale University in lecture form during 1957. After considerable expansion, it was published as one of the series of books produced by the Addison-Wesley Company and presented by the United States Government to foreign delegates at the United Nations Conference on the Peaceful Uses of Atomic Energy, Geneva, 1958. It is now available in a different binding published in Great Britain by Methuen.

Prof. Seaborg has a well-established place in the discovery and elucidation of the complex chemistry of the transuranium elements, and any new publication by him is deserving of our close attention. This book is not, however, written for the specialist in this field and is of quite a different character from the highly successful volume "The Chemistry of the Actinide Elements" written in collaboration with J. J. Katz. Moreover, much of the basic material has appeared previously.

There are four main sections. The first is historical, beginning with a detailed description of the discovery of plutonium early in 1941, and continuing through the development of methods for its large-scale separation, with some digressions on the related actinide elements. This section is not easy reading despite the introduction of a considerable number of personal recollections of important events: the inclusion of long lists of names in the running text is distracting. The emphasis is on the chemists whose contribution to the success of the war-time project for the synthesis and separation of plutonium was only briefly mentioned in the Smyth Report of 1945. Although the reviewer is not in a position to judge the accuracy of detail in the accounts given of this very early work in the United States, some errors

and misleading statements were detected in the brief references to the British project. As examples, no distinction is made between R. W. Spence (of Los Alamos) and R. Spence (of Harwell) on p. 73 and in the index, and the work of Welch and collaborators on plutonium compounds (pp. 87-88) is erroneously quoted as having taken place at Harwell rather than at Windscale. The brief description of the Chalk River Laboratories (p. 73) does not mention the important laboratory-scale development of the Windscale plutonium separation plant during the period 1946-48.

The second section of the book, in which the chemical properties of the actinide elements are discussed briefly in a correlative manner, is more digestible. Although one must agree with the author that the main points of the actinide concept are now well established, there will still be many chemists reluctant to see the undiscovered element 104, instead of thorium, taking the *eka* hafnium position in the periodic table. At the end of the book there is a shorter fourth section in which Prof. Seaborg attempts to extrapolate the generalizations he has derived to predict the chemical and nuclear properties of elements well beyond those which have yet been successfully synthesized. The magnitude of the experimental problem of isolating such elements is illustrated by a detailed description of the discovery of element 101. Since an average of only one atom of element 101 was expected to be produced in each experiment, the subsequent separation and identification must rank as one of the most outstanding feats in the history of chemistry.

The most valuable part of this book is the third section, which deals systematically with the nuclear properties of the trans-uranium elements. However, there is here, as in the rest of the book, a complete lack of detailed reference to sources of information.

In summary, the book, though containing much material of interest is written in such a way as to fall rather awkwardly between two stools. Specialists in the field will prefer other expositions on the subject by the same author, while the layman interested in scientific matters will find difficulty in following the book, as a considerable background of scientific knowledge is required for a full understanding of even the historical sections.

The book is well produced, with a commendable lack of typographical errors. J. K. DAWSON

SCIENCE EDUCATION

The Challenge of Science Education

Edited by Joseph S. Roucek. Pp. xii + 491. (New York: Philosophical Library, 1959.) 10 dollars.

WHEN *Sputnik* was announced to a startled world in October 1957 the reaction in the United States was immediate and vigorous, but no where was it more unsettling than in certain radical proposals for revolutionizing the American educational system by copying that of the U.S.S.R. This book is an attempt to make a first systematic survey of the post-*Sputnik* educational practices in the field of science in the United States, the U.S.S.R. and Britain. The work is edited by a former Czech, who commences with a brilliant, short historical account of the impact of science upon human thought and behaviour. More than thirty collaborators are each responsible for a chapter and these include Dr. James R. Killian

lately consultant to President Eisenhower, and Dr. Werner Heisenberg. The contributions differ in size and value as is to be expected, and the treatment of the subject is generally diagnostic and experimental rather than conclusive. Standards and content in American science education vary more by reason of geographical location, religious and political factors than they do in Britain, though so far as the last is concerned, even here it still remains to be seen whether politics, which has invaded the field of secondary education, as in Derbyshire, will prove harmful to science teaching at a high level in the grammar schools. The salary levels, which affect the recruitment of suitable men and women to teach science, operate in the United States more forcibly than in Britain, and there is the added difficulty of the lower rating in social status "Don't become a teacher," said the head of one science college in the United States, "we want to be proud of all our men."

Werner Heisenberg's defence of a background education in the classics in relation to his own mental development as a theoretical physicist is most interesting and suggestive and so are the chapters on new approaches to mathematics teaching by using the theories of sets and probability. The underlying tone of the book is by no means optimistic. There is a quotation from Don K. Price ("Government and Science") who concludes that "The role of world leadership is an uncomfortable one, it requires a steadiness of purpose, an economy of our energies and a breadth of philosophy that have never been characteristic of American temper."

The short account of science education in Great Britain (though it might have been more accurate to say England) by Dr. Kenneth Laybourn of Bristol and the longer account of the U.S.S.R. by L. A. D. Dollin of Vermont are very useful summaries.

The documentation at the end of each chapter is excellent. Every chapter is worth reading and pondering on, particularly by those who are interested in science and mathematics teaching, but generally by those who have any interest in maintaining the free world. W. L. SUMNER

SIR CHARLES HASTINGS

The Life and Times of Sir Charles Hastings, Founder of the British Medical Association

By William H. McMenemey. Pp. xii + 510 + 32 plates. (Edinburgh and London: E and S Livingstone Ltd, 1959.) 50s. net.

IN 1951, Dr. W. H. McMenemey was invited by the Council of the British Medical Association to deliver the first Sir Charles Hastings memorial oration, for which task he was singularly well equipped, for he had worked for several years as pathologist at Hastings's own hospital, and in 1947 had made a name for himself with his scholarly and charmingly written "History of the Worcester Royal Infirmary." An elaboration of this oration, "The Life and Times of Sir Charles Hastings" is a huge tome, to which the hackneyed phrase "labour of love" may unhesitatingly be applied. It will for long remain the standard biography of the founder of the British Medical Association and of the architect of the Medical Act of 1853. Dr. McMenemey possesses a scholar's conscience in consulting original sources and he quotes extensively and happily from con-

temporary medical periodicals, newspapers, minutes and letters, yet he wears his learning lightly and unobtrusively, and his style is both elegant and delightful. Some readers might criticize his story on the grounds that it is too detailed and too discursive, and that the lengthy accounts of his contemporaries detract from a true appreciation of the subject proper of the biography, but even those who would have preferred a more succinct narrative will yield to none in their admiration for an invaluable work of reference.

We meet Charles Hastings as a medical student at Edinburgh, where he developed "a catarrhal inflammation of the lungs", which was treated by the distinguished physician, James Gregory, and we learn that this malady inspired his lifelong interest in diseases of the chest. In 1820 was published his classic "Treatise on Inflammation of the Mucous Membrane of the Lungs", which was translated into German two years later. We accompany him to Worcester, where he was appointed physician to the Infirmary, and watch him first using the stethoscope in the summer of 1820. We read how he founded, and edited, the *Midland Medical and Surgical Reporter* in 1828, and in 1832 launched the Provincial Medical Association, which was watched by Thomas Wakley in London "carefully and with considerable suspicion". Little did Wakley realize that one day it would grow into a British Medical Association. Hastings was "the pivot around which the Association revolved, for they all looked to him for guidance and inspiration". We are told that he narrowly escaped becoming mayor of Worcester, paying a fine of £50 for having refused office. We see him in the role of naturalist and in his company attend a dinner where twenty toasts were drunk. "When the celebrants finally arose they had completed just over six wonderful hours of feasting and conviviality." It is interesting to find that in 1844 a National Association of General Practitioners was formed with seventeen branch secretaries.

Lavishly and fascinatingly illustrated, Dr McMenemey's book bristles with bitter controversies in "disturbed and disputatious" meetings. It concludes with a bibliography of Hastings's writings, a general bibliography, and a model index. I like the chapter headings.

W R BETT

PANBIOGEOGRAPHY

Panbiogeography or an Introductory Synthesis of Zoogeography, Phytogeography, and Geology, with Notes on Evolution, Systematics, Ecology, Anthropology, etc

By Léon Croizat. Vol 1. The New World. Pp 1018. Vol 2a. The Old World. Pp iii+1-771. Vol 2b. The Old World (continuation). Pp iii+772-1731. (Codicote, Nr Hitchin. Wheldon and Wesley, Ltd, 1958) £16 10s (paper bound)

IT is a distinct understatement to call this enormous work unusual. Published in three separate books making up two volumes which weigh something like ten pounds unbound, it contains 2,700 pages and probably at least a million words. To this must be added that it is highly prolix and repetitive, that it is written in a peculiar brand of semi-colloquial idiomatic English which often obscures the author's exact meaning, and that it contains too many animadversions on biologists with whose views Dr Croizat is not in accord. In short, the author seems to have

put almost every possible obstacle in the way of the reader who wishes first to understand and then carefully to consider his opinions. This is all a great pity because there are two excellent reasons at least why this *magnum opus* should on no account be regarded as unreadable and therefore safely to be ignored.

The first reason is that the book is a vast compendium of information about plant and animal distribution which is arranged and discussed on a geographical and not a taxonomic basis, thus making it much more valuable than it might otherwise be. Indeed, the broad sweep of its geographical background is one of the book's best features. The first volume begins with an introduction, which concludes with a remarkable piece of self-criticism by the author, and is thereafter concerned with the New World in general and then with Venezuela, Colombia, Ecuador, the West Indies and Galapagos (that is, with several crucial areas) in particular. The first book of the second volume deals with Africa, Eurasia, Malaysia and Australasia. The second book covers Polynesia and is thereafter made up of conclusions, a long epilogue on evolution, and various addenda, of which the most extensive is one on physical anthropology. The chapter of conclusions is the shortest of all the chapters but also the most readable.

The second reason is that Dr Croizat is a man of quick intelligence who has for years pondered over many fundamental problems of biology, not only in its narrower sense, but also in its wider philosophical expression in which it comprehends the whole history of the human race and of its thought. His comments and beliefs on many such subjects are interlarded, as it were, through his immensely long recital of the data of biogeography, but they often reveal great discernment and may therefore be forgiven for any digressions they cause.

As regards biogeography Dr Croizat's main thesis is that plant and animal distribution, using this word in its more particular sense of 'dispersal', must not be studied in isolation, it is simply one aspect of the three basic factors of evolution, namely time, space and form. To quote his own words, his book "replaces the Darwinian understanding of 'species' originating at some definite spot on the map and 'migrating' via 'occasional means' with a fitting understanding of form-making and translation in space as a single process".

Thus, this vast book is, in essence, a study in evolution, chiefly, but by no means only, from the biogeographical point of view. It is clearly inspired by the author's discontent with the approaches to this subject of Darwin, Wallace and some of their successors, and so it is yet another contribution to the swelling stream of opinion that the general biological outlook which we now call Darwinism, however great its value may have been in the past, is no longer a suitable vehicle for progress in the biological sciences.

The maps, with which the book is liberally supplied, are open to some criticism. Most of them might be clearer and too many of them are drawn on Mercator's projection, which is quite unsuitable for depicting biological distributions. Also, they are too plentifully supplied with arrows purporting to show movement along various 'tracks' of migration. It is easy enough to postulate tracks of this sort but it is quite another thing to produce satisfactory evidence to show which way along them movement has been.

RONALD GOOD

Plant Growth Substances

By Prof L J Audus Second edition (Plant Science Monographs, No 1) Pp xxii+554+34 plates (London Leonard Hill (Books), Ltd, 1959) 65s net

TO produce within a single volume a comprehensive and up-to-date treatment of a subject which is developing so rapidly as plant growth substances is no mean achievement. Yet in this second and revised edition of his book, Audus has done this with considerable success. As in the first edition, physiological aspects of growth regulating activity receive careful attention throughout, but in addition a new chapter on the mechanism of action of the auxins, dealing with more fundamental physiology, is now included. Other changes in the book are shown in the more detailed treatment given to flowering control and chemical control of sexual processes in lower plants and to non auxin type growth substances. The chapter on the chemistry of the auxins has also been considerably expanded.

Although this is an excellent book, it is perhaps pertinent to ask whether it is attempting to cater for too many classes of reader. In the reviewer's opinion, most of the contents are far beyond the reach of the "non-scientific layman", whose requirements would perhaps be met better by a book written specifically for him.

With this reservation, the present volume can be confidently recommended. It is well produced with excellent photographs and diagrams. Many references to original work are given and appendices relating to the practical use of growth substances in agriculture and horticulture are provided. R. L. WAIN

The Design of Physics Research Laboratories

A Symposium held by the London and Home Counties Branch of the Institute of Physics at the Royal Institution, 27 November, 1957 Pp 108 (London Chapman and Hall Ltd, New York Reinhold Publishing Corporation 1959) Published on behalf of the Institute of Physics) 21s net

THE proceedings of the symposium on "The Design of Physics Research Laboratories" held on November 27, 1957, at the Royal Institution and organized by the London and Home Counties Branch of the Institute of Physics have now been published in book form. A report of the symposium appeared in *Nature* (181, 90, 1958). The symposium was very timely and extremely successful. It was attended by some 400 architects, physicists and others interested in the design of research laboratories, and the book contains a full account of the proceedings including the discussion and many of the photographs which were presented as lantern slides. Nobody who is about to plan a new physics laboratory or an extension to an existing laboratory should omit to read this volume first. It contains a wealth of excellent hints and reminders, and may save much expense in assisting to avoid faulty design and much time in providing quick and accurate reference to the authoritative literature. It is difficult to summarize the contents, but all those who have had experience of planning buildings and the responsibility of supervising the construction will agree most wholeheartedly with the statements that properly planned sound construction using lasting and easily maintained materials is the most economical, and that regular site meetings should take place between the user of the building, the architect and the most essential

person, whom Mr. Emerson calls "the building supervisor" and who should be the sole official channel of communication between the various parties concerned in the building of the laboratories. S. WEINTROUB

Aromatic Substitution

Nitration and Halogenation. By Dr P. B. D. de la Mare and J. H. Ridd Pp vii+252 (London Butterworths Scientific Publications, New York Academic Press Inc, 1959) 50s

THIS book deals with the nitration and halogenation of aromatic compounds. Two introductory chapters cover the basic principles of electrostatic theory and methods used to investigate reaction mechanisms. Next follows a group of four chapters dealing with methods of nitration and the mechanism of the nitration reaction, and then a further group of four chapters dealing likewise with halogenation. The authors then review substitution in diphenyl, in polycyclic hydrocarbons, in non benzenoid hydrocarbons, and in heterocyclic systems, and substitution reactions involving displacements of groups other than hydrogen. The final chapters deal with molecular orbital calculations of reactivity and with linear free energy relationships.

The authors have succeeded in giving an excellent well written and critical account of their subject. Although the book is both short and readable no important aspect seems to have been omitted and no important papers overlooked. The authors have not been afraid to express forceful opinions on a variety of controversial issues—a pleasant phenomenon in this era of depressingly uncritical compilations. The book is, moreover, very well produced and the price most reasonable. It can be strongly recommended to any chemist interested in organic reaction mechanisms. M. J. S. DEWAR

Constitutional Diagrams of Uranium and Thorium Alloys

By Frank A. Rough and Arthur A. Bauer (Addison Wesley Physics Books) Pp vi+154 (Reading Mass Addison Wesley Publishing Company, Inc 1958) 5 dollars

THIS book, which supersedes the Battelle Memorial Institute publication, "Compilation of U.S. and U.K. Uranium and Thorium Constitution Diagrams", is a new compilation of United States and United Kingdom uranium and thorium constitutional diagrams. The book is divided into two major sections, one for uranium and the other for thorium. Each section is preceded by a short account of the transformation temperatures and crystal structures of the base metal. The method of presentation is the constitution diagram, with a short account of the investigations on the system, the essential data on the crystallography of the compounds and a list of references for each alloy. Most of the references are unclassified, but in several systems, where the unclassified literature is incomplete, some classified references are given. The various systems are listed in alphabetical order and include both binary and ternary alloys. The information on each alloy is quite comprehensive and the form of presentation is neat and concise. This publication will be extremely useful as a reference book to everyone interested either from a theoretical or practical point of view, in the alloys of uranium and thorium. D. E. R. HUGHES

SHIP HYDRODYNAMICS LABORATORY, FELTHAM

ON October 19, H.R.H. the Duke of Edinburgh opened at Feltham the new Ship Hydrodynamics Laboratory of the National Physical Laboratory.

Since 1932, when No. 2 Tank was built at Teddington, test work on models of new ships has increased in volume to a point where it has seriously impeded research. At the same time, thanks to the steady investigations undertaken over the past fifty years, research requirements have themselves changed. Increasing emphasis is falling on the seagoing qualities of ships, particularly at high speeds, and the facilities at Feltham have been specially designed for these requirements. It is expected that, in general, tests of commercial ship-models in smooth water will continue to be carried out at Teddington, while tests of commercial models in rough water and a great deal of the research will be done at Feltham. This research will include theoretical and experimental studies of ship motions in regular and irregular seas, together with a study of full-scale multi-directional sea states, propeller and hydrofoil cavitation and ship vibration. Various other research projects formerly followed at Teddington will be carried over to Feltham, where larger models can be used than is possible in the existing tanks, these will include skin friction of smooth and rough surfaces, ship-model

correlation, wave-making resistance and boundary layer investigations.

The design of the new Laboratory (Fig. 1) was developed by the Ship Division of the National Physical Laboratory working in collaboration with the Chief Architect's and Chief Engineer's Divisions of the Ministry of Works. The principal facilities at Feltham comprise a towing tank, a sea-keeping and manoeuvring basin and a propeller water-tunnel for cavitation research.

The ship-testing tank is the largest of its kind in Britain. It is 1,300 ft long, 48 ft wide and 25 ft deep. Its length, which is almost double that of the No. 2 Tank at Teddington (680 ft), is necessitated by the requirements of testing models in irregular seas or at high speeds and the use of larger models of multi-screw ships. In sea-keeping tests the model must be run through regular and irregular seas for long enough time to obtain complete cycles of motion and also to ensure a long enough steady run for making measurements at high speed. The original design was for a length of 1,800 ft, but this had to be reduced in order to keep within the funds available, and the present length represents the minimum for fulfilling these requirements. The site, however, has been planned so that the additional length can be added in the future.

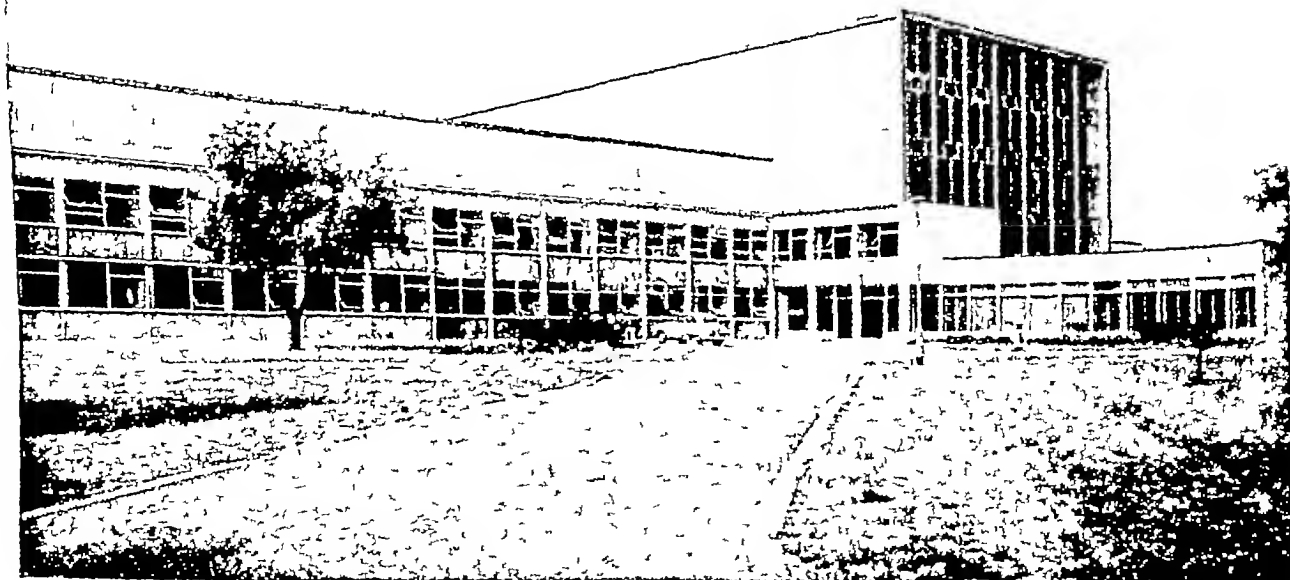


Fig. 1 Ship Hydrodynamics Laboratory of the National Physical Laboratory

[Crown copyright reserved]

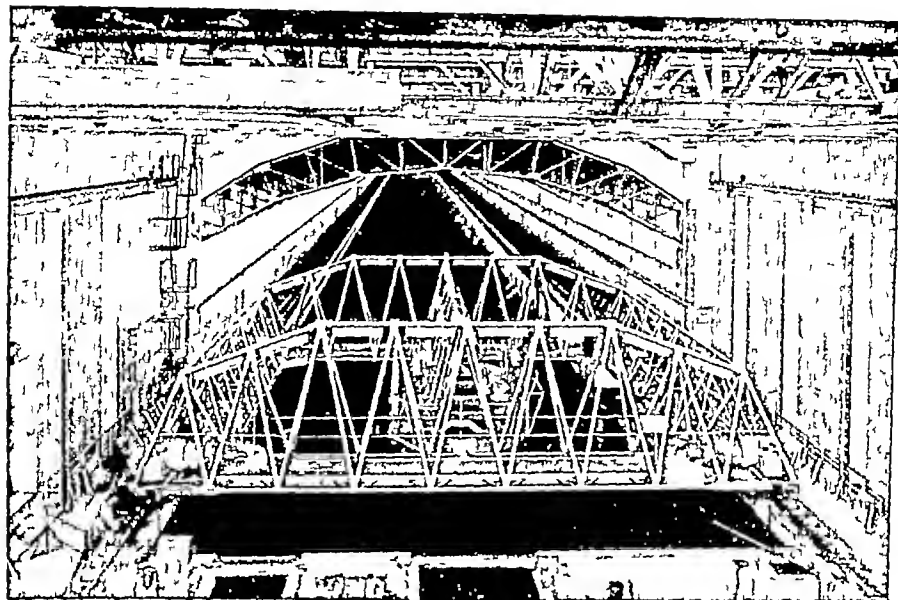


Fig. 2. Carriage and main towing tank 1300 ft long

[Crown copyright reserved]

The tank itself has been built of reinforced concrete sections. It is above ground level, as the expense of keeping out the subsoil water would have been heavy in this area, where the water table is very near the surface. Special care has been taken in the heating and ventilating arrangements to keep an even temperature in the building in order to maintain accurate rail alignment, avoid condensation effects on electrical equipment and ensure a reasonably constant nominal water temperature of 60° F.

The towing carriage (Fig. 2) is designed to tow ships' models up to 5 tons in weight and 40 ft in length. The maximum speed attainable is 50 ft/sec, but this would not be used with heavy ship models. The carriage has four girders forming a square frame work 50 ft x 50 ft externally, completely open inside, giving a space 36 ft. square. Into this centre space a fore and aft girder containing dynamometers and other instrumentation can be placed in a number of positions to give flexibility in carrying out different types of tests.

To decrease the effects of track deflexion and thus assist in providing undisturbed and uniform motion the carriage is driven by four twin wheel self steering bogies on which the frame is in effect pivot-mounted via a system of rubber compression springs. Each bogie is powered by a 300 h.p. peak rating d.c. motor. The total peak power of 1,200 h.p. has been calculated to provide, with adequate margin, sufficient power to accelerate the carriage, which will weigh nearly 40 tons fully equipped, at the maximum rate without wheel slip. This value will have to be determined precisely by experiment, but will be of the order of 0.1g. Wind tunnel tests have been made on a model of the carriage frame to help assess accurately the wind loadings at high speed.

The carriage is equipped with a speed holding servo which will maintain any set test speed between 10 and 50 ft/s within 0.1 per cent of the set speed. Much study has been given to the braking system necessary. The normal method of braking will be electrical but at high speeds a system of mechanical friction brakes will be brought into use, which are spring operated and held off pneumatically so that they fail to safety in the event of loss of air supply. To limit the duration of the test run track switches have been installed to bring on both electrical and mechanical brakes and bring the carriage to rest with a maximum deceleration rate of 0.25g. Should all these systems fail, an aircraft arrestor gear has been fitted, with cables on each side of the tank. A shock absorbing nylon harness on the underside of the carriage will engage hooks located on the inside face of the tank walls.

The investigation of the behaviour of vessels in a seaway demands the generation of regular and irregular wave systems in the tank. A wave-maker has been installed at one end of the tank capable of making waves up to 40 ft in length and 2 ft. in height from crest to trough with an infinite variety of possible combinations within these limits. The wave-maker takes the form of a wedge-shaped plunger 17 ft in height which spans the tank and tapers almost to a point at the bottom. The front face is curved to follow a theoretically ideal contour and is true to within $\pm \frac{1}{8}$ in. over the whole frontal area. The plunger moves vertically on slides on the end wall of the tank and is driven by hydraulic rams from a pump which operates normally on a sinusoidal pressure cycle to give a regular train of waves. By varying the pressure cycle it will be possible to generate irregular wave systems more typical of

average ocean sea-states To prevent reflexion of the waves from the other end of the tank, an end beach has been provided This consists of a curved sloping surface, continuous below water and slotted in and above the water It can be raised or lowered by means of buoyant chambers

When tests are being made with a model in smooth water, she creates her own wave system, and time has to be allowed between successive runs to allow these waves to die down In order to reduce this waiting time to a minimum, a similar beach is fitted in front of the wave-maker and can be raised to the surface when required In addition, there are side beaches consisting of continuous lengths of curved flaps on either side of the tank which are hinged to the tank walls so that they can either be raised into a vertical position clear of the water when making waves or let down and partly submerged for still-water testing

In long towing tanks the behaviour of models can be studied under conditions of head-on or stern-on waves It has long been desired at the National Physical Laboratory to carry out tests in waves at different angles to the heading of the model and in confused seas and to investigate manoeuvring qualities generally This will now be possible at Feltham, with the new manoeuvring and sea-keeping basin (Fig 3), which is 100 ft square with a depth of water of 8 ft A plunger-type wave-maker has been fitted along one side capable of producing waves up to 15 ft long and 9 in high A beach has been fitted on the opposite side It is intended later to fit another wave-maker on an adjacent wall, and thus may be articulated, to enable confused seas to be generated.

Models up to 10 ft. in length can be used in this tank, and as they are to be free-running, they must carry their own source of power and instrumentation They must therefore combine lightness with strength, and will in general be made of fibre glass plastic They will be radio-controlled from shore, and the instrumentation in the models will either record its own data or telemeter them ashore The Control Mechanisms and Electronics Division of the Laboratory is assisting in the development of a tracking system

The new water tunnel (Fig 4) is intended primarily for research work on propellers up to 24 in in diameter and can also be adapted for testing hydrofoils and similar bodies This work is likely to grow in importance with the increasing demand for high speeds in ships of all classes The tunnel is one of the largest of its type, with a circular closed test section 44 in in diameter, it is designed for a maximum water velocity in the working section of 50 ft/s

The tunnel shell is arranged as a rectangular circuit of which the upper horizontal limb is at ground-level This portion includes the contraction section, where the water is accelerated to the working section velocity, the working section itself and the transition and diffuser sections, where the speed of the water is gradually reduced before entering the suction side of the pump The remaining portions of the tunnel form a U-shaped circuit descending 180 ft into the ground and forming a 'resorber' This is designed to subject the water to an additional static pressure head during transit, when all bubbles created by cavitation at the model and released into the water stream are re absorbed into solution

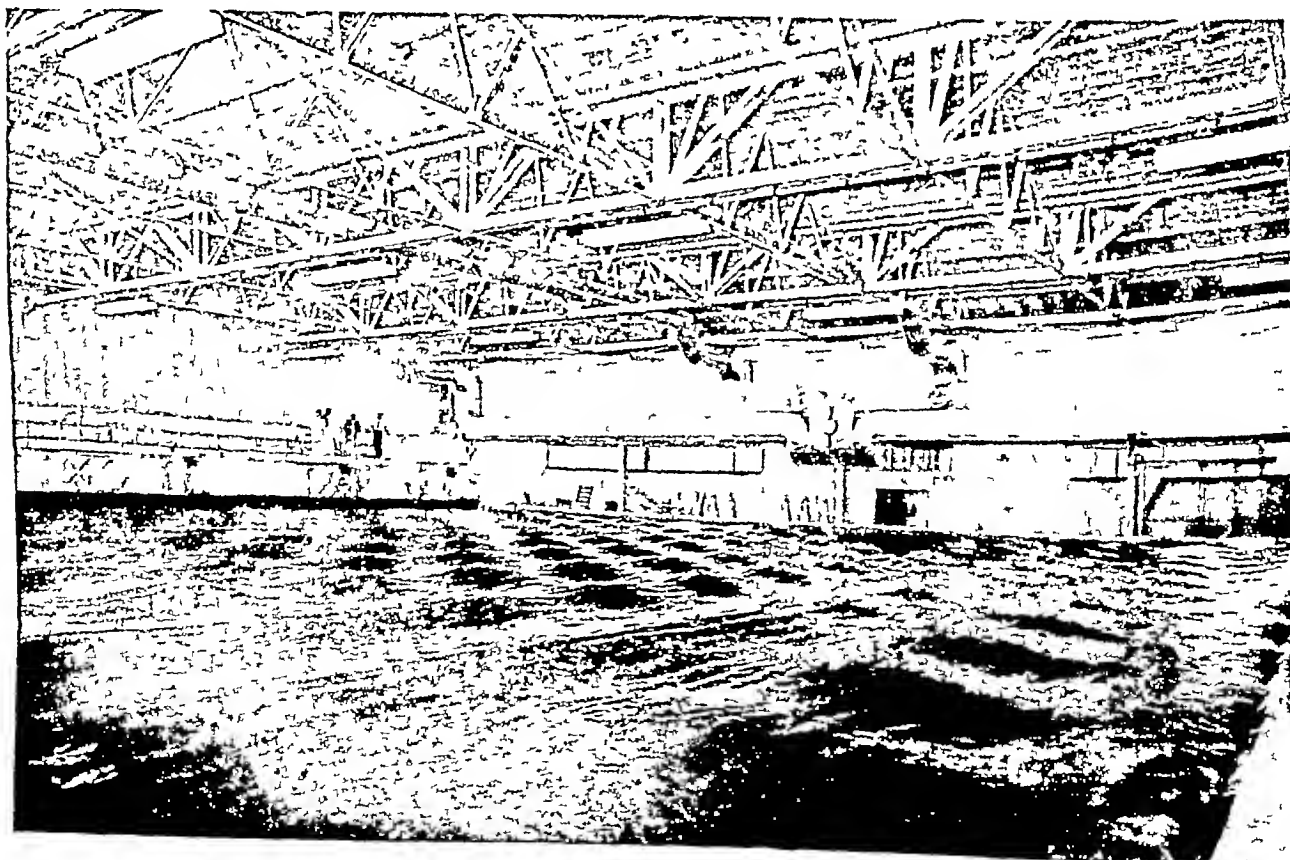
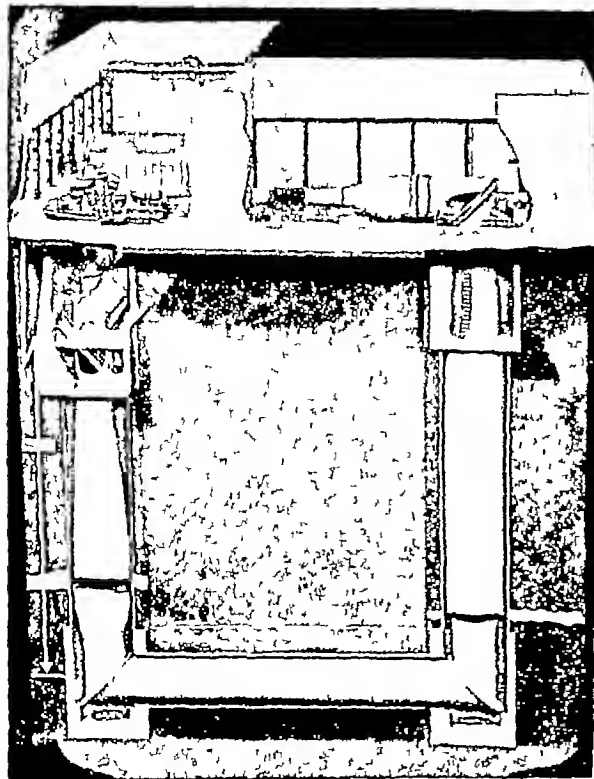


Fig 3 Sea keeping tank

[Crown copyright reserved]



[Cross copyright reserved]

Fig. 4 Model of the water tunnel showing underground portion

The water will be circulated around the tunnel by a 92 in diameter vertical variable pitch pump driven at a maximum speed of 220 rev/min by an 850 h.p. mean continuous rating vertical d.c. motor which is equipped with automatic speed holding equipment designed to hold any set speed with an accuracy of 0.1 per cent.

The model propeller is mounted on a downstream shaft, fitted with thrust and torque dynamometers and driven by a 300 h.p. motor. The pressure in the test section can be varied from near zero to 6 atmospheres absolute. The tunnel is fitted with stroboscopic lighting and high speed photographic equipment.

There are a number of small laboratories devoted to the development of new instrumentation, a photographic room and a vibration laboratory containing a water tank 20 ft by 14 ft and 6 ft deep for experiments on virtual mass and similar problems.

The Laboratory is fully equipped with workshops for making wax, wood and plastic hull models, and casting and finishing propeller models in bronze. The office block includes a handsome library, a dining room and kitchen. The offices and workshops have been occupied since August 1958 and much of the new instrumentation has been built in the shops.

The new Ship Hydrodynamics Laboratory will be under the personal direction of Dr. F. H. Todd, superintendent of the Ship Division of the National Physical Laboratory.

LOCALIZATION AND ASSAY OF RESPIRATORY ENZYMES IN SINGLE LIVING CELLS

Absorbancy Measurements on the Nebenkorn

By DR. ROBERT P. PERRY*, DR. BO THORELL, DR. LENNART ÅKERMAN
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A STUDY and selection of appropriate optical electronic and photoelectric components now permits remarkable sensitivity in the detection of small changes of absorbancy caused by enzymic reactions in living materials. In the case of suspensions of whole cells or cell particles, a detectability of 10^{-11} mole can be achieved without difficulty in a 1 cc cuvette of a recording spectrophotometer¹. Microspectrophotometry affords an even more favour-

able situation for the study of small amounts of biological materials in that measurements can be localized to specific parts of single living cells, and the cells themselves may be selected on the basis of temporal or morphological criteria. Hitherto however it has been used mainly for the evaluation of substances present in relatively high concentrations such as proteins and nucleic acids² and for studies of the formation of hemoglobin in erythroid cells^{3,4}. So far only limited success has been had in measuring those pigments of the single cell which are present

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in 'enzyme concentrations, since this requires sensitivities in measuring changes of absorbancy between one-tenth and one per cent over an aperture of about a micron

This communication reports the application of a combination of a highly sensitive recording circuit and the microscopic technique⁵ which permits the assay of the cytochromes localized in single mitochondrial aggregates, particularly the 5- μ diameter *Nebenkern* of grasshopper spermatids, with an accuracy of several per cent. This sensitivity allows the detection of 10^{-20} mole or 6,000 molecules of the cellular enzyme, cytochrome *b*. The following communication describes localized measurement of the fluorescence of pyridine nucleotide of the *Nebenkern* and that of mitochondrial aggregates of other types of cells with a sensitivity comparable to that of this instrument

The optical system used is similar to that described by Thorell and Åkerman⁴. It employs a 250 mm focus, grating monochromator, a 1.6-mm Grey reflecting water-immersion condenser and objective (N.A. = 1.0), and a 3.5 \times quartz ocular which projects the beam on to a vibrating mirror assembly. The photomultiplier is type 1P28 and operates in the range of total voltage 400–650 V. The tungsten lamp is given an overvoltage of approximately 30 per cent to provide adequate illumination. The spectral interval of the monochromator is approximately 3 m μ . The amplitude of the vibrating mirror corresponds to approximately 12 μ . The hole in front of the photocell corresponds to a 1.5 μ diameter aperture.

The electronic circuit incorporates the dynode feedback circuit of Picard⁶ as previously used by Yang⁷ and Åkerman⁸. The circuit is insensitive to grid and dark currents, and will operate at very low signal-to-noise ratios due to a switching circuit that adds a signal to the phototube output exactly equal to that of the reference signal (~ 1 V). Thus the output wave-form consists of alternate pulses reference beam, dark, measuring beam, dark, in a balanced wave-form with no 'pips' for equal reference and measurement signals (Fig. 1). This signal can be highly amplified without amplifier overload and demodulated to give appropriate signals for control of the dynode voltage (reference minus dark) or measurement of absorbancy (reference minus measure). The noise-level of the spectrophotometer at 420 m μ is about 10^{-4} in optical density units with a 2.5 sec time constant.

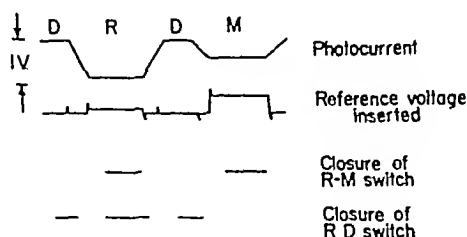


Fig. 1 Wave-form diagram illustrating the principle of operation of the electronic circuit of the microspectrophotometer. As indicated in the left-hand scale, the amplitude of the wave-form is slightly less than 1 V. The top trace represents the wave form of the photocurrent after electron amplification. The portions labelled *D* are those corresponding to the dark interval and those labelled *R* and *M* refer to the intervals during which the light passes through the material in the reference and measuring areas. The second trace represents the wave-form after 1 V has been inserted into the wave-form at intervals *R* and *M*. A measurement of the absorbancy difference between the *R* and *M* optical paths is made by a closure of the *R-M* switch. Control of the dynode voltage for the photocell in response to any deviation of the *R-D* difference from 1 V is measured by the closure of the *R-D* switch (*MD* - 82).

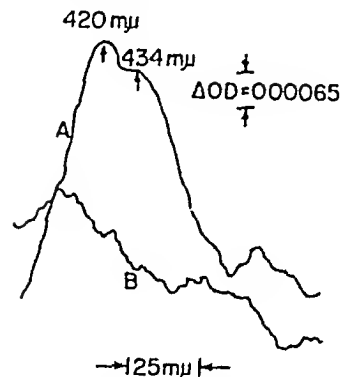


Fig. 2 Spectrum of anaerobic spermatid. Trace *A* represents the difference of absorbancy between the *Nebenkern* and the adjoining free space. Trace *B* represents the difference between the cytoplasm of the cell and the adjacent free space. The recording is on a linear wave length scale (*RP* - 1).

Spermatid preparations were made from mature grasshoppers by Belar's method⁹. The cells were confined between a slide and coverslip suspended in about 3 μ l of buffer. Aerobic conditions were obtained in glucose-free suspensions for approximately 1 $\frac{1}{2}$ hr observation. Thereafter cell respiration exhausted the oxygen and the material contained in the suspension became anaerobic. By this simple method it was possible to obtain, in one experiment on a single *Nebenkern*, spectra corresponding to the oxidized and reduced forms of the cytochromes. If glucose was added to the buffer, anaerobic conditions were attained a few minutes after preparation. The anaerobiosis was monitored by the inclusion of some human erythrocytes under the coverslip, and the time of anaerobiosis was checked from measurements of the characteristic shift of the haemoglobin absorption bands⁴.

Fig. 2 shows two traces obtained from a single anaerobic spermatid in a preparation treated with glucose. Curve *A* illustrates the absorbance of the *Nebenkern* measured with respect to the surrounding free space, curve *B* records the absorbance of the cytoplasm of the spermatid, also with respect to the surrounding free space. The *Nebenkern* shows an absorption maximum at 420 m μ with a distinctive shoulder at 434 m μ .

Observations of the *Nebenkern* in a glucose-free suspension 70 min after closing the preparation with a coverslip show a single peak at approximately 413 m μ , such as that shown in Fig. 3. Other experiments in which the spermatid respiration was inhibited by iodoacetate show, for a considerable interval, the single peak characteristic of the cytochromes, mainly in the oxidized state.

The measurement of the *Nebenkern* under aerobic or anaerobic conditions invariably gives clear Soret

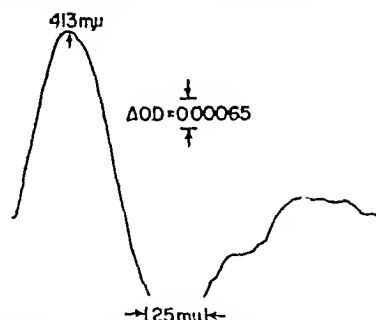


Fig. 3 Spectrum of aerobic spermatid *Nebenkern* versus nucleus. Spectrum recorded 70 min after preparation of glucose free material (*RP* - 6).

peaks 413 m μ for aerobic conditions and 430 and 434 m μ for anaerobic conditions. These are almost identical with the theoretical composite curves constructed from the known spectra of reduced or oxidized cytochromes *a*, *a*₃, *b*, and *c* mixed on an approximately equimolar basis. Preliminary attempts have been made to examine the alpha bands of the cytochromes, but inadequate sensitivity is available with the light intensity, photosensitivity and response times used at present. However some encouraging preliminary results have been obtained with liver cells, as described in the third communication of this series.

The curves of cytoplasm or nucleus versus free space are monotonic functions which may show a systematic deviation corresponding to about 2×10^2 optical density units per 100 m μ change of wave length. The direction of the shift is variable and depends upon the combination of instrumental error and differences of light scattering in the specimen.

Errors due to the motion of the cell can be readily observed and precautions are taken to record only those cells which are immobilized at the glass surface by surface tension or are entangled in the tails of mature sperm. The error due to motion can be negligible under favourable conditions compared to the intrinsic noise of the spectrophotometer. The average reproducibility for several curves is approximately 3×10^{-4} optical density units.

The remarkable absorption of the *Nebenker* and the lack of any significant absorption, in this wave length range, of the cytoplasm give direct support to the current idea that the bulk of the respiratory activity is associated with the mitochondrial bodies. The experiments reported here show that the *Nebenker* contains *in vivo* at least 50 times more cyto-

chromes per unit volume than any other comparable part of the cell.

An estimate of the concentration of cytochrome in the single *Nebenker* based upon these data ($\Delta O.D.$ at 425-430 m μ = 5×10^{-3}), an extinction coefficient of reduced cytochrome *b* of 100 cm⁻¹ m μ ⁻¹ and an estimate of 60 per cent contribution of cytochrome *b* to this peak, gives an effective concentration of 36 μ moles per litre over a $7.5 \mu^3$ volume of the *Nebenker*. Assuming equimolar amounts of the four principal cytochromes, the total cytochrome concentration is 144 μ moles per litre or about 10^4 molecules per μ^3 . If the difference of optical density is expressed in terms of the amount of cytochrome *b* in a $7.5 \mu^3$ volume, one obtains 5×10^{-10} mole or 30 000 molecules. Since the signal to noise ratio is about 50:1, the error in detection corresponds to 10^{-10} mole or 6,000 molecules. This value compares very favourably with that obtained by any other method for the determination of the amount of an enzyme concentration *in vivo*.

This investigation was supported in part by grants from the National Science Foundation, the U.S. Office of Naval Research, and the Swedish Medical Research Council.

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Fluorescence Measurements of Mitochondrial Pyridine Nucleotide in Aerobiosis and Anaerobiosis

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SPECTROSCOPIC observations of the large pyridine nucleotide content of isolated mitochondria were recently supplemented by the demonstration of the intensified and shifted fluorescence of this substance in mitochondria.¹ These results direct attention to the possibility of a close relationship between the blue autofluorescence of the living cells and that of the reduced pyridine nucleotide component of the mitochondria.¹⁻³ This communication describes photoelectric measurements of fluorescence of mitochondrial bodies in the grasshopper spermatocyte. The localization of blue fluorescence in mitochondrial aggregates has been demonstrated, and quantitative measurements of the kinetics of changes in response to aerobiosis and anaerobiosis have been made. A comparison of the fluorescence of mitochondrial aggregates and the neighbouring cytoplasm during this change from aerobiosis to anaerobiosis may lead to a much clearer understanding of the dynamics of interaction of the cytoplasmic and mitochondrial pyridine nucleotide *in vivo*. While the present technique has been applied only to cells showing large mitochondrial aggregates, the excellent performance obtained under these conditions may allow this study

of much smaller numbers of mitochondria. The combination of this instrument for measuring the mitochondrial pyridine nucleotide with that of a sensitive microspectrophotometer (see preceding communication) for the study of the cytochromes may provide a new method for following metabolic changes in cytologically defined parts of the living cell.

The 1,000 watt *AH0* mercury arc illumination was filtered by means of a water cooled Corning 584 filter (Marshall, personal communication), and by an "Eppendorf" 306 m μ multi-component filter. Dark field cardioid illumination of the sample was observed through a 100 \times adjustable aperture lens set at N.A. = 1.00 and a 10 \times ocular. A 60 c/s vibrating diaphragm⁴ with an effective 5 μ aperture sweeps through an effective distance of 15 μ and allows comparison of the intensity of fluorescent portions of the cell and the adjacent free space by means of an electron multiplier photocell. The intensity of the a.c.-operated mercury lamp reaches a maximum at the excursions of the vibrating diaphragm (see Fig. 1). Simultaneously an electronic switch communicates signals to a storage condenser so that the difference of the intensities at the peaks of

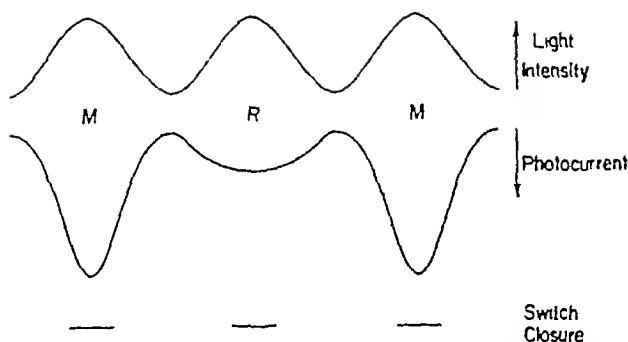


Fig. 1 Wave-form diagram indicating the time relations of the light intensity, photocurrent, and switch closure for the microfluorimeter. The top line represents the time variation of the intensity of the mercury arc lamp. The modulation frequency is 120 c/s, and the amplitude of modulation is nearly 100 per cent. The second wave form is that of the photocurrent after electron amplification. (An increase of current is indicated by a downward deflexion.) This wave-form is in response to a fluorescent object in the *M* position of the aperture, and the surrounding free space in the *R* aperture, the distance between *M* and *R* is approximately 15μ . As indicated at the bottom of the trace, the closure of a synchronized mechanical switch is coincident with the peak of the *M* and *R* wave forms. The electronic circuit measures the difference between the amplitudes of the photocurrent at the *M* and *R* intervals ($M/R - 83$).

the excursions of the diaphragm are recorded by a millivoltmeter, the sensitivity of which is 1 mV for 10^{-16} amp of primary photocurrent. The average signal from the mitochondrial aggregate or *Nebenkern* (4×10^{-16} amp) gives a signal-to-noise ratio of the order of 30:1 with a time constant of about 2 sec.

Localization of fluorescence in grasshopper spermatid

Fig. 2a represents recordings of fluorescence intensity as a function of time for two positions of the measuring aperture with respect to the cell. At the left of the graph, the abrupt downward deflexion of the trace indicates opening of the photocell shutter and the maximal downward deflexion corresponds to the intensity of fluorescence of the *Nebenkern* measured with respect to the free space surrounding the cell. By an adjustment of the air pressure on the movable stage⁸ the cell is moved so that one aperture coincides with the cytoplasm. Here a 50 per cent diminution of the intensity is noted. The specimen (moved a distance of about 5μ) is then returned to its initial position so that the *Nebenkern* again coincides with the aperture, and the previous value of fluorescence intensity is obtained. The record ends with the closing of the shutter. In this way the fluorescence intensities of different portions of the cell can be scanned. A schematic diagram of such a study (Fig. 2b) indicates intensity measurements corresponding to the free space, cytoplasm, and *Nebenkern*, the width of the rectangles corresponding to the half-power response of the measuring aperture. These results suggest that the fluorescence of the cell is highly localized in the *Nebenkern* body.

The study of many anaerobic spermatids having *Nebenkern* indicates that the ratio of the fluorescence signal of the *Nebenkern* to that of the cytoplasm varies from a minimum of 1.7:1 to a maximum of 6:1, the average for ten cells being 3.3:1. The variation of these values may be due to a number of factors, for example, the position of the *Nebenkern* or the thickness of the cytoplasm in which a measurement is being made or the metabolic state of the spermatid. A significantly higher fluorescence has been observed in the nucleus than in the cytoplasm, values ranging as high as 2:1. However, the biochemical significance of fluorescence other than that of the *Neben-*

kern requires studies of its biochemical response to different oxidation-reduction conditions as described below.

Biochemical response of the intensity of fluorescence

In order to subject the *Nebenkern* of the living cell to a metabolic change which would specifically identify its fluorescence with that of mitochondrial reduced pyridine nucleotide of the respiratory chain, we have followed its time course in the transition from aerobic to anaerobiosis (see Fig. 3). As described in the preceding communication, glucose free spermatids will exhaust the oxygen under a coverslip in about 90 min. In the microfluorimeter, a coverslip of smaller diameter and a smaller liquid volume are used. It is calculated that anaerobiosis can be expected in about 40 min. The right hand portion of Fig. 3 (open circles) shows the fluorescence as a function of the time after excluding air from the preparation. The fluorescence of the *Nebenkern* rises slowly for 40 min and then abruptly until a total of 60 min has elapsed. Thereafter, the fluorescence of the *Nebenkern* is constant. Measurements of the cytoplasmic fluorescence (solid circles) indicate no rise of fluorescence over the 90 min interval and there is some indication of a slight decrease. In order to avoid prolonged ultra-violet radiation of a particular cell, three cells were studied in the course of the experiment and they are identified by the numbers along the abscissa. In order to diminish instrumental error and any differences between the cells which might contribute an error to the right hand portion of the figure, the results are plotted in the left-hand portion in terms of the ratio of the *Nebenkern* fluorescence to the cytoplasmic fluorescence; it is seen that the fluorescence increases slowly for the first 40 min, and then rises abruptly between 40 and 55 min to reach a plateau which is maintained thereafter. This behaviour is characteristic of the transition from the oxidized to the reduced state of mitochondrial pyridine nucleotide in the transition from aerobic to anaerobiosis.^{1,2}

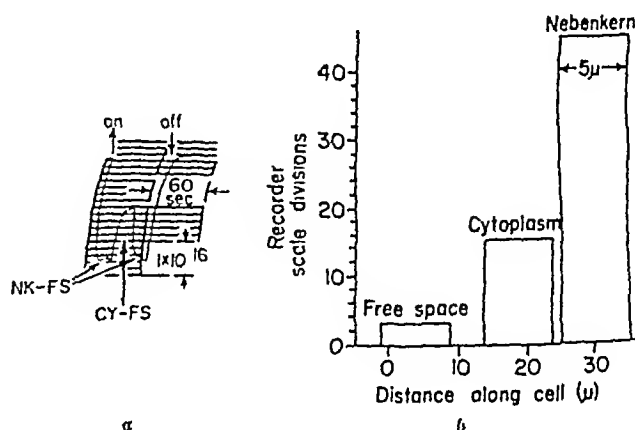


Fig. 2a An example of the measurement of the fluorescence intensity of two portions of the grasshopper spermatid under anaerobic conditions. The phototube shutter is opened and closed at the points labelled 'on' and 'off'. The time scale runs from left to right, the initial reading is made with the measuring aperture on the *Nebenkern* and the reference aperture on the free space (NK-FS). The specimen is then moved 5μ by means of a flexible quartz plate, after which the tracing records the fluorescence intensity of the cytoplasm (CY-FS). The specimen is then returned to the initial position (NK-FS) and the shutter is closed. The scale indicates the primary photo current (1×10^{-16} amp per 5 scale divisions) (025a).

Fig. 2b Scan of fluorescence intensities of anaerobic grasshopper spermatid. The cell is moved with respect to the measurement aperture by means of the flexible quartz plate and positions are chosen with the measurement aperture on the free space, cytoplasm, and *Nebenkern*. The cell boundary is approximately at the 10μ position on the scale of the abscissa (020a).

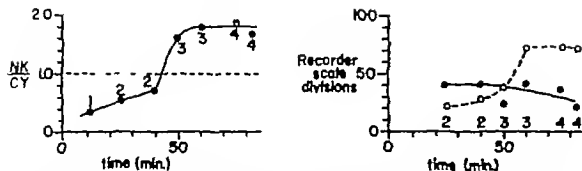


Fig. 3. Time-course of the fluorescence changes of the *Nebenkern* (open circles) and the cytoplasm (solid circles) of a grasshopper spermatid during the aerobic-anaerobic transition. On the right, the independent determinations in the cytoplasm and on the *Nebenkern* are plotted. On the left, the data of the two measurements. The abrupt discontinuity at 45 min. corresponds to the expected time for the exhaustion of oxygen under the cover slip. The numbers adjacent to the circles refer to the cell which is under observation (922a, b).

These results appear to identify the *Nebenkern* fluorescence with that of reduced pyridine nucleotide. If we assume that the cytoplasmic fluorescence is also due to pyridine nucleotide, these results suggest that there is no rapid change of the oxidation-reduction state of cytoplasmic pyridine nucleotide of the grasshopper spermatid associated with the aerobic-anaerobic transition.

Studies of other cells. Cells which do not show a distinctive localization of mitochondria as does the grasshopper spermatid, do not permit a distinction between cytoplasmic and mitochondrial fluorescence. However, in the anaerobic state the greater fluorescence of mitochondrial material would lead at least to a preponderance of mitochondrial effects. For example, observations of the effects of the transition from aerobiosis to anaerobiosis can be observed by measurements of the brighter portions in the cytoplasm of ascites tumour cells. In these cells the fluorescence is constant for about 10 min., rises for an interval of 10 min. and then remains approximately constant (Fig. 4). A comparison of this graph with the right hand portion of Fig. 3 (open circles) shows that the percentage increase is considerably less for a cell in which both cytoplasmic and mitochondrial fluorescences are summed. In fact a curve similar to that of Fig. 4 can readily be constructed from the results of Fig. 3 if one plots the sum of mitochondrial and cytoplasmic fluorescence as a function of time.

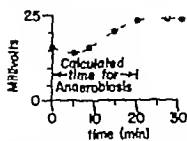


Fig. 4. Time-course of the fluorescence changes of an ascites tumour cell during the aerobic-anaerobic transition. The recording is taken from what appears to be a mitochondrial aggregate in the cytoplasm of the cell. "Calculated time for anaerobiosis" represents the number of minutes it should have taken the suspension to become anaerobic if the respiratory rate measured in the bulk phase were valid for the microscopic sample (923a).

It would appear therefore that in spite of the inferior localization obtained with the ascites tumour cells substantially the same results are obtained in the aerobic-anaerobic transition. Similar results have been obtained for pentaploid yeast cells, and preliminary studies of the application of this method to the kinetics of transfer of mitochondrial material from the mother to the daughter cell in budding yeast have been made.

Discussion. The blue autofluorescence of living cells and tissues has been indirectly associated with mitochondrial bodies by Sjöstrand¹, who has studied in detail the fluorescence characteristics of thiamin and frozen dry sections of axons and of riboflavin in acid treated groups of kidney cells (Sjöstrand, unpublished work). However no detailed investigations of the fluorescence of the living tissue were possible due to its relatively lower intensity. Independent developments in the study of fluorescence of solutions of reduced pyridine nucleotide by Boyer and Theorell⁴ and by Duyens and Kronenberg⁵ have shown a characteristic shift and an enhancement of this fluorescence in the presence of enzymes which will bind the coenzyme. The peak of this fluorescence is approximately 443 mμ. Duyens and Ames⁶ have recorded a similar fluorescence in suspensions of yeast cells. Spectroscopic observations of the high content of pyridine nucleotide in isolated mitochondria⁷ have led to a study of their fluorescence⁸. Here again a maximum at 443 mμ is obtained suggesting that the reduced pyridine nucleotide of the mitochondria is in a bound form, and therefore that the blue autofluorescence of mitochondria of living cells may well be associated with its bound reduced pyridine nucleotide. The experiments reported here verify the localization of a fluorescence characteristic of reduced pyridine nucleotide in the mitochondrial aggregate of the grasshopper spermatid and also show that it has excitation and emission characteristics which are not inconsistent with those of reduced pyridine nucleotide. However, the following kinetic data give the most direct support for this supposition.

First the change of fluorescence in the grasshopper spermatid occurs at the time expected for anaerobiosis in view of the calculated respiratory activity of the cells. Second, the change of fluorescence is an increase, as expected from studies of suspensions of mitochondria or intact cells that is where increased reduction of pyridine nucleotide occurring in the aerobic-anaerobic transition leads to increased fluorescence of intramitochondrial pyridine nucleotide. Thirdly, the fact that the *Nebenkern* shows some fluorescence in the aerobic state is consistent with the observation of a partial reduction of pyridine nucleotide in the steady state of metabolism provided substrate is present. Thus reduced pyridine nucleotide could readily account for nearly all the fluorescence of the *Nebenkern*. This confirms observations of suspensions of liver mitochondria in which complete oxidation of intramitochondrial pyridine nucleotide removes the bulk of fluorescence that is excited in the wave length region 340-360 mμ (ref. 2).

The fact that fluorescence of the *Nebenkern* is considerably less than that of the cytoplasm in the aerobic cell and increases to a value considerably greater than in the anaerobic cell is also significant. Since pyridine nucleotide is present in the cytoplasm and may well be bound to dehydrogenases and hence have shifted and intensified fluorescence it appears reasonable to attribute the cytoplasmic fluorescence at least in part, to this substance. On this basis we conclude that a change in the oxidation-reduction state of the mitochondrial pyridine nucleotide by a factor >3 has no measurable effect upon that of

the cytoplasm this is a demonstration *in vivo* of the phenomenon of impermeability of mitochondria to reduced pyridine nucleotide. While this phenomenon has been accepted on the basis of *in vitro* experiments¹⁰, the possibility existed that the impermeability of the mitochondrion may have been acquired during isolation, for example, by its envelopment in the endoplasmic reticulum (ref. 11, also personal communication). Within the framework of the assumptions here, we can put forward evidence, at least for the grasshopper spermatid, of the unreactivity of the mitochondrial membrane to cytoplasmic pyridine nucleotide *in vivo*. This observation is of considerable importance in the study of metabolic control and in the dynamics of interaction of intracellular bodies¹². In cells that fail to show the extent of mitochondrial aggregation observed in the *Nebenkern*, we are at present unable to give further data on this point.

Our thanks are due to Dr. R. P. Perry for advice and criticism, and to Miss Georgann Cullen for assistance in these studies.

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Absorbancy Measurements on Liver and Kidney Cells

By DR. BO THORELL and PROF. BRITTON CHANCE

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IN the multicomponent reaction system of the living cell, the organization and spatial distribution of the different enzymes are of fundamental importance. During the past decade, much data have been obtained about the localization of enzymes in various cellular structures. A further step towards a more integrated and physiologically adequate picture of the cell functions can be made if these enzyme systems are studied *in situ*.

This communication reports the localization and assay of respiratory enzymes (cytochromes) in areas of 1.5 μ diameter in the cytoplasm of single, living rat liver and kidney cells under different external conditions as regards the oxygen tension, namely, under aerobic and anaerobic states. The analyses were made by recording the specific light absorption (magnitude about 1 per cent) in the Soret wave length region with the highly sensitive microspectrophotometer outlined in the first communication of this group.

Single parenchyma cells from the liver or kidney-cortex of adult Wistar rats were teased out in a drop of Krebs-Ringer solution on a microscope slide with a small scalpel and a needle. After a coverslip had been put on, the cells were washed with a few drops of Krebs-Ringer solution sucked through the preparation by a piece of filter paper. To obtain anaerobiosis, ethanol-treated, starved yeast cells were incorporated in the preparation prior to sealing it with paraffin wax around the coverslip edges. Without the yeast, aerobic conditions of the cells were obtained for several hours. The state of each preparation was checked by measurement of the haemoglobin absorption bands in some added human erythrocytes¹.

The microspectrophotometer is described in detail elsewhere². The microscope optics were a 1.0 mm. Grey reflecting water-immersion condenser and 1.0 N.A. objective. A 3.5 \times quartz ocular projected the image via a vibrating mirror assembly¹ on to the photomultiplier aperture. The location of the cell image on the light-receiving system was controlled by means of an interchangeable cross-hair

The areas in the cell selected for absorption measurements were 1.5 μ in diameter. The 'reference area' in the preparation was at a distance of 12 μ from the measurement area and care was taken to choose as clear a space as possible to provide 'absolute' spectra.

On the light-absorption records obtained, an empirical wave-length calibration was made by tracing the 415-m μ maximum of the erythrocyte oxyhaemoglobin with the identical wave-length scanning speed and time constant as in the other measurements. In this way the cytochrome absorption maxima could be estimated within ± 2 m μ .

Figs. 1a and b show typical sets of absorption curves from points in the cytoplasm of single liver and kidney cells, where the anaerobic state was ensured by the presence of respiring yeast cells. In the various curves three distinctive absorption maxima or 'shoulders' appear at 415, 423 and 445 m μ .

If the yeast cells were omitted and the density of the rat parenchyma cells was low enough to permit the aerobic state during several hours, the changes in the state of the respiratory enzymes could be

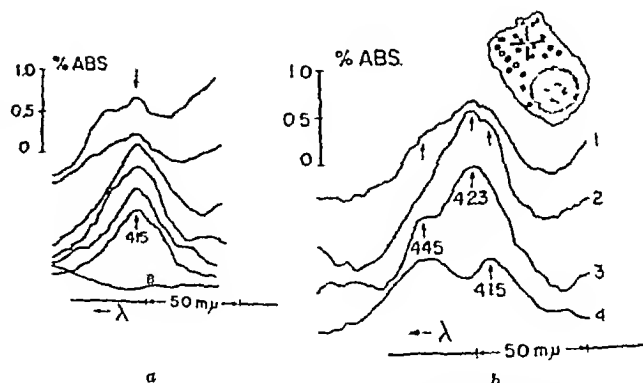


Fig. 1a. Group of absorption spectra from different points in the anaerobic liver cell cytoplasm. Trace B represents a base-line (free space) versus another free space. The records are on a linear wave length scale.

Fig. 1b. Absorption spectra from adjacent sites (1-4) in the cytoplasm of an anaerobic kidney cell. The locations of the four different areas correspond approximately to the four arms of the cross in the inset diagram.

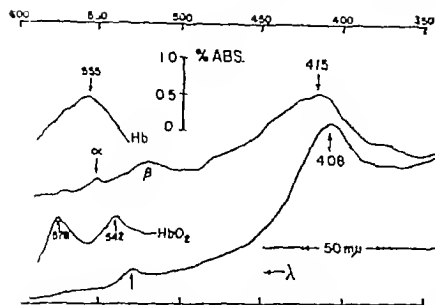


Fig. 2. Spectra from an area of 1.5μ diameter in a liver-cell cytoplasm during the aerobic (bottom record) and subsequent anaerobic (top record) states. The second spectrum was recorded after an interval of 30 min. during which the hemoglobin absorption of an adjacent human erythrocyte shifted as shown by the two left-hand records.

recorded within the same, single cell. Fig. 2 shows such an experiment, in which the hemoglobin absorption of an adjacent erythrocyte was also recorded. The reduction of the red cell hemoglobin which in this particular experiment preceded by about 20 min. the absorption changes in the intracellular cytochromes indicated that the oxygen concentration in the medium was less than 20×10^{-4} mole per litre.

The results show that absorption bands of the haemoprotein type can be obtained from small areas ($\approx 1.5 \mu$) in the single intact mammalian cell. The shift in the absorption maxima which occurred parallel with changes in the oxygen tension indicates that the specific absorptions are due to respiratory enzymes. The orders of magnitude of the absorptions measured in the single liver cell (about 1 per cent) are the same as can be calculated theoretically for cytochromes^{1,2}.

If the spectra obtained from the single intact cells are compared with the spectra of purified cytochromes the main peaks at 408_{ox} and 415_{red} , 423_{red} and 445_{red} will correspond to the Soret absorption bands of cytochrome *c*, *b* and *a* respectively.

The strictly quantitative interpretation of the absorption spectra from such optically inhomogeneous materials as liver and kidney cells is more difficult than in the case of the geometrical

uniform *Nebenkeren* (see first communication). The obviously multicomponent curves in Fig. 1b were obtained within a very small optical cross sectional area (about $2 \times 1.5 \mu^2$). The different proportions of the components found at adjacent sites can be explained either by the presence of structures containing varying proportions of cytochromes, or by changes in the layering of a few distinct structures along the microspectrophotometric light path through the cell.

If the present *in vivo* microspectrophotometric results are compared with the data on enzyme distribution obtained from the bulk isolation of cellular components, some apparently contradictory points emerge. The rather pronounced absorption band 408_{ox} - 415_{red} in practically every part of the liver cell cytoplasm indicates large amounts of a cytochrome unlike *b*. The same absorption bands are also present in the large particle free homogeneous cytoplasmic area (endoplasm) of the ultra-centrifuged but otherwise intact liver cell³. Cytochrome *b*, which can be isolated from the 'microsomal' liver cell fraction, has bands (413_{ox} - 423_{red})⁴. Different explanations for this discrepancy can be put forward for example, that the isolated microsomal fraction might constitute only a minor part of the endoplasm and that a cytochrome might have been lost during the isolation procedure. Some support for the existence of a difference between the spectral character of the DPNH reducible pigments and that of the isolated microsomes is emerging from studies of suspensions of liver cells (Chance and Rutter unpublished observations). In any event the studies reported here underline the importance of structural interpretations of absorption spectra obtained microspectrophotometrically from the highly complex enzyme system of the living cell.

The main conclusion emerging from the results described is that it is possible to analyse components of the respiratory system and to define the metabolic state of parts of the single intact mammalian cell.

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CELL AND ORGAN CULTURE

TECHNIQUES of cell cultivation are being increasingly applied in all fields of biological research. Recent developments in these methods and in their application to cancer research were described by four speakers at a session of Section I (Physiology and Biochemistry) of the recent British Association meeting at York. Cell and organ culture techniques make possible the rapid proliferation of animal and human cells outside the body, and the maintenance *in vitro* of small organs or sections of organs in a healthy condition. It was appropriate that the chair man on this occasion was Dr. E. N. Willmer, one of the leading authorities on tissue culture techniques and research in the United Kingdom.

The first paper was concerned with recent technical advances in cell culture and was given by Dr. J. Paul

(HERT Tissue Culture Laboratory, University of Glasgow). As Dr. Paul explained, tissue culture really began fifty years ago with Dr. Ross Harrison's demonstration that axons would grow out of nerve cells cultivated on frog lymph. Although the principles of the technique were at that time clearly stated only a few biologists followed up this work with enthusiasm and success. One of the common objections to tissue culture in its first years was that the cells which grew were 'nothing one thing nor another'. When tissues were explanted in a way which encouraged the rapid multiplication of cells the organized pattern of the organ was destroyed and the cells which appeared could only be classified in the most cases as either fibroblastic or epithelial. If the original morphology was retained, the cells developed

abnormal features and deteriorated too rapidly for useful investigations to be undertaken. An outstanding achievement in the pioneer phase was the demonstration in Alexis Carrel's laboratory that avian cells could be induced to multiply indefinitely. This particular cell strain lasted for thirty years—several times the life span of the fowl—and only died out when there was no one available to keep up the routine feeding and sub-culturing.

Dr Paul described, with the aid of excellent diagrams, how the mechanization of the technique during the past ten years had led to its increasing use in research laboratories and in the pharmaceutical industry. Although the hard work of developing correct procedures had been done before 1949, the impetus for a rapid advance came from the demonstration by Enders and his colleagues that poliomyelitis virus would multiply in cultures of non-nervous origin. This was followed by the successful use of trypsin for producing suspensions of living cells from body tissues, a technical trick which made easier the large scale cultivation of cells. Cultures of this type grow in an unorganized manner, and they may, as occasionally happens, produce permanent cell strains. Cells cultured from tumour tissue also grow indefinitely, and these permanent strains of different origin are available to any laboratory for investigations on their nutritional requirements and metabolism, and for virus and cancer research.

Such strains are, of course, specially adapted to grow in culture conditions and genetically, they may form a most heterogeneous population. Another technical advance which opened the way to the study of the genetics of somatic cells was the discovery that single mammalian cells could be induced to multiply and form clones with distinctive features. This was first accomplished by Dr Katherine Sanford at Bethesda, who developed an ingenious, although tedious, method of cultivating single cells within capillary tubes. Easier methods of cloning cells from permanent strains have since been devised, and the sublines are being used to study, for example, variations in the malignancy of cells and their response to irradiation.

The second paper in the session by Dr O. A. Trowell (Medical Research Council Radiobiological Unit, Harwell), was an entertaining account of the principles and practice of organ culture. The aim of this technique is to preserve the normal histology and functioning of the organ cells outside the body. Its success largely depends upon suppressing the outgrowth of cells, the principle originally demonstrated by Dr Honor Fell in the cultivation of embryonic limb buds. Dr Trowell explained that the business of physiology is to find out how the animal body works and that the logical approach is to study the different organs one at a time. This can be done either by observing the behaviour of the organ in the intact animal in various states of bodily activity or by cutting the organ out of the body and studying its behaviour and capabilities under artificial but completely controlled conditions. These approaches are complementary, and his own choice was to study the isolated organ *in vitro*. The outcome of this approach depended upon keeping the tissue alive as long as possible, since there are many physiological and pathological responses of organs which take several days to develop. Dr Trowell had, therefore, set out to study systematically the conditions which would maintain organ tissue in a healthy condition for a week or more.

The diffusion of oxygen and nutrients into all the cells of the organ culture can only be ensured by using tiny organs 2 mm in diameter, such as pituitary, thyroid, adrenal, ovary and lymph nodes of rats and mice. With larger organs, it is necessary to cut off 2 mm sections of tissue. Cultivation by immersion of the tissue in the medium proved unsuccessful because of the low solubility of oxygen, and efficient stirring of the medium only increased cellular damage. The oxygenation problem is solved by allowing the organ cultures to project into the gas phase. The tissues are, consequently, supported on a stainless steel grid, covered with fine tissue paper which is level with the surface of the medium. The grid, in its shallow dish, is kept in an atmosphere of oxygen at body temperature inside a sterile aluminium container. With this apparatus, many organs can be kept alive for as long as nine days, each 1 in square grid can carry up to twenty cultures, and the medium can be sucked off and replaced without disturbing the tissues. Culture conditions are completely standardized by the use of a chemically defined medium.

Larger organ cultures would be an advantage, and Dr Trowell hopes to achieve this by using tissue from horses and cows which have 'built into' their cells a much lower oxygen consumption and metabolism than is found in the cells from rats and mice. Cultures of cow tissue have shown that this is a feasible way of overcoming the limiting effect of oxygen diffusion. By adopting a 'mixed grill' technique, different organs, for example, endocrine organs and their target tissues can be cultured in the same vessel, and their histology can be correlated with metabolic effects revealed by the changing composition of the medium.

The two remaining papers were concerned with the application of cell and organ culture in cancer research. Scientists and laymen who are still not convinced of the connexion between lung cancer and cigarette smoking ask for direct proof of the causal relationship. For the most sceptical, it is not sufficient to show, as has been done, that cigarette tar and the carcinogens it contains produce tumours in experimental animals; the only acceptable proof is that they induce malignancy in human lung cells. The organ culture technique used by Dr Ilse Lasnitski (Strangeways Research Laboratory, Cambridge) provides the most direct experimental approach possible. Dr Lasnitski described how she prepared lung cultures from human foetal tissue and how the explants would, under normal conditions, show the characteristic formation of bronchioli *in vitro*. The normal histology of these lung cultures and the abnormal changes produced by 3,4 benzpyrene and three types of cigarette smoke condensate in the medium were beautifully illustrated by microphotographs of stained sections of the tissue. Two or three days of exposure to the carcinogen stimulated division of the epithelial cells, and in some sections taken from cultures about three weeks later cell proliferation had completely obliterated the lumen of the bronchioli. During the early stages the normal ciliary and secretory activity of the epithelium was intensified by the carcinogen, but later the cells lost the characteristic features of bronchial epithelium. Occasionally, cells with abnormal mitotic chromosomes were found in the treated cultures. Dr Lasnitski made it clear that there is, as yet, no proof that cancerous cells had been produced in these experiments. The changes observed might be precancerous, but proof of malignancy would only be obtained if treated cultures

would produce tumour like growth after hetero transplantation into experimental animals

The usefulness of organ culture was further illustrated by Dr Lasnitski's research on another form of cancer. Malignancy of the prostate gland in men is one of the hazards of old age and it is of particular interest to the investigator that this type of cancer can temporarily be controlled by treatment with female sex hormones. Cultures of mouse prostate gland were exposed to a chemical carcinogen, thus time 20 methylcholanthrene and again the epithelium of the alveoli became hyperplastic and produced a histology similar to that of skin. Dividing cells with polyploid chromosomes were frequently seen in the cultures. As in cases of human tumours, the cell proliferation was dependent upon the hormone, since the hyperplastic action of the carcinogen was abolished by the presence of oestrogen in the medium and preserved by the male hormone, testosterone. Dr Lasnitski concluded by describing briefly investigations on the metabolism of these cultures. Autoradiographic studies, undertaken with Dr S R Polo, showed that the carcinogen stimulated deoxyribonucleic acid synthesis in the epithelial cells but inhibited deoxyribonucleic acid synthesis by fibroblast after 2-8 days treatment. Amino-acid uptake from the medium was investigated in collaboration with Dr J A Lucy and it was found that leucine and iso leucine were well utilized by normal and treated cultures. However the uptake of arginine associated with normal cultures was decreased after a period of exposure to methylcholanthrene.

In the fourth paper Dr I Leslie (Department of Biochemistry Queen's University, Belfast) described the search for metabolic features which distinguish normal and cancer cells, and the opportunities provided by cell culture for tackling this problem. Three cell types are being studied in Belfast. Normal cells are represented by short-term cultures of human foetal tissues, and malignant cells by the HEP 1 strain, derived from a human carcinoma at the Sloan Kettering Institute for Cancer Research, New York. The HLM strain came from liver cell cultures prepared from a human foetus in 1950. Unlike the other cells grown from this foetus, the HLM cells grow indefinitely in culture and, in this respect they resemble the HEP 1 carcinoma cells. This 'transformation of normal cells to an apparently 'immortal' form is not uncommon in cell culture and the process is open to investigation. It is important to find how far transformed cells resemble cancer cells and how far they retain the properties of the parent cells. The way in which these cells derive their energy from glucose was investigated in 1956 in collaboration

with Drs W C Fulton and R Sinclair. According to Warburg's original concept the unique property of malignant cells is their ability to grow by means of the energy of fermentation, that is to say, the enzymic conversion of glucose to lactic acid. During proliferation in cell cultures, however, the normal (foetal) cells showed more intensive fermentation than the carcinoma or the transformed HLM cells. Other investigators have reported similar results, and Warburg's recent studies on monolayer cultures of monkey kidney cells have caused him to change fundamentally his emphasis on fermentation as the essential feature of malignancy.

The explanation of cancer has therefore to be sought elsewhere in the metabolism of the cell. Since 1953 when Watson and Crick first described the deoxyribonucleic acid molecule and its process of replication, knowledge of cellular physiology has been progressing rapidly. As a working basis, Dr Leslie suggested that cancer metabolism can be defined in terms of the biochemical events which lead to the continued replication of deoxyribonucleic acid and which are out of control of the normal restraints imposed by the adult organism. It is necessary to study the metabolic events leading to deoxyribonucleic acid synthesis and to find which are essentially different in normal and cancer cells.

Four possible defects in cancer cells were discussed and illustrated by observations on cell cultures. The defects were: abnormal chromosomes producing modified cell proteins; the channelling of compounds into the synthesis of nucleic acids; the deletion of enzymes controlling the degradation of nucleic acids and proteins; and the loss of control over growth because of the altered response of cancer cells to hormones. Evidence for enzyme deletion as a vital defect has come principally from biochemical investigations on liver tumours at the McArdle Memorial Laboratory, Madison, and the Montreal Cancer Institute. Now the absence of xanthine oxidase and arginase in both transformed and carcinoma cells is an example of this type of defect in permanent cell strains. The failure of the HEP 1 cells of corneal origin to respond to oestradiol (although they respond to insulin) is possibly linked to the recent discoveries by American groups that oestradiol is the co factor for a transhydrogenase system, and that this enzyme is much reduced in certain tumours. It would however, be wrong to suppose that there is one vital defect common to all tumours. The encouraging features of current research are that the key problems in tumour metabolism can be clearly specified and that the techniques for solving them are available.

I LESLIE

OBITUARY

Prof F S Bodenheimer

FREDERICK SIMON BODENHEIMER, who died in a London hospital on October 4 from internal complications after a successful eye operation, was born in Cologne on June 6 1897, son of Max Bodenheimer, one of the founders of the Zionist movement. As a schoolboy, he was attracted to biology but was persuaded to study medicine which offered a more certain future, at Frankfurt and Bonn. His main interest was, however, still in zoology, and he obtained his Ph.D. at Bonn in 1921 with the intention of

specializing in entomology and going to Palestine to work there. He studied at the School of Agriculture in Geisenheim and after spending half a year at Portici with Silvestri and Grandi, accepted an appointment as entomologist in the new agricultural research station of the Jewish Agency at Tel Aviv, where he worked during 1922-28.

His studies during that period were concentrated on economic entomology, culminating in a book, "Die Schädlingfauna Palästinas (1930)" but his interests were wider and his energy so inexhaustible

that he succeeded, at the same time, in producing two volumes of the "Materialien zur Geschichte der Entomologie" (1928-29) and in carrying out an expedition to the Sinai with Dr O Theodor to settle the problem of the origin of manna, which proved to be the excretion of a coccid (*Najacoccus serpentinus*) on tamarisk. In 1928, he was appointed a Research Fellow, and in 1931 professor of zoology at the newly founded Hebrew University at Jerusalem. This opened a period of most fruitful research on a variety of biological problems, resulting in a long series of publications, the total of which during his life exceeded four hundred, including a number of books, apart from those already mentioned, he published "Animal Life in Palestine" (1935), "Prodromus Faunae Palaestinae" (1937), "Problems of Animal Ecology" (1938), "Animals in the Bible Lands" (1949, 1956), "Citrus Entomology in the Middle East" (1951), "Insects as Human Food" (1951), "The History of Biology" (1958), and "Animal Ecology To-day" (1958). His last book, just published, "A Biologist in Israel", is an extensive autobiography, and, at the same time, as he described it to me, "a history of a generation of ecologists".

Bodenheimer travelled extensively, in 1931, after a term as a visiting professor at Minneapolis, he went around the world, stopping where he would, during 1938-41 he was a visiting professor at Ankara and played a prominent part in developing entomological work in Turkey, in 1943 he was invited to Iraq to study the locust problem there, in 1955 he lectured in the University of Durham on Canon H. B. Tristram and visited Finland, in 1956 he went to Australia

for a Unesco meeting on the Climatology of Arid Zones and took in South Africa *en route*. Wherever he went, he lost no opportunities of learning at first hand all that could be learned of local biological problems and institutions and workers.

His main life-interest was animal ecology in the broadest sense. His earlier published books on the subject did not receive sufficient recognition, since he had to write in English, which was not his own language, and many of his original ideas have been offered in a not easily digestible form. Moreover, he was never easily satisfied with formal definitions of concepts and always searched for other than the accepted solutions of such basic problems as the equilibrium in animal populations, animal communities, the interaction of environment and heredity, etc. On many of these points he was outspokenly critical of views of others, but his criticisms were always such as not to annoy, but to stimulate.

As an entomologist, Bodenheimer left a great heritage, but he was also well known to mammalogists for his studies on the vole (*Microtus*) populations in Palestine, and before his death he prepared a revision of Canon Tristram's work on the mammals of Palestine.

His many travels and his deep interest in the work of others have made Bodenheimer well known to a large number of biologists all over the world and his early death will be deeply regretted by many. His wife Mrs Rachel Bodenheimer, who accompanied him on many of his travels, made friends wherever she went. Their many friends will share her feeling of loss.

B. P. UVAROV

NEWS and VIEWS

Chief Scientist of the Ministry of Supply

Dr R. Cockburn, C.B., O.B.E.

ON October 1, Dr Robert Cockburn took up the post of chief scientist of the Ministry of Supply. Cockburn gained his first degree at the University of London when he was only nineteen, adding to it later both the M.Sc. and the Ph.D. From 1930 he taught science at the West Ham Municipal College, and at the same time conducted research on the effects of electron transit time in very high-frequency oscillators, until, in 1937, he joined the Radio Department of the Royal Aircraft Establishment, Farnborough, where he was engaged in the development of a new very high-frequency communication system for the Royal Air Force. From 1939 until 1945 Cockburn was at the Telecommunications Research Establishment, Malvern, where he and his team developed and used radio counter-measures of all kinds in the protection both of targets in Britain and British bombers operating over enemy territory. For his outstanding work he was appointed O.B.E. in 1946. He spent a short period at Chalk River and at Harwell, until in 1948 he became scientific adviser to the Air Ministry. He stayed there for five years, joining the Ministry of Supply in 1953, where he has been successively responsible for research and forward thinking in all applications of electronics, for the organization of all the research and development programmes in this field, and since 1956, as con-

troller of guided weapons and electronics, for the whole field of research, development and production of these equipments.

Cockburn brings to his new post exceptional practical knowledge of the operational use and technical requirements of systems that he gained in the Second World War, the intimate knowledge of the Services that he acquired when at the Air Ministry, and the inside knowledge of the Ministry of Supply gathered in the three senior appointments that he has already held there. He adds these to his wide basic scientific knowledge and his international standing and prestige as a scientist who has concentrated on the special problems of defence. His appointment is warmly welcomed by his professional colleagues, Service and scientific, throughout the many circles in which he is well known.

Engineering at Leicester.

Prof. E. W. Parkes

DR E. W. PARKES has been appointed to the new chair of engineering in the University of Leicester. Dr Parkes was born at Sutton Coldfield in 1926, and was educated at King Edward's School and St John's College, Cambridge, where he gained first-class honours in the mechanical sciences tripos in 1945. After leaving Cambridge, he worked for a year at the Royal Aircraft Establishment and for two years with the Hawker Siddeley group on the design and testing of aircraft structures. He returned to

Cambridge in 1948 to study the elastic stresses in flamed beams. In 1950 he was appointed University demonstrator and afterwards lecturer. He was elected into a fellowship at Gonville and Caius College in 1954 and in 1957 was appointed tutor. Dr Parkes's main fields of research are the inelastic dynamic behaviour of structures and the behaviour of structures subjected to temperature variation. He is particularly interested in repeated thermal loading phenomena such as incremental collapse under thermal cycling. In the industrial field Dr Parkes has acted as consultant on the design of crane jibs, tall towers, bridges, boilers and vacuum vessels. He has lectured on his work on thermal stresses on a number of occasions in Denmark and Sweden and is at present spending six months as visiting professor at Stanford University, California, working in the same field.

Highway and Traffic Engineering at Birmingham

Prof J Kolbuszewski

Dr J Kolbuszewski, who has been appointed to the chair of highway and traffic engineering which has recently been established within the Department of Civil Engineering at the University of Birmingham, joined the University as a lecturer in 1951, the title of reader in soil mechanics being conferred on him in 1957. During the past three years he has been in charge of the Graduate School of Highway Engineering and the Graduate School of Foundation Engineering. Originally, Dr Kolbuszewski graduated from the University of Lwów, where he was afterwards a lecturer in civil engineering. He served throughout the Second World War with the Polish, French and British armies. After the War he studied at the Imperial College, London, where he obtained his Ph.D. degree. He was a member of the staff of the Polish University College, London, from 1946 to 1950, joining as a lecturer and being promoted to professor and director of studies in 1947.

Dr Kolbuszewski's research interests have been principally concerned with problems in soil mechanics and foundation engineering, and in particular, with problems arising in connexion with pressures under pavements and the trafficability of beaches. A few years ago he carried out some original experiments in the Sahara Desert, when he obtained some interesting information regarding the bearing capacity of wind-deposited sands.

Radiation Protection

The occupational hazards associated with radioactive materials have for a generation been under periodic review by the International Commission on Radiological Protection, which is a commission set up by the International Congress of Radiology and by national bodies. In the United States this is the National Committee on Radiation Protection, which issued its latest report on June 5 (US Department of Commerce National Bureau of Standards Handbook 60 Maximum Permissible Body Burdens and Maximum Permissible Concentrations of Radio-nuclides in Air and in Water for Occupational Exposure, Pp viii+95 Washington, D.C. Government Printing Office, 1959 35 cents). The chairman of the sub-committee responsible for this report is also chairman of the corresponding international committee. It can therefore be taken that this document is in many respects a preview and abbreviated version of the corresponding recom-

mendations of the International Commission on Radiological Protection which are now in press.

Previous figures for permissible body burdens of radioactive nuclides were given in 1953. The basis for recommendations concerning permissible exposure was revised recently (Recommendations of the International Commission on Radiological Protection, September 9, 1958 Pergamon Press London, 1959). This has led to corresponding revision to smaller permissible body burdens only for nuclides which result in irradiation to the whole body. However, new biological data and improved methods of calculating physical doses have led to a complete reassessment of values. This has allowed permissible figures for some nuclides to be increased notably twice as much strontium 90 as before is now allowed. At the time this produced a furore in the American daily press. On strictly logical grounds the committee could have raised the value five-fold. That it did not do so indicates that judgment and opinion as well as numbers have been used rather than strict logic. After all, the figures are not magical: they are still capable of revision in the light of further information and experience after a further quantum.

International Council of Scientific Unions

THE financial statement of the International Council of Scientific Unions for the period November 1, 1957, to December 31, 1958 (pp 12 The Hague International Council of Scientific Unions, 1959) records an excess of expenditure over income for the period of 16 038 dollars, in spite of a further increase in the income from member unions to 2,852 dollars. The 67 428 dollars received from national members during the year includes 20 898 dollars representing annual dues previously in arrears. The increase in expenditure from 42,070 dollars in 1956-57 to 88 130 dollars is attributed to the increasing scientific activity of the Council the higher costs of running the Secretariat mainly due to increased staff the heavy costs of holding the 1958 General Assembly and Meeting of the Executive Board in the United States and the establishment of a Secretariat in The Hague, apart from the fact that running expenses are for fourteen months instead of the normal twelve. For the triennium 1959-61 the eighth General Assembly adopted a budget of 58 000 dollars per annum, and the Assembly also strongly endorsed the decision of the Executive Board to establish a capital fund.

University Foundation of Belgium

DURING the academic year 1957-58 the University Foundation of Belgium distributed subsidies totalling 4 858,002 francs and 2 441,600 francs in awards for ordinary studies. Of the latter, 1 940,500 francs went to the University of Louvain 718 000 francs at the University of Ghent, 350,000 francs at the University of Brussels and 108,500 at the University of Liège. Of the 107 awards 32 were in science, 4 in pharmacy, 33 in medicine 1 in veterinary medicine 3 in dental science 32 in engineering 4 in agronomy, 5 in political, social or administrative science, 5 in commercial or economic science or finance and 4 in applied psychology and vocational guidance. Five awards were made for courses of study abroad: four in France and one in Switzerland. Subsidies for the publication of scientific works amounted to 458 500 francs and to periodicals to 3 188 000 francs while

scientific associations received subsidies amounting to 606,000 francs. The thirty-eighth annual report of the Foundation (Fondation Universitaire Trentehuitième Rapport Annuel, 1957-1958. Pp 148. Bruxelles: Fondation Universitaire, 1959) which gives these figures, includes a list of beneficiaries during the year, as well as some notes on institutions with which the Foundation has connexions. It also includes a list of bursars for 1958-59 under the Belgian American Education Foundation, Inc., both in Belgium and in America. Of the 29,651 university students enrolled in 1957-58, 81.5 per cent were men and 18.5 per cent women. 11.35 per cent were in science, 25.33 per cent in medicine and pharmacy, 11.62 per cent in applied science, 2.52 per cent in agronomy, 6.15 per cent in social, political and economic science, and 13.16 per cent in commercial science. Of 4,770 diplomas obtained in 1956-57, 630 were in science, 1,035 in medicine and pharmacy, 33 in veterinary medicine, 405 in applied science, 151 in agronomy, 266 in social, political and economic science, and 654 in commercial science.

Industrial Psychology Grant Increased

THE Department of Scientific and Industrial Research is to continue its annual grant to the National Institute of Industrial Psychology for a further five years. The amount is to be raised from £4,000 to £6,000 a year, on the understanding that the Institute will increase to £9,000 a year its own income from membership subscriptions and special contributions for long-term research. The Department of Scientific and Industrial Research is also to add another £100 a year for every £100 of grant earning income which the Institute can obtain in excess of the qualifying £9,000 up to a maximum of another £6,000 a year. This means that if the Institute can raise £15,000 a year from industry, the Government will give it £12,000. The grant and the grant-earning income have to be put in a special fund and used only for long-term research. Among research projects now in train are: an inquiry into workers' attitudes to the opportunities and rewards offered by their jobs, which may have a bearing on personnel policies; an investigation into the relation between satisfaction and efficiency on the job; a study of industrial management structure and efficiency; and experiments on tests for manual skill. The Institute has received many inquiries from industry recently about the special tests it has devised for selecting suitable school-leavers to be engineering apprentices.

Australian Atomic Energy Commission Research Grants

RESEARCH grants totalling almost £28,000 have recently been awarded by the Australian Atomic Energy Commission in support of research under contract in seven Australian universities. Fields covered include chemistry, physics, geology, mining, electrical, metallurgical and chemical engineering, and the biological sciences. The grants have been made for work in fields which will contribute to the Commission's own work in developing civilian uses of atomic energy.

Alkali and Similar Works in Britain

THE ninety-fifth report of the Chief Inspector on Alkali, etc., Works in England and Wales covering the year 1958 notes an increase in the number of

works registered under the Act from 872 at the end of 1957 to 2,160 at the end of 1958. It also shows an increase in the number of separate processes from 1,733 to 3,412 in consequence of the extensions of the list of scheduled works and of noxious or offensive gases under the Alkali, etc., Works Order, 1958. Many of the new registrations relate to very large undertakings, particularly as regards the non-ferrous metal and steel industry and the newer electric power stations. The result of these increases is that the staff of the inspectorate has been increased, and it will now be necessary to adjust the internal organization. The 7,142 visits and inspections during the year included 255 special visits by the chief and deputy chief inspectors and 32 by Mr W. A. Damon, the former chief inspector, who continues to serve in a special advisory capacity. Several visits were again paid to establishments of the Atomic Energy Authority, and discussions with the Authority during 1958 covered problems arising out of the nuclear power problem, particularly as regards the increased scale of processing uranium for use as a fuel and of irradiated uranium from the projected nuclear power installations. Considerable interest has been shown by local authorities in clean air matters and in the processes scheduled by the 1958 Order, and friendly and adequate liaison and co-operation appear to have been established. There were twelve infractions of pre-1958 processes compared with seventeen in 1958, and of these, six related to escapes of acid gases in excess of statutory limits and six to failure to use 'best practicable means'. The Chief Inspector for Scotland reports 213 visits during the year, including 27 in connexion with the Alkali, etc., Works (Scotland) Order, 1958, mainly about points of doubt in applications to register. In the course of 89 chemical tests, three infringements were found, two in chamber sulphuric acid plants, which appeared to be quite inadvertent, and one at a plant for concentrating sulphuric acid. Two further infringements were noted during visual inspection of premises registered for distillation of tar.

New Journal of Psychopharmacology

LITERATURE on psychopharmacology has hitherto either appeared as contributions to symposia, of which the past years have seen ever-increasing numbers, or been scattered in the periodicals of many disciplines, such as psychology, psychiatry, physiology, biochemistry and pharmacology. *Psychopharmacologia* is a new journal aiming at finding a single home for the investigations on the effect of drugs on behaviour carried out by workers with the greatest variety of training (Vol 1, Fasc 1. Pp 78+10. 9.60 DM. Maximal preiss 1959, 40 DM. Maximal-preiss 1960, 80 DM. Berlin: Springer Verlag, 1959). There will be some overlap with the recently launched periodical *Biochemical Pharmacology* as there will be with the *Journal of Neurochemistry*, but interest in this field has been so great in recent years that the editors will experience little difficulty in obtaining manuscripts of the highest standard. Papers will be accepted in English, French or German. The advisory board is recruited from Western Europe and North America. The first number contains a review and a number of original articles and makes interesting reading. It is to be hoped that psychopharmacologists, while keeping up with their own discipline, will find time to read yet another integrating journal.

Bird Paintings of the Eighteenth Century

THE Trustees of the British Museum have published an account of "Some Eighteenth Century Bird Paintings in the Library of Sir Joseph Banks (1743-1820)", by Averil Lysaght (*Bull. Brit. Mus. (Nat. Hist.)*, Historical Series, 1 No. 6 Pp. 251-371 + plates 35-37. From the Museum 40s.). This collection, ultimately passing to the British Museum, included the work of various artists accompanying Captain Cook on his three voyages. These are of interest to systematists in that some of the drawings rank as the types of the then newly discovered species, the actual specimens having deteriorated or perished. The record is of all the more value in that some of the species have meanwhile become greatly reduced in numbers and geographical incidence if not extinct. Owing to the accident that some of the illustrations remained in Bloomsbury when others were transferred to South Kensington in 1880, these were overlooked by Bowdler Sharpe and others. The task of making a new assessment was originally suggested by the late Sir Norman Kinnear.

Microcard Adapter for 'Dagmar' Microfilm Reader

THE Dutch 'Dagmar' microfilm microfiche reader which was introduced into Great Britain in 1957, has proved itself to be a good, cheap, portable reader with many attractive features. It has been made even more versatile by the addition of a microcard adapter. This has been developed in the library of the Manchester College of Science and Technology and it is now being manufactured for sale to others. Anyone already owning a 'Dagmar' can effect the alteration necessary to take the adapter in a few moments. A small hole has to be cut in the front panel above the lens and a triangular casting bolted on. This takes the condenser system of the adapter and positions the illumination so that it shines down on to the microcard which is in the glass microfiche holder. The adapter is being distributed by Trow Microfilming Ltd., 22 Park Lane Croydon at about £10.

Museum of Applied Science, Victoria

THOSE engaged in museum work have often deplored the name but have failed to find an adequate substitute. The Report of the Museum of Applied Science for the year ended June 1958 states that the Trustees have unanimously recommended that the term 'Institute' shall replace 'Museum' and they trust that the necessary legislation to effect the change shall be introduced. It is felt that the new title will indicate more clearly the present functions and activities especially as the displays interpret the rapid and continuing advances in applied science and technology. The International Geophysical Year was well publicized both by means of special displays and booklets.

Cancer Current Literature Index

THE Excerpta Medica Foundation, which has its main office in Amsterdam, provides a monthly comprehensive series of abstracts on branches of medicine, one of which is devoted to cancer. The August issue of the cancer section is a sizeable volume of 170 pages containing nearly 600 abstracts. The Foundation has now, in collaboration with the U.S. Cancer Society, begun the production of a still more con-

densed form of abstracts which consists only of title author and reference to publication. The first number (September) is a guide to 300 papers dealing with different aspects of cancer research. The aim of this publication, which has been made possible by a grant from the U.S. Cancer Society, Inc., New York, is to provide a regular up to date index of the bibliographical references to the world's literature in the field of cancer. The "Cancer Current Literature Index" will appear at intervals of two to three weeks. Each yearly volume will contain approximately 4,500 references from some 3,000 medical journals published all over the world, including those from the U.S.S.R.

Cattle and Buffaloes of India

ABOUT 20 per cent of the total number of cattle in the world exist in India, and while at present they are mainly used for draught purposes, their potentiality at present but poorly developed for milk supply is great. Improvement of these cattle for milk production would not only supply one of the main nutritional needs of the Indian peoples but also would improve the economic position of the peasant farmer by giving him the weekly income which he does not receive from crop farming alone. One of the steps towards an improvement is the holding of cattle shows for the development of special breeds. A bulletin published by the Indian Council of Agricultural Research on "Bovine Stars of India" illustrates some of the best individual cattle of different breeds exhibited at four Regional and the All India Cattle Shows in 1955 (Indian Council of Agricultural Research Misc. Bulletin No. 82 Pp. ix + 20. Delhi: Manager of Publications 1957 Rs. 2.37 4s.). It is stated that some of the cattle have been given prizes for being the best milch type but the absence of any actual records of production to go with the photographs is to be regretted. Since the buffaloes and native Zebu breeds of cattle have a high degree of heat tolerance it is on their improvement rather than by the introduction of European breeds lacking heat tolerance that the future milk supply of India lies. Bulls and cows of some twenty six breeds of cattle and three breeds of buffaloes have been photographed against a squared background which enables one to judge actual size and an attempt is to be made to record body measurements at future shows. Some good draught type cattle are also illustrated but one wonders how long it will be before they are replaced by mechanization.

Pest Control

THE Ministry of Agriculture Fisheries and Food has published under the title 'Infestation Control a Service to Agriculture and Food Storage' (pp. iv + 32 + 12 plates. London: H.M. Stationery Office 4s.) a pamphlet describing the research carried out by its officers on the problems of infestation control in farms and warehouses, together with a brief history of the subject in Great Britain. The work falls into two main parts: one dealing with the insect pests of stored foodstuffs the other with vertebrate enemies such as rodents and birds. By what must be regarded as a political accident vertebrates are covered whether they attack crops in the field or in store whereas the invertebrate field pests are the responsibility of another section of the Ministry. Both parts of the pamphlet cover a surprisingly wide range of topics in which the application of scientific method

has made important contributions to public health or profit. These concern especially the control of insect pests by chemical means and the development of new techniques for baiting rodents and, more recently, the development of anti-coagulant poisons. Perhaps characteristically in Britain, the pioneer work was done in the universities and received final Government blessing during the Second World War. There is a useful list of papers published by members of the infestation control division during the past fifteen years.

Nitrogen Replenishment in the Soil

LAND fertility improvement was the theme of the presidential address by Dr N. R. Dhar, of the University of Allahabad, this year to the Indian Society of Soil Science held at Delhi. He points out that the amount of fertilizer used in the world is still very inadequate and production of nitrogen fertilizer appears to be lagging behind production of phosphate and potash. Under-developed countries are poorly equipped with nitrogen-fixation factories because of the high capital investment involved. Dhar estimates that approximately one hundred million tons of fixed nitrogen is necessary for the food supply of the world, but present production is less than eight million tons. This emphasizes the importance of other nitrogen sources. For example, legumes probably fix five million tons of nitrogen and rain contains about ten million tons. It is also pointed out that the amount of nitrogen lost in refuse from urban areas is about equivalent to the amount of nitrogen supplied to world crops as fertilizer. Even in highly organized agriculture such as in the United States, more nitrogen is removed from the soil than returned as fertilizer, resulting in an annual deficit of six million tons. This translated into world figures means a loss of about fifty million tons of nitrogen a year. This annual loss must be compensated in permanent agriculture by natural methods of recuperation. By making assumptions concerning the amount of carbon added to the earth by photosynthesis and the proportion of this which in turn is oxidized, it is estimated that one hundred and ten million tons of nitrogen a year is fixed by natural processes. Hence this is the chief natural source of soil nitrogen and far exceeds the amount supplied by fertilizers.

Tectonics in the U S S R

A GREAT advance in tectonics was made by the publication of the tectonic map of the Soviet Union in 1957 on the scale of 1:5,000,000, published on nine sheets. This map is coloured vividly in accordance with the orogenic age of the formations, with tints and shadings indicating various folding phases and structural features. The map was compiled by a number of geologists under the direction of N. S. Shatsky, one of the foremost tectonists in the Soviet Union. It was accompanied by an explanatory memoir written by N. S. Shatsky and A. A. Bogdanov. A small-sized variant of this map is published by Y. A. Kosygin (*Priroda*, 8, 21, 1958) as an illustration for his article dealing with new methods applied to the study of tectonic structure of the Earth's crust by means of deep stratigraphical boreholes. This method, according to the author, is particularly suitable for the study of the 'cover' of ancient 'platforms' and also for the preparation of 'palaeogeological' maps of the 'floor' of the 'cover'. In another article Y. A. Meshcheryakov (*Priroda*, 9, 15, 1958) discusses

'neotectonics'—a term proposed by V. A. Obruchev for the study of the recent or near-recent movements of the Earth's crust. In this article he gives a 'neotectonic' map of the European part of the Soviet Union and a generalized map of the world showing regions of recent elevation and depression as well as the earthquakes zones. This map shows that the modern regions of elevation are not confined to the areas of Quaternary glaciation and therefore cannot be explained by the hypothesis of glacial isostasy control.

Meteorological Data

RADAR is a powerful tool for the meteorologist in the detection of precipitation as it is the only means of locating the positions of all precipitation falling at above a certain moderate rate and at any one time within a distance of the order of 100 miles from the transmitter. The strength of the radar echo is proportional to ND^6/L^4 , where N is the number of drops in unit volume, D the drop diameter and L the wave length of the radar. The echo intensity thus increases very rapidly with the size of the drops. The advantage of a very short wave-length is, however, offset by increased attenuation of the beam by precipitation and the water vapour and oxygen of the air, and by engineering difficulties of obtaining adequate radiant power. In practice, wave-lengths in the region of 3–10 cm are mostly used, giving admirable representation of moderate and heavy rain at distances up to 100 miles or more. Radar is of great value for guiding aircraft in and out of airfields to avoid highly turbulent thunderclouds, in forecasting the approach to cities of thunderstorms with their effects on public transport and demand for lighting, and also in the study of cloud structure and hydrology. The subject is comprehensively discussed in all its aspects in a recent report by the World Meteorological Organization prepared by a Working Group of the Commission for Instruments and Methods of Observation under the chairmanship of Mr. R. F. Jones, of the Meteorological Office (Technical Note No. 27. Use of Ground-Based Radar in Meteorology (Excluding Upper-Wind Measurements). Pp. xvi+80. Geneva: Secretariat of the World Meteorological Organization, 1959. 9 Swiss francs). This describes the basic theory, types of radar and display, recording and transmitting the information, the types of radar echo associated with clouds and precipitation, echoes from other phenomena such as smoke, insects and birds, the practical applications and the use of radar in research.

European Nuclear Energy Project, *Dragon*

THREE engineers, one from Switzerland and two from Italy, arrived in Britain on September 21, representing the advance guard of some ninety European engineers and scientists who, with 160 from the United Kingdom, will comprise the international staff of the *Dragon* project of the Organization for European Economic Co-operation at the Atomic Energy Establishment, Winfrith, Dorset (see *Nature*, 183, 507, 1959).

Harwell Reactor School Courses

STANDARD Course No. 20 of the Harwell Reactor School will commence on January 4 and continue until April 29, 1960. These courses, which began in September 1954, are designed to train engineers

in the techniques of reactor construction and operation, particularly in connexion with nuclear power stations. A special course for senior technical executives, the tenth of its kind, will be held during May 8-20, 1960. Application forms and details of both courses can be obtained from the Principal Reactor School, Atomic Energy Research Establishment, Harwell, Didcot, Berks.

University News

Oxford

It is announced that the Medical Research Council has provided a grant not exceeding £1 100 for the year beginning October 1 for scientific assistance in a study of X ray analytical methods of insulin and related structures, to be carried out in the Laboratory of Chemical Crystallography under the direction of Dr D M Hodgkin. A grant not exceeding £5 700 for the three years beginning October 1 has been provided by the United Kingdom Atomic Energy Authority for studies in interferometric spectroscopy to be carried out in the Clarendon Laboratory under the direction of Dr H G Kuhn, and in addition a further grant not exceeding £1,250 during the period October 1, 1959 to September 30, 1960, for work on the constitution of bismuth rich alloys being carried out in the Department of Metallurgy under the direction of Prof W Hume-Rothery.

The United States Public Health Service has provided a sum of 14,100 dollars for the year which commenced September 1 for the continuation of research on vision and light quanta, being carried out in the Department of Physiology by Dr M H Parnane, under the direction of Prof E G T Liddell.

Grants are to be received from the Department of Scientific and Industrial Research as follows: £1 000 for the year beginning October 1, for research on some natural products with biological activity, to be carried out in the Sir William Dunn School of Pathology under the direction of Dr E P Abraham £1,500 for one year as from October 1, for research into perceptual limitations in high speed performance, to be carried out in the Institute of Experimental Psychology by Dr H Kay, under the direction of Prof R C Oldfield, £22,860 for the three years ending September 30 1962, for an investigation of the geological age of rock series by methods based on natural radioactivity being carried out in the Department of Geology under the direction of Prof L R Wager, £1,220 for equipment for research on the biochemical mechanism of cell division, to be carried out in the Department of Biochemistry under the direction of Sir Hans Krebs; £25 725 for the period October 1, 1959 to July 31 1962 for an investigation of materials using magnetic resonance and double resonance techniques to be carried out in the Clarendon Laboratory under the direction of Prof B Bleaney £17 610 for the period October 1, 1959 to July 31 1962, for an investigation of nuclear orientation and nuclear cooling in magnetic fields to be carried out in the Clarendon Laboratory by N Kurtz under the direction of Prof B Bleaney. The Ministry of Supply has provided a grant not exceeding £1,175 for the year as from September 1, 1959 for the continuation of an investigation of fluorocarbon hydrates being carried out in the Department of Biochemistry under the direction of Dr P W Kent £2,200 is to be expended from the University General Fund on alterations to the Department of Zoology in order to provide additional teaching space.

Mr F A Burchardt director of the Institute of Statistics who died on December 21, 1958, has been succeeded by E F Jackson, Fellow of St Antony's College.

World Meeting on Veterinary Education

A world meeting on veterinary education to be held in London during April 25-20 1960, is being convened by the Food and Agriculture Organization. The meeting will be held at Church House Westminster, by invitation of H.M. Government and will be attended by participants from most parts of the world, including the Far East Latin America, the Near East and Africa.

British Society of Rheology

The British Society of Rheology has announced the following officers for the year 1959-60: *President* Dr H Kolsky (Armament Design Establishment), *Hon. Secretary* Dr M F Culpin, *Hon. Treasurer* Mr O C Mill, *Hon. Editor (Bulletin)* Mr J F Hutton (Shell Research, Ltd.), and *Hon. Editor (Abstracts)*, Dr J C Vernon.

British Electronic Achievements

The scheme for awarding annual premiums for articles on electronics, organized in the past by the Radio Industry Council (London) is now under the joint sponsorship of the Council and of the Electronic Engineering Association. Articles published during 1959 will be considered by the panel of judges early in the New Year and explanatory leaflets can be obtained from the Electronic Engineering Association, 11 Green Street London W1 to which also eligible articles should be submitted before the end of the year.

The Annual Review of Pharmacology

ANNUAL REVIEWS, INC, of Palo Alto California announces the organization of a new series 'The Annual Review of Pharmacology'. The first volume is scheduled to appear in April 1961. Prof Windsor C Cutting, of Stanford University, has been appointed as editor, and Prof Henry W Elliott, of the University of California as associate editor. Members of the Editorial Committee, under whose direction the Reviews will be organized are initially as follows: Windsor C Cutting (chairman), Bernard B Brodie, National Heart Institute, Maynard B Chonoweth, Dow Chemical Co, Louis S Goodman University of Utah, G B Koelle, University of Pennsylvania, Chauncy D Leake, Ohio State University, and Maurice H Seavers University of Michigan.

Announcements

Mr A PERERA representing Ceylon has been appointed chairman of the Executive Council of the Commonwealth Agricultural Bureaux, in succession to Dr J G Malloch. Mr C K Reheman representing Pakistan, has succeeded Mr Perera as vice chairman.

ERRATUM In the communication entitled 'Pro duction of Serum Albumin and of Globulins', by Prof E Brode *et al.*, in *Nature* of August 1, p 381 the penultimate line of column 1 should be at the foot of column 2. Further, Dr Leslie's strain referred to in column 2 should be *HLB* and not *HIM* as printed.

THE EUROPEAN ORGANIZATION FOR NUCLEAR RESEARCH

PRESENT STATUS

THE European Organization for Nuclear Research (CERN) has in operation a synchrocyclotron, accelerating protons to 600 MeV and is in course of constructing an alternating-gradient synchrotron which is designed to accelerate protons up to 25 GeV. In addition to these two accelerators, CERN is building up on its site at Meyrin, near Geneva, experimental equipment and services comparable with those existing or being built at Brookhaven and Berkeley in the United States and at Dubna in the USSR.

The synchrocyclotron, which has been running for more than a year and in recent months has operated for 95 per cent of the scheduled time, is yielding an ever-increasing flow of experimental results. Analysed beams of mesons, neutrons and protons are available in two experimental halls on either side of the machine. The most recent experiments which have been completed include a charge-independence experiment concerning the ratio of the cross sections of the reactions $p + d \rightarrow H^3 + \pi^+$ and $p + d \rightarrow He^3 + \pi^0$, which should be (apart from Coulomb and mass correction) exactly 2. The experimental accuracy achieved was 5 per cent, which is perhaps the most precise confirmation of charge-independence yet obtained at high energies. An experiment in an earlier stage is examining the neutron groups from the reactions $\pi^- + p \rightarrow \pi^0 + n$ and $\pi^- + p \rightarrow \pi^- + n$ with 70 MeV pions. This has already yielded an accurate value of the π^0 mass. Two experiments which are now being designed are on the scattering of μ -mesons by nuclei (for which a focusing channel for muons is under construction) and an experiment for the accurate measurement of the anomalous part of the magnetic moment of the muon. Two experiments using hydrogen bubble chambers are just starting, the first, using a 25 cm diameter chamber brought to CERN by an Italian group, deals with the scattering of 350 MeV pions by protons, and the second, using a 30 cm diameter chamber built at CERN, deals with the double production of π -mesons. Many other experiments are being carried out with the synchrocyclotron by teams of CERN physicists and by visiting groups from the member countries of CERN. About 30 per cent of the running time of the machine is scheduled for these visiting groups, which include teams from Padua, Utrecht, Harwell and University College, London.

The magnet units of the 25 GeV proton synchrotron, one hundred in number and weighing in total 4,000 tons, are mounted in the machine building, a subterranean annular tunnel covered with 3 m of earth. Pulsing tests on the magnet, using the rectifier-inverter set and generator, began in the latter part of July. The vacuum system, a 620 m long elliptic tube pumped by fifty vacuum pumping stations, is nearly assembled, as are the sixteen radio-frequency accelerating stations. Two tanks of the three tank linear accelerator, which will inject protons with an energy of 50 MeV into the synchrotron, are working, giving 3.5 m amp of 30 MeV protons.

Considerable thought has gone into the planning of the experimental apparatus to be used with the 25 GeV accelerator and into the layout of this apparatus in the experimental halls. The largest

pieces of equipment being built at CERN are a 2 m long liquid hydrogen bubble chamber, a 1 m diameter propane bubble chamber and a 2 m long gas Čerenkov counter. The propane chamber, complete with its magnet, giving a field in the chamber of 18,000 gauss, weighs about 100 tons and is planned to come into operation in the middle of next year. The hydrogen chamber and its magnet weigh about 600 tons and are scheduled for operation in 1962. A French group from the Centre d'Études Nucléaires, Saclay, will bring an 80 cm long hydrogen bubble chamber to CERN towards the end of 1960 and a British group plan to bring an even larger hydrogen chamber in 1961. Another French group, from the École Polytechnique, Paris, plans to bring a 1 m long propane bubble chamber next year. These 'visiting' bubble chambers will be used at CERN by mixed teams of CERN physicists and the physicists coming with the chambers. Initially, the 30 cm diameter CERN hydrogen bubble chamber will be used for exploratory experiments. To get momentum analysed and purified beams of particles to these bubble chambers and to counter experiments, systems of bending and focusing magnets have been designed and ordered and a 30 m long beam separator is in course of study. Direct current generators, totalling 8 MW capacity, are being installed to power these experimental magnets.

Although about 500 sq m of floor area are at present available for experiments with the proton synchrotron this space will be fully occupied by experimental equipment within a year or so of the accelerator coming into operation. A new experimental area, foreseen for use in 1962 will provide special buildings for the very large hydrogen bubble chambers and a 600 m long flight path for the beams of particles emerging from the synchrotron. This long flight path is necessitated by the extreme difficulties encountered in trying to distinguish between different types of particles at such high energies where all particles, irrespective of their rest mass, are travelling at very nearly the velocity of light. It is possible to discriminate between different particles only after they have travelled hundreds of metres, when the small relative velocity differences of the particles have resulted in a time separation which can be measured by electronic discriminators with resolution times of a few nanoseconds (10^{-9} sec).

The analysis of the bubble chamber photographs will be carried out with semi-automatic measuring machines, designed at CERN, similar to those already in use at the Radiation Laboratory at Berkeley. The output of these machines, in digital form, is fed into the Ferranti Mercury computer now in operation at CERN, for spatial reconstruction and kinematic analysis of events.

In addition to the experimental groups using the 600 MeV synchrocyclotron and planning experiments with the 25 GeV synchrotron, there is a strong theoretical group established at CERN which not only contributes to pure theory, but also takes an important part in the initial planning of experiments and in the interpretation of the experimental results. Among the problems studied by this group are those of parity conservation in strong and weak

interactions, particularly how it is possible to reconcile the violation of parity in strong interactions involving K mesons with the quasi conservation in nuclear interactions involving π mesons. Another problem being studied relates to the magnetic moment of the μ meson.

Apart from the two accelerators, their experimental programmes and theoretical work CERN is carrying out a basic research programme on new methods of accelerating particles the results of which can be used as a basis for future machines and to improve the existing machines. The Accelerator Research Group is at present studying intersecting beam machines that will yield energies in the centre of mass system higher than is practicable with existing machines using targets in which the bombarded nuclei are at rest, very high current machines using

beam stacking techniques, and plasma accelerators that can either be used as high-current machines or to provide by means of very high circulating electron beam currents, intense magnetron guide fields for heavier particles. Several experimental plasma betatrons have been built and an electron beam stacking model is now being planned which will provide a flexible experimental tool for investigating stability problems in high-current beams and in intersecting beam machines.

The total staff of CERN is nearly a thousand, about two hundred of which are physicists and engineers and in addition to staff appointments CERN offers fellowships to enable physicists from all over the world to participate in the work of the Laboratory. About sixty physicists are currently using these fellowships at CERN.

THE BRITISH COMPUTER SOCIETY FIRST CONFERENCE

IN view of the widespread interest in computers nowadays, particularly in the fields of science and engineering it is perhaps a little surprising that the British Computer Society should have held only its first conference last June. However, as the president, Dr M. V. Wilkes, reminded us, it was not the first time that a conference of those interested in computing had been held at Cambridge, the last one being almost exactly 10 years previously, when the subject was in its infancy. The rapid growth of interest in the subject is instanced by the capacity attendance of 330 at the conference and by the increasing membership of the British Computer Society, which is now more than 2 000, drawn from a wide variety of backgrounds.

These differing backgrounds accounted for the considerable range of topics discussed, running from the structure of myoglobin through automatic programming and logical design to the problems of auditing accounts kept by computers. The work currently being done by Perutz, Kendrew and others on protein structures would scarcely have been possible without the use of fast computing machinery and Dr J. C. Kendrew, in his interesting address, brought out clearly the importance of the existence of, and of further developments in these powerful tools. He described the work recently done on the structure of myoglobin, mainly using X-ray diffraction techniques applied to structures into which a heavy atom had been artificially introduced by chemical methods. Photographs of diffraction patterns from single crystals have enabled the broad outlines of the structure to be determined and a model of the polypeptide chain to be built up. It is hoped next to determine the detailed atomic positions within the structure by more sophisticated techniques. These techniques will involve processing very large amounts of data, some thousands of reflections being obtained from the X-ray apparatus.

All these must be included in the refinement calculations which result in the tabulation of electron density values over a hundred or more two-dimensional Fourier sections through the crystal, each section involving evaluations at many hundreds of points. The processing will thus require not only very rapid calculation facilities but also adequate support equipment for input of data and output of results.

Furthermore, myoglobin is one of the simpler protein structures, so that future advances in this field will undoubtedly require the fastest and largest equipment available.

Developments in very fast computers were described in a crowded session by Drs T. Kilburn (Manchester), M. Lehmann (Israel), and N. C. Metropolis (Chicago). Dr Kilburn described the *Muse* project which is now in an advanced stage of planning to build a computer at the University of Manchester with speeds of operation in the millimicrosecond range. This machine like most other modern developments will rely primarily on transistors and magnetic cores as fundamental elements for storage, arithmetic operation, and control. The arithmetic unit a prototype of which has been built and is now being tested, is capable of carrying out multiplications and additions on numbers in floating point representation in less than 2 microseconds and administrative instructions will be carried out in less than 1/5 μ sec. The main storage is to be on magnetic cores with an access time of 2 μ sec. However, overlapping of operations in some parts of the machine will reduce the effective access to 1/2 μ sec. In addition, a special store is also provided from which words can be read in about 1/7 μ sec. but into which writing is restricted. A wide use of time sharing is to be made in controlling input, output and bulk storage mechanisms such as magnetic tapes. Up to 16 magnetic tapes and in addition, up to 16 slower mechanisms can be feeding into or be fed by the computer simultaneously, the computer control scanning these units in sequence at a pace sufficiently rapid to allow inspection of each one at a suitable interval.

It is hoped that this very powerful machine will be working in just over two years time, and that copies will later be available commercially.

Dr Lehmann described a fast but comparatively small computer which is being designed for the Israeli Ministry of Defence. This will include an 8 000 word drum and a core store of 128 words and is expected to be very cheap to produce although comparable in speed with many of the large machines of to-day which cost hundreds of thousands of pounds.

Dr Metropolis described the computer being developed at the University of Chicago under his direction. This machine is to be in the same speed range as the

Muse, but is not planned, at present, on quite such a large scale. Nevertheless a core store of more than 8,000 words with an access time of 2 μ sec is to be provided, and there is provision for at least four magnetic tape mechanisms to be attached to the machine. Two very interesting features are the proposed structure of the arithmetic unit and a new method of number representation: it is intended to incorporate the arithmetic unit is to be built on the same principle as that of the *Maniac* at Los Alamos, using asynchronous circuitry, but will include many additional cross-connections between registers to facilitate rapid arithmetical working. A number representation, called 'significant digit' representation, will be used. This is a form of floating point representation which avoids the appearance of many meaningless digits at the end of approximate numbers, while retaining a few guarding digits against rounding errors.

An important application of fast machines is to problems in supersonic flow-past aerofoils and other surfaces. An interesting contribution to this subject was made by Mr D. S. Butler of the Armaments Research and Development Establishment, who described some recent work he has carried out on this problem.

In order to calculate the lines of flow around and pressures on a solid figure in a supersonic airstream it is necessary to solve a hyperbolic partial differential equation in three variables. He discussed various methods of doing this and made particular reference to the method of characteristics, a powerful technique for solving equations of this type. He went on to describe a particular example of stationary flow around a body shaped like a delta-wing aircraft and showed how the calculations had been carried out in this case using the computer at Fort Halstead, a Ferranti Mk 1*.

Other topics at the conference which excited considerable interest concerned the control of production in factories and the application of operational research techniques to this and allied problems. Mr F. Bryon of Imperial Chemical Industries described an application of punched card machinery to factory control, and Mr J. Harling of Urwick, Orr and Partners dealt very interestingly with the use of computers for operations research. An application of one of the latter techniques within the Shell group of companies

formed the subject of a later address by Mr C. S. Galor. There were also sessions on keeping accounts by computer, on auditing the accounts so kept, on the training and selection of programmers, on automatic programming, and on working experience with magnetic tape mechanisms. On the mathematical side, Dr A. S. Householder of the Oak Ridge National Laboratory, Tennessee, directed attention to some of the pitfalls in the techniques commonly used on computers. In particular, he considered the stability of two methods of inverting a matrix, and concluded that the method of rotation is not more stable than the method of elimination, although an argument can be adduced to the effect that it is. After this paper, as after all the formal papers presented, there was a lively discussion, in which many of the delegates took part.

A wide ranging review of the state of the computing art was given by two speakers, Mr J. A. Goldsmith of Robson, Morrow and Co., and Dr A. S. Douglas of the University of Leeds. Mr Goldsmith noted that delivery of 76 installations of electronic computers had so far been made in the United Kingdom and that 33 were on order, although recently the tempo of orders had slackened. Much of the work in the commercial field had so far been unambitious and the results somewhat disappointing. He felt that it would be 5-10 years before computers played a full part in helping management to control their organizations. Dr Douglas reviewed the work of computers in British universities. Much work has been done in training in their use at the postgraduate level, and he felt that this could well be extended to the undergraduate level. He discussed the problem confronting universities in the installation and use of large scale machinery, and suggested that it would be desirable for three or more of the large fast computers such as *Muse* to be installed in universities, where they would act (on a service basis) as focuses for local computer users. He gave details of serviceability and use of typical present-day university installations, and concluded that a high standard of efficiency can be attained.

All the sessions were very well attended throughout. It is intended in the future to hold annual conferences of the Society at various centres in the United Kingdom, the next conference being planned for June or July 1960.

A. S. DOUGLAS

THE INTERNATIONAL INSTITUTE OF REFRIGERATION

THE first International Congress of Refrigeration was held in Paris in October 1908. Shortly after this, in January 1909, the International Association of Refrigeration was established, following the suggestion of Kamerlingh Onnes, the name being changed to the International Institute of Refrigeration just after the First World War. The organization has therefore just celebrated its jubilee.

The general objective of the Institute is the development of the science and techniques of refrigeration in the international field. It promotes scientific research, as well as the teaching and popularization of refrigeration and its application in all fields, particularly in food preservation, health and industrial processes. The International Institute of Refrigeration headquarters are in Paris.

The main tasks of the Institute are determined by the general conference, at present presided over by Dr Ezer Griffiths. This meets every four years, at the same time as an International Congress of Refrigeration, also organized by the Institute. Executive power is vested in an executive committee. A technical board, of which Dr J. C. Fidler is the current president, co-ordinates the scientific and technical activity of nine commissions, which between them cover all aspects of refrigeration matters from fundamental research to applications in agriculture, transport, etc.

The tenth International Congress of Refrigeration was held in Copenhagen during August 19-26 and was attended by about 1,500 delegates from all over the world. About 300 scientific and technical

papers were discussed at plenary sessions and at meetings of all the commissions held during the period of the Conference

The Institute publishes six times a year a Bulletin which appears in both English and French, the two official languages of the Institute. The Bulletin contains abstracts of scientific and technical articles and information about current research in refrigeration and on other refrigeration activities from all over the world. The Institute also publishes the works of its various commissions.

Full membership of the Institute is restricted to the governments of member countries, which at present number 35, including the United Kingdom, the United States and the USSR. The United Kingdom interests in the Institute are co-ordinated by the Department of Scientific and Industrial Research, with the advice of a Standing Committee

representing research, institutional and industrial interests in Great Britain.

In 1952, the Institute introduced associate membership available to qualified firms, institutions or individuals active in the science or in the industry of refrigeration. The annual subscription is about £13 for firms and institutions and £3 10s for individuals. Associate members receive the *Bulletin* and the proceedings of the nine international commissions of the Institute, together with the texts of reports presented. Associate members may participate in the work and the meetings of the commissions in which they are interested and can also use the services of the large library of the Institute. Applications for associate membership may be made to the Director of the International Institute of Refrigeration, 177 boulevard Malesherbes, Paris (17^e).

STERIC ASPECTS OF THE CHEMISTRY AND BIOCHEMISTRY OF NATURAL PRODUCTS

THE interest taken in stereochemical problems by chemists and biochemists alike has been greatly increased in recent years, and the Biochemical Society recognized this fact by arranging a symposium on "Steric Aspects of the Chemistry and Biochemistry of Natural Products" which was held in the Senate House of the University of London on June 30. The chairman of the morning session, Prof. A. Neuburger (London), discussed some of the main trends of recent work in this field and emphasized the importance of stereochemistry in modern enzymology.

Dr W. Klyne (London) then discussed in a comprehensive manner the types of evidence used for establishing relative or absolute configurations of asymmetric compounds. The term 'absolute configuration' can now be used with confidence, as Bijvoet and his colleagues working in Utrecht have demonstrated by means of a special X-ray technique that the Fischer convention for glyceraldehyde happens to be correct. Dr Klyne pointed out that the most satisfactory method of correlating two asymmetric compounds is by a chemical reaction which does not involve the asymmetric centre. The second type of approach is concerned with chemical reactions in which one or more of the linkages of the asymmetric atoms are broken. The stereochemical correlation in this situation must be based on kinetic and other evidence and must involve certain assumptions about the mechanisms of the substitution concerned.

Dr Klyne then went on to discuss the deductions which can be made from studies of asymmetric synthesis methods used successfully by Prelog and by Cram. Another type of approach which was developed mainly by Fredg in Sweden, and which is probably not sufficiently widely known, is based on the study of melting points of mixtures of a compound of known configuration and a structurally similar compound of unknown configuration. If the two compounds have opposite configurations they may form in the solid phase a quasi-racemic compound and this can be deduced from the melting point curve.

Reference was also made to the information obtained from the applications of X-ray analysis

especially to compounds with more than one asymmetric centre. Finally methods were discussed which depend on a numerical comparison of the values of optical rotations of structurally related compounds. These calculations and deductions have in the past been largely based on measurements at a single wave length and have indeed yielded much valuable information. In recent years this tool has been made more powerful by extending the measurements to the whole visible and a large part of the ultra-violet range of the spectrum. In this development (rotatory dispersion) Djerrn of Detroit has taken the leading part.

Stereo aspects of the biosynthesis of terpenes and steroids were considered by Dr D. Arigoni (Zurich) who discussed first the formation of an isopentenyl derivative from acetate. The early stages of the synthesis consist of a condensation of acetyl-CoA with acetyl-CoA to give the CoA derivative of β -hydroxy β -methylglutaryl acid. The latter is then reduced, probably through the aldehyde acid, to β -3-dihydroxy β -methylvaleric acid or mevalonic acid. The absolute configuration of this compound has been unambiguously related recently by Eberle and Arigoni to that of quinic acid, which in turn had been established by Dangl and Fischer in 1950 by relating it to glyceraldehyde. Dr Arigoni then referred to the stereochemical problems involved in the conversion of isovaleryl β -methylglutamic acid, which occurs through the CoA esters of β -methylcrotonic acid and β -methylglutamic acid. The hydration of the double bond and the carboxylation of methylcrotonic acid must be stereospecific and this is also likely to apply to the reduction of mevalonic acid to mevalonic acid. The next steps in the reaction sequence are the simultaneous decarboxylation and elimination of the tertiary hydroxyl group from the pyrophosphate of mevalonic acid to give isopentenyl pyrophosphate and the isomerization of the latter to give dimethylallyl pyrophosphate. It can be postulated that the isomerization is stereospecific and Dr Arigoni thought it probable that only one of the two hydrogen atoms of isopentenyl pyrophosphate is involved in the isomerization.

The allyl compound is assumed to react with the isopentenyl pyrophosphate, resulting in the formation of a new C—C bond. This reaction must again have stereospecificity, since the new double bond produced usually has a *trans* configuration, but Dr Arigoni stressed the fact that the detailed mechanism of the formation of this condensation is not yet securely established and he suggested that experiments involving labelling with deuterium and determining the axial or equatorial position of the deuterium in a suitable cyclization product are likely to give further information.

Dr Arigoni pointed out that steric factors had to be taken into account in any attempts which were made to explain the actual cyclization and the rearrangements which either follow the cyclization proper or are coupled with it. Otherwise, it would be difficult to explain the formation of diastereoisomers from one single aliphatic precursor, squalene. If a carbonium ion is involved in cyclization reactions, it can only have a structure which preserves the original configuration, a 'bridged ion' fulfils this requirement and addition of this relatively stable species to a base or nucleophilic substance ('anti-planar addition') will produce only one isomer. The postulate of antiplanar addition imposes restrictions on the type of folding and it appears that only the chair-type and boat-type of folding explain, for example, the formation of both lanosterol and tirucalol from *all-trans* squalene. Experimental evidence for the theory is provided by the work of Bloch and by that of Cornforth and Popják. Further interesting examples from the work of Dr Arigoni himself and from that of Prof Birch were given, showing the application of stereochemical rules to the biogenesis of terpenes, but a note of caution was sounded against the assumption that the configuration of the A/B ring junction is always the same.

Steric aspects of drug action were discussed by Dr R. B. Barlow (Edinburgh), who began his talk by emphasizing the distinction first made by Stephenson between affinity or adsorbability of a drug to a receptor site, and efficacy, that is, the ability of the adsorbed drug to start a sequence of reactions which can be observed in a pharmacological experiment. While it is possible to make definite statements about the steric arrangement of drugs, ideas on the stereochemistry of receptors are generally based on somewhat uncertain deductions made from structures of active compounds and those of their antagonists.

Dr Barlow illustrated his talk with examples from the field of drugs resembling acetylcholine either in its muscarine-like or nicotine-like function or of compounds antagonizing such action. For nicotine-like activity the molecule should contain a cationic head such as a dimethylamino or trimethylamino group and a partial positive charge at a distance similar to that which separates the ether oxygen of acetylcholine from the charged nitrogen atom. In nicotine itself the two optical isomers have identical pharmacological activities. The constitution and stereochemistry of muscarine have recently been worked out and it is found that it has three centres of asymmetry. Dr Barlow then discussed the activities of the various stereo-isomers of muscarine and of various synthetic substrates resembling this substance pharmacologically, such as acetyl- β -methylcholine. In this case the (+)-isomer is reported to be about 200 times as active as the (–)-isomer. Dr Barlow then mentioned the importance of steric factors in flexible molecules and he pointed out that

in these cases it is more difficult to arrive at quantitative conclusions. In particular, the work of Schueler was discussed in detail and some recent criticisms of his calculations were mentioned. Dr Barlow then dealt in some detail with diquaternary bases, such as various esters of aliphatic dicarboxylic esters containing two quaternary basic groups, such as suxamethonium. The many examples which were considered illustrated the difficulties which still exist if one attempts to correlate the stereochemistry of the compounds under consideration with their biological activity.

The last paper of the morning session was given by Dr G. A. J. Pitt (Liverpool) on behalf of Prof R. A. Morton and himself, and dealt with *cis-trans* isomers of retinene in visual processes. Dr Pitt briefly discussed the chemistry of retinene (vitamin A aldehyde) and that of vitamin A, and in particular referred to the early work of Pauling which predicted the existence of the following four isomers: all-*trans*, 9-*monocis*, 13-*monocis*; and 9,13-*dicis*. These four isomers of retinene and vitamin A have been synthesized, but it has been possible to prepare two other retinenes and vitamins A containing a *cis* linkage in the 'hundred' 11-position. No 7-*cis* vitamin A has yet been prepared and it seems almost certain that 7-*cis* isomers cannot exist, as in such a molecule there would be considerable steric interference. Dr Pitt then referred briefly to the occurrence of *cis*-isomers in Nature, and mentioned that the thermodynamically most stable isomer and the one found most commonly in Nature is the all-*trans* isomer. He then reviewed the isomerization of the various retinene isomers and their absorption spectra. The importance of the *cis-trans* isomerization was appreciated when Hubbard and Wald found that the retinene which united with opsin was the 11-*cis* form. The 9-*cis* form also reacted with opsin but the resulting complex has not been found in Nature. The main effect of the introduction of a *cis*-bond at the 11-position is that it produces a bend of the side chain whereas in the all-*trans* isomer the side chain is straight. When rhodopsin is illuminated it breaks down to the protein opsin and a retinene, but the latter was found, rather surprisingly, to be the all-*trans* isomer. This all-*trans* retinene liberated by the bleaching of rhodopsin does not give rhodopsin again when mixed with the opsin *in vitro*, and strong evidence has been obtained by Hubbard that the utilization of the *trans* isomer in a more complex system is caused by the presence of an enzyme called retinene isomerase, which changes the all-*trans* retinene to the 11-*cis* isomer. Dr Pitt discussed this enzymic isomerization in more detail and then went on to report on recent work which has been done on invertebrate rhodopsins, dealing in particular with indicator yellow. He also gave an account of the effect of light on various rhodopsins under a variety of conditions, but it would be impossible to summarize adequately the rather complicated relationships which have been established, mainly due to the work of Hubbard and Wald.

The chair was taken for the afternoon session by Prof S. Peat (Bangor), all three papers were devoted to various aspects of stereospecificity in enzyme action. Dr E. C. Webb (Cambridge), who dealt with hydrolytic enzymes, treated some general matters relevant to all enzymes. He emphasized that enzymic catalysis is at least a two-stage process, and that steric factors may be important both in the formation and in the breakdown of the intermediate

enzyme-substrate complex. To be of real value any comparison of substrates should involve measurement of both the Michaelis constant (K_m) and the reaction velocity, as measures of the two stages.

Examples considered included α -esterases and lipases, cholinesterases, glycosidases, lactonases, peptidases, arginase and fumarase. For the cholinesterases knowledge has accumulated which permits the representation of the catalysis in terms of anionic and esteratic sites on the enzyme surface. The high specificity of glycosidases is well known, and this is paralleled in the recently studied group of lactonases. Proteolytic enzymes may be used, thanks to their high stereospecificity as tools for the resolution of synthetic amino-acids. Work on the behaviour of synthetic substrates as competitive inhibitors of α -chymotrypsin emphasizes the importance of distinguishing the two stages of enzyme action.

In conclusion, the importance of Ogston's concept (1948) of three-point attachment between enzyme and substrate was emphasized. This idea explains very simply the formation from a symmetrical substrate (C₂X₂YZ) of an asymmetrical product (C₂X⁺YZ). Ogston has recently discussed this concept further (1958).

Dr H. Gutfreund (Sharnfield) in discussion considered further the specificity of α -chymotrypsin in the reactions of which three stages can be distinguished ($E + AB \rightleftharpoons E \cdot AB \rightleftharpoons EA + B \rightleftharpoons E + A + B$).

Prof E. C. Slater (Amsterdam) dealt with oxidation-reduction enzymes. He began by considering dehydrogenases which act on hydroxy acids and more complex systems which can (indirectly) transform one enantiomer into the other (commonly but wrongly called racemases). After a brief discussion of amino acid oxidases the greater part of the paper was devoted to stereospecificity of hydrogen transfer in the reactions of pyridine nucleotide dehydrogenases. These compounds are dinucleotides, one unit of which is the nicotinamide group which can undergo reversible oxidation and reduction at N and C-4. The elegant work of Vennesland's school in Chicago using substrates and enzymes labelled with deuterium has shown that these dehydrogenases fall into two classes: these are distinguished by the fact that they add hydrogen at C-4 of the diphosphopyridine nucleotide molecule on opposite sides. Other related work dealt with reactions involving cytochrome *c*, flavin and orotic acid.

An important extension of Vennesland's work was the preparation of stereospecifically labelled and

optically active CH₃CHDOH. Alternative mechanisms of action for a typical dehydrogenase have been suggested by Dixon and Wöhls in their classic textbook on "Enzymes", and by Van Eyk, Kaplan *et al*. Finally, succinic dehydrogenase which involves another type of stereospecificity was introduced.

Dr H. R. Levy (Chicago) emphasized in discussion that the stereospecificity in the reactions of pyridine nucleotides is another example of the ability of enzymes to distinguish between two identical groups and gave further examples. Dr W. Klyne directed attention to the important work of Prelog on microbiological oxidations and reductions of simple deoalones and related compounds. The pictorial treatment of these reactions may constitute a valuable extension of Ogston's concept of three-point attachment.

Dr G. R. Barker (Manchester) dealt with enzymes of nucleotide metabolism. He began by outlining current views on the biosynthesis of D-ribose and 2-deoxy-D-ribose: the important routes leading to ribose involve the 5-phosphates of D-xylulose and D-ribulose. The formation and fission of glycosidic bonds in nucleosides was next considered: these reactions are generally phosphorolytic and not hydrolytic. The stereochemistry of analogous chemical syntheses of nucleosides has been studied with respect to relative configurations at C-1 and C-2 and it is necessary to consider how far the stereospecificity of the enzymic reaction is attributable to the enzyme, and how far it is inherent in the nature of the reaction catalysed. The answer at present is that both factors are involved.

The formation and fission of internucleotide links in polynucleotides were then discussed. Pancreatic ribonuclease degrades ribopolynucleotides via nucleoside 2,3' (cyclic) phosphates to 3 phosphates, and the steric factors involved in this and the reverse reaction were considered. Finally the polynucleotide phosphorylase was considered: many reactions require a polynucleotide 'primer' the composition of which determines that of the polymer formed: this is a direct demonstration that the primer acts as a template.

All three papers emphasized in different ways the essentially complementary nature of enzyme and substrate and the two (or more) stage character of the enzyme-substrate reaction.

A. NEUBERG
W. KLYNE

OIL IN NAVIGABLE WATERS

IT is now 60 years since a group of representatives of the interests in Great Britain which are most affected by oil pollution formed themselves into the Coordinating Advisory Committee on Oil Pollution of the Sea under the chairmanship of Mr James Callaghan, M.P. In 1953 this Committee organized an international conference in London which called for a meeting of governments of all maritime countries to take action to prevent the growing pollution of the oceans of the world. This request met with considerable success, for an inter-governmental conference was held in 1954, at which an international convention was drawn up. This Convention came into force in July 1958, and has been ratified by the

United Kingdom, Belgium, Canada, Denmark, Finland, France, the Federal Republic of Germany, the Irish Republic, Mexico, the Netherlands, Norway and Sweden.

The Convention does not prohibit the discharge of waste oil entirely, but merely within certain zones and the countries which observe the Convention represent only about one half of the world's tanker shipping, notable omissions being the United States, U.S.S.R., Poland, Italy, Panama and Liberia. The Coordinating Advisory Committee on Oil Pollution of the Sea therefore decided to organize an international conference to discuss, among other aspects, how far the 1954 Convention had been effective in

diminishing the contamination of coasts and beaches, and the destruction of bird life. This Conference was held in Copenhagen during July 3-4. It was presided over by Mr James Callaghan, M P, with Dr Boje Benzon (chairman, Danish National Section, International Council for Bird Preservation) and Hr Ekspeditionssekretær Sven Lunddahl (Secretary, Danish Council for the Prevention of Oil Pollution of the Sea) as vice chairmen.

The meeting was very well attended, and included a wide range of interests, for among those present were representatives of government departments of transport and commerce, ship owners, port authorities, ship repairers, seamen's unions, sea fisheries associations, local authorities, pleasure resorts, tourist organizations, hotel and restaurant associations, and conservation, ornithological, and humanitarian organizations, of many countries, together with the diplomatic representatives of nineteen nations. In addition, seven international bodies, the Inter-governmental Maritime Consultative Organization, the Food and Agriculture Organization, the Council of Europe, the International Union of Biological Sciences, the International Council for Bird Preservation, the International Union for the Conservation of Nature and Natural Resources and the World Federation for the Protection of Animals were represented.

The Conference was opened by Mr Helge Juul, deputizing for the Danish Minister of Commerce, and the first section of the proceedings was devoted to a review of the situation arising from the 1954 intergovernmental Conference. In a paper on the working of the Oil in Navigable Waters Act, 1955, Mr D C Haselgrove, under-secretary, U K Ministry of Transport and Civil Aviation, pointed out that the provisions of this act go beyond the basic requirements of the 1954 Convention, and quoted as an example that the sea zones in which British ships registered in the United Kingdom must not discharge oil extend beyond the zones laid down in the Convention. He paid a warm tribute to the ready co-operation of British ship owners, dock and harbour authorities, and the oil industry. Capt K C Angus, Marine Regulations Branch, Department of Transport, Canada, in a report on the preventive measures taken by the Canadian Government, stated that the coasts of Newfoundland suffered most from oil pollution, and after them the eastern maritime provinces and the St Lawrence river, but the whole Atlantic coast was subject to heavy and habitual contamination. He stressed the value of weight of public opinion, and directed attention to the fact that in many countries only a very small percentage of the population was aware of the existence of oil pollution and its serious consequences. Mr Lester A Giles, jun, American Humane Education Society, in association with Mr John W Mann, State Department, Washington, D C, announced that an inter-departmental Committee had unanimously adopted a draft report for submission to the Secretary of State, recommending that the United States accept the 1954 Convention with reservations of a technical nature, a statement that was received with acclamation.

In a paper dealing with the working of the Convention from the point of view of British tanker and oil companies, it was recalled that since the Second World War the use of oil, and consequently the number of tankers, had increased enormously, and that ownership was now spread over a great variety of flags, some quite new to shipping, and it was urged

that universal ratification be strenuously pursued. In the discussion regarding methods of cleaning cargo tanks which followed, Mr A Logan (Shell Tankers, Ltd) uttered a word of warning regarding the indiscriminate use of chemicals, and pointed out that the use of large amounts of detergent might lead to a situation even more destructive and less manageable than that arising from the original oil sludge.

Disposal of oil waste and facilities in ports were dealt with by speakers from Denmark, the Netherlands and the United Kingdom. Mr S Glazenburg (Netherlands) forecast that the consumption of 134 million tons of oil by European countries in 1957 would rise to a consumption of 190 million tons in 1963 and 340 million tons in 1975, with a corresponding expected rise in refinery capacity, particularly in Western Europe. Comparatively more oil products would be exported from Western Europe, and in proportion to this increase in oil movements the problem of the disposal of oil residues would become more acute.

Speaking for 43 coastal municipalities in the Netherlands the Burgomaster of Bergen described the system of weekly reports on the condition of the beaches in Holland which are summarized annually in order to give a general survey of the amount of oil pollution during the year. He urged that municipalities in other countries should organize similar surveys and that the information should be co-ordinated on an international scale. From the point of view of tourism it was pointed out by Mr Eric D Croft, director-secretary of the British Hotels and Restaurants' Association, that dollar earnings from tourism exceed the total value of exports of cars and Scotch whisky together from the United Kingdom to the United States, and he stressed the serious loss to the tourist trade presented by pollution of beaches.

Reports, on the destruction of birds by waste oil, received from Canada, the German Federal Republic, the Netherlands, Newfoundland, Poland and the United Kingdom, showed that in the Netherlands it was estimated that a minimum of 20,000 and a maximum of perhaps 50,000 birds are destroyed annually, and that 50 different species have been affected, in Newfoundland all species of sea-birds around the coasts are victims, further evidencing the great toll of sea birds which has been continuing for more than forty years.

Major Bertil Funck (Sweden) directed attention to the recurring pollution of the Baltic, especially east and south-east of the island of Gotland. Under the Convention there is an area in the Baltic, south-east of Gotland, 50 nautical miles from the island and the mainland, where discharge of oil is permitted. He emphasized that the Baltic is too small in area for oil discharge, and proposed that a resolution be passed seeking to obtain the inclusion of the Baltic as a prohibited zone for oil discharge. He also recommended that the whole North Sea should similarly be declared a prohibited zone.

The representative of the secretary-general of the Inter-governmental Maritime Consultative Organization, Kommerserådet G M E Bøös, stated that the bureau functions for the International Convention for the Prevention of Pollution of the Sea by Oil had been discharged by the United Kingdom up to June 15, 1959, when the Organization took over the duties and obligations conferred upon it under the terms of the Convention. Among other responsibilities the Organization would have the duty of convening a further conference to review both the

working of the Convention and the possibility of bringing about complete cessation of discharge of persistent oils into the sea. In resolving to take over its functions, however, the Organization pointed out to the governments concerned that, owing to other urgent tasks, it would not be possible to convene a further conference before 1961. Mr B55e ended on a personal note, stating that though the convening of a further conference on oil pollution was not an obligation made under the Convention, he would characterize it as a moral undertaking inspired by the first resolution of the 1954 Conference. The aim of that resolution was certainly the same as the object of the present conference, namely, the complete avoidance of discharge of persistent oils into the sea, which, so far as was known, was the only entirely effective method of preventing oil pollution.

Two resolutions were adopted by the conference. The first urged that the governments of countries which had not yet ratified the Convention of 1954 should do so, that further efforts should be made to

impress upon governments and upon ship owners and ship's officers and crews the serious consequences arising from the discharge of oily wastes into the sea, that all necessary facilities be provided for the disposal of oily wastes in main ports and harbours, that technical research into means of avoiding discharges of oily wastes into the sea be intensified, and the results made widely known through the Inter-governmental Maritime Consultative Organization, that with a view to achieving the aim of total avoidance of the discharge of persistent oils into the sea, the governments and the Organization should make preparations for holding a further inter-governmental conference as soon as possible.

The second resolution, though reiterating the only effective solution of the problem, proposed in the meantime an extension of the prohibited zones for oil discharges in such areas as the Gulf of St Lawrence, the Grand Banks of Newfoundland, and the eastern seaboard of North America and also in the Baltic and North Seas.

P. BARCLAY-SMITH

RADIOACTIVATION ANALYSIS

NEW methods of chemical analysis using techniques derived from nuclear physics were discussed at a Symposium on Radioactivation Analysis held in Vienna during June 1-3. Sponsored by the International Atomic Energy Agency and the International Council of Scientific Unions, the meeting brought together research workers from twenty-one countries for the first international conference on a subject of rapidly growing importance in many branches of science, medicine and industry.

An introductory survey by G. B. Cook (Atomic Energy Research Establishment, Harwell) was followed by reviews of the uses of activation analysis in geochemistry (W. Hart, Max Planck Institute of Chemistry, Mainz), biochemistry and medicine (J. M. A. Lenihan, Western Regional Hospital Board, Glasgow) and metallurgy (J. Hoste, University of Ghent). P. Leveque (Centre d'Etudes Nucleaires Saclay) spoke of applications in industry and G. W. Leddicotte (Oak Ridge National Laboratory) described recent developments in the United States. Several shorter contributions were also given.

Most analytical methods depend on the behaviour of electrons. Activation analysis depends on the properties of the nucleus. In particular the radioactivity induced by bombardment with neutrons or other particles. Many elements have isotopes which decay slowly enough for the assay to be done a day or two after irradiation, but work on short-lived activities can only be done close to a neutron source. A reactor is the instrument of choice for activation analysis, but more modest facilities are often serviceable. Discharge tubes using the deuterium-tritium reaction give neutron fluxes as high as 10^{12} n/cm²/sec at moderate cost. Useful work has been done with the lower fluxes provided by radium-beryllium or antimony-beryllium sources; a recent innovation is the americium-beryllium source, which has the merit of freedom from residual γ ray emission.

Since nearly seventy elements become appreciably radioactive after a few hours exposure inside a nuclear reactor of moderate thermal neutron flux (10^{12} n/cm²/sec) the irradiated sample generally contains

several different activities. Fortunately many of the common matrix elements (aluminium, silicon, iron, carbon, nitrogen, oxygen) have relatively small cross-sections for thermal neutron capture. Differences in half-life and decay energy between trace element and matrix or between different trace elements in the sample are also advantageous.

The isolation of individual activities for radioactive assay may often be achieved by γ ray spectroscopy, but a preliminary chemical separation is generally advisable, even when dealing with short-lived nuclides. When once the experimental material has been irradiated, along with a known amount of the element under investigation (to serve as a standard) the isolation may be simplified by the addition of a stable carrier in any desired amount. Another useful advantage of the activation method is that contamination of reagents, often a source of trouble in the micro-determination of trace elements, need not be considered at all.

The sensitivity of thermal neutron activation analysis for trace estimation is remarkable. Many elements can be estimated at levels of 10^{-8} to 10^{-11} gm using a neutron flux of 10^{12} n/cm²/sec acting on a 1 gm sample. The detection of trace elements by this method has been useful in several industrial problems, notably the measurement of deliberate or fortuitous contamination in semiconductor materials. Applications in the oil industry are so numerous (and so important financially) that many companies have acquired neutron sources of their own. A typical problem, in which conventional methods of analysis are not sufficiently sensitive, is the control of vanadium which acts as a catalyst poison in cracking operations and as a corrosive agent in fuel oils.

The same element is important in a different connection as a constituent of high alloy steels. Here the activation method of analysis is valuable for its speed and accuracy. A 10 second irradiation at a flux of 10^{11} n/cm²/sec, is sufficient for analytical determinations using the isotope vanadium-52 (half-life 3.8 minutes). In prospecting for vanadium a useful technique is to lower into a borehole a neutron

generator After a few minutes the generator is replaced by a scintillation counter to estimate the vanadium-52 activity

In geochemistry, where the study of natural radioactivity has been of prime importance for more than half a century, the new possibilities offered by activation analysis have been welcomed A powerful technique for age determination in rocks and meteorites depends on measurement of the relative abundance of parent and daughter nuclides in a natural radioactive decay process Useful improvement in sensitivity can be expected where one or both of the nuclides can be subjected to activation analysis Potassium/argon and rubidium/strontium ratios are readily measured in this way Uranium-238 can be estimated down to a limit of 10^{-12} gm by the reaction $^{238}\text{U}(n, \gamma\beta)^{239}\text{Np}$ For uranium-235 the limit of sensitivity so far achieved (at the Argonne National Laboratory) is 5×10^{-11} gm, using the reaction $^{235}\text{U}(n, f)^{140}\text{Ba}$

Activation analysis of biological material has attracted relatively little attention, though the method has many interesting potentialities Several elements, including vanadium, manganese and cobalt, are important to plants or animals but their function in human nutrition is still obscure, through lack of sufficiently sensitive analytical methods The role of vanadium in dental caries and of manganese in bone formation were two of the subjects suggested for study by activation analysis Many problems in dental science and in animal biochemistry are also awaiting exploration by activation methods

Arsenic is an element of continuing interest in clinical science, partly because of its increasing uses and hazards in agriculture and partly because it is the only component of tobacco smoke known to be carcinogenic in man Arsenic levels in normal tissue are too low for accurate estimation in living subjects by conventional methods Activation analysis has been used in several investigations of arsenic poisoning, whether accidental or homicidal An unusual toxicological experiment was the recent study by activation analysis of the remains of Erik XIV, a sixteenth-century Swedish king who died in

mysterious circumstances These tests gave support to the theory that he was poisoned by mercury, said to have been administered in a dish of pea soup

Although thermal neutrons are the most versatile agents for activation analysis, fast neutrons have some distinctive applications The estimation of traces of oxygen has been done satisfactorily by mixing the experimental sample with lithium fluoride and irradiating with fast neutrons to produce the reaction $^7\text{Li}(n, \alpha)^3\text{H}$ followed by $^{16}\text{O}(^3\text{H}, n)^{18}\text{F}$ (half-life 112 min) The limit of sensitivity of this method, as practised at Harwell, is $5 \cdot 10^{-7}$ gm of oxygen Protons have been used for the estimation of boron in silicon, a test of considerable importance to transistor manufacturers Neutron activation yields no suitable isotopes but fast protons induce the reaction $^{11}\text{B}(p, n)^{11}\text{C}$ (half-life 20.4 min) The silicon provides an internal standard by the reaction $^{30}\text{Si}(p, n)^{30}\text{P}$ Concentrations of boron as low as 1 in 10^9 have been measured in this way Proton activation is useful also for the estimation of boron in germanium Deuterons provide the best method for the estimation of magnesium in iron, by the reaction $^{24}\text{Mg}(d, \alpha)^{22}\text{Na}$ An internal standard is given by the reaction $^{56}\text{Fe}(d, \alpha)^{54}\text{Mn}$

Two conclusions emerged from the symposium The first is that any laboratory using conventional methods of chemical or spectrographic analysis would do well to explore the possible advantages of activation methods for some of its work The second is that activation analysis, though superficially a simple technique, requires considerable skill in nuclear physics and in analytical chemistry for the full realization of its possibilities

The success of the meeting was enhanced by the genial hospitality of the sponsors and by the agreeable atmosphere of the magnificent new conference suite of the International Atomic Energy Agency in the Hofburg The proceedings of the symposium will be published shortly in book form A long-awaited manual of experimental procedures is in an advanced state of preparation at Oak Ridge

J M A LENTHAN

THE CAPE TOWN SCIENCE EXHIBITION, 1959

ENCOURAGED by the success of the Science Exhibition held in Cape Town in March 1958, the Cape Council of the South African Association for the Advancement of Science, in collaboration with the Royal Society of South Africa, organized the second Science Exhibition in more spacious surroundings (10,500 sq ft) during the period April 6-11 After introductory addresses by the chairman of the Organizing Committee and vice president of the South African Association for the Advancement of Science, Dr Ronald Singer, and by H M Astronomer at the Cape, Prof R H Stoy, the Exhibition was officially opened on the evening of April 6 before a distinguished audience of scientists, industrialists and educationists by His Excellency the Governor-General, Dr E G Jansen

Dr Jansen stated that the Exhibition must be of particular interest to the layman, "because although one does not always understand all that science has

to teach us, one realizes the importance of science and scientific research especially in the troublous times in which we live, and where science has, to a large extent, changed the life of civilized man and touches our everyday life at every point"

Dr Jansen indicated that it is a rather startling thought that, according to some reports, the Soviet Union is more advanced than any other country, not only in certain fields of scientific research but also in the number of men and women receiving education and training in science and scientific methods "The question arises as to whether sufficient is being done in that direction in our country If we believe that the future of the country is in the hands of the youth of to-day, we should surely see to it that the education of our boys and girls is in the hands of men and women most fitted for the task, and who are devoted to their work It follows that they should

be adequately remunerated and enjoy fair conditions of employment."

The organizing committee produced a handsome brochure of 48 pages, providing not only a guide to the twenty-seven exhibits but also a general description of the scientific methods behind each exhibit. In the introduction, Dr Singer stated that 'the Exhibition is an attempt to present to the lay public interesting aspects of modern scientific research and the application of science to industry and commerce. Some, if not most, of the important research projects and applications of research to industry in South Africa have been carefully assembled for the public of Cape Town and environs. A wider understanding of scientific endeavour and its vast potential will inspire lay individuals and give them some insight into the multitude of problems besetting almost every aspect of our daily lives—which we generally take for granted. Ignorance of these matters must only provide a false sense of security—an acceptance without contemplation' which can only end in a degeneration of our standards of civilization.

The exhibits (fixed at twenty-seven because of the limitations of space) were of three types—pure science, applied research and modern technical equipment. The South African Council for Scientific and Industrial Research presented a display depicting the nature and scope of its nine national research laboratories (roughly as outlined in *Nature* 183 853 1959), a demonstration on the electro-dialysis process for desalting water and a poster-demonstration of the theme 'The Planet Earth' emphasizing the international character of the recent International Geophysical Year. The methods of geophysical research were dramatically illustrated. The United Kingdom Information Office presented an impressive display outlining Britain's role in the development of power from the atom. Models of Calder Hall and Zets provided the basis of the exhibit.

The Division of Fisheries presented its integrated programme of pelagic fish research indicating the types of problem investigated and the directions in which the research has progressed. It clearly outlined the essential part it played in the £15 million fishing industry. In addition the Fishing Industry Research Institute at the University of Cape Town provided an exhibit covering three aspects of its research—electrical thermometers on board ships, protein analysis and the bacteriology of fish.

The South African Broadcasting Corporation provided a unique studio to display the great deal of research and development work that lies behind a modern transmission system. The methods used to minimize distortion and noise were demonstrated. The South African Railways and Harbours exhibit demonstrated centralized traffic control, the draught arrangement and problems in modern locomotives and the ultrasonic testing of materials.

The tellurometer microwave system of precise measurement of distance (an electronic device which measures distance between a master unit at one end and a remote unit at the other by phase comparison of a number of pattern frequencies) was invented in South Africa and is now used in many parts of the world. This was one of the exhibits by a number of industrial and commercial firms, including modern methods of sock making, the scientific aspects of a modern motor-car, echo-sounders, industrial closed-circuit television, automatic alarm equipment on sea-going vessels, modern metal spraying equipment, prevention of corrosion, atomic power in the

oil industry, the bacteriology of canned foods, the standardizing of colours of printing inks, etc.

The South African Trigonometrical Survey exhibited the methods and techniques in modern survey operations. The Division of Entomology indicated the more important aspects of two of its research projects on forest and timber insects. Dr S. H. Skuse exhibited his ingenious and simple equipment used in studying the habits and nature of some of the 400 species of ants in South Africa. The South African Museum's exhibit demonstrated a 14 ft fibre-glass cast of a slab of rock containing the foot-prints of three mammal-like reptiles which lived 200 million years ago in Beaufortland.

The South African Association for the Advancement of Knowledge and Culture displayed methods of promoting science education.

The most dramatic and most popular exhibit was that of the Department of Surgical Research of the University of Cape Town, which had a working heart-lung machine, and films and slide demonstrations on open heart surgery. Approximately twenty people a day were treated for syncope by the St John Ambulance Brigade.

Films of scientific interest were screened throughout the daily 12 hr period when the Exhibition was open in a specially erected cinema inside the hall.

Approximately 17,000 people of all races visited the Exhibition in comparison with 5,000 who attended the 1958 Exhibition. As a result of the sale of the brochure and the renting of exhibition space to commercial firms, more than £1,200 was collected. Most of this money will form the basis of a fund to provide scholarships to suitably qualified young men and women who wish to take up science as a career.

This Exhibition is part of an ambitious programme on which the Cape Council of the South African Association for the Advancement of Science has embarked during the past three years to stimulate an interest in and an understanding of the progress of modern science among non-specialists and laymen. The Council organizes four to five science film shows a month which attract capacity audiences and in addition, fortnightly luncheon film shows are put on at the South African Museum (where there is at present also a planetarium attracting visitors). Through the Council's initiative, refresher courses for science teachers are now regularly provided at the major South African universities and at present the first in a series of autumn lectures (based on the Christmas Lectures in the United Kingdom) is being arranged for senior pupils at schools in and around Cape Town. Regular conversations are held and last year the Council organized the Darwin-Wallace centenary week of exhibitions, lectures and symposia on evolution. A special committee is investigating science teaching and particularly mathematics in schools and making recommendations for improvement to the educational authorities. The formation of a Parliamentary and Scientific Committee is being mooted, and the Cape Council is already planning for the Diamond Jubilee Congress of the Association in 1962, when it hopes to invite distinguished scientists from overseas.

The Cape Council of the South African Association for the Advancement of Science firmly believes that in providing these services to the lay public it will eventually produce noticeable effects on the future leaders of not only science but also politics, religion, ethics and moral philosophy.

RONALD SINGER

Table 1 AFTERSHOCKS OF THE YELLOWSTONE PARK EARTHQUAKE OF AUGUST 18 (ALL DURING AUGUST)

| Initial day and time (G M T) | | | | Epicentre | | Magnitude Richter Scale |
|---------------------------------|------|--------|--------|--------------|---------------|-------------------------------|
| Day | Hour | Minute | Second | Lat (° N) | Long (° W) | M |
| 18 | 07 | 54 | 32 | 45 | 111 | — |
| 18 | 15 | 26 | 06 | 44½ | 111 | 0½ |
| 19 | 04 | 04 | 03 | 45 | 111½ | 0 |
| 19 | 19 | 06 | 29 | 45 | 111½ | — |
| 19 | 19 | 43 | 45 7 | 45 | 110½ | — |
| 19 | 21 | 45 | 57 | 45 | 111½ | — |
| 20 | 10 | 59 | 11 | 45 | 111 | — |
| 20 | 10 | 11 | 27 | 45 | 111 | — |

From the first of these epicentres earthquakes on June 27, 1925, reached intensity 10 on the Rossi-Forel Scale and caused greatest damage at Man-

hattan, Logan, Three Forks and Lombard. From the second location shocks in October and November, 1935, attained maximum intensity 9 on the Rossi-Forel Scale. However, minor shocks of intensity 4-5 (R F Scale) from an epicentre in Yellowstone National Park, Wyoming (44° N, 111° W), occurred at various times from August 24 to December 22, 1930. In 1947 (November 23) at 09h 46m 05s G M T, a shallow focus earthquake from an epicentre 44½° N, 111½° W reached a magnitude 6½ on the Richter Scale. Earthquakes are always liable to recur at or near old epicentres.

Aftershocks of the earthquake of August 1959 so far listed by the United States Coast and Geodetic Survey are given in Table 1 although smaller shocks are said to have occurred at intermediate times.

E. TILLOTSON

A THEORY OF AGEING

THE theory of ageing put forward by Szilard¹ refers explicitly to mammals. It is the purpose of the present communication to point out that this theory cannot explain ageing in *Drosophila*, since it is inconsistent with two experimental observations. This of course does not prove that it cannot explain ageing in mammals, but reasons will be given for doubting that it does so.

Szilard postulates the random occurrence of 'hits', each hit rendering ineffective the genes of a whole chromosome, or perhaps of a large segment of a chromosome. A cell becomes ineffective either when two homologous chromosomes have each suffered a hit, or when one of a pair of homologues has suffered a hit, and the other carries an inherited 'fault'. By a fault is meant a recessive gene which in homozygous condition renders the cell inviable, or incapable of performing a necessary function in the adult organism. Death occurs when some predetermined fraction of the cells initially present is in this way rendered ineffective, Szilard suggests that this fraction is of the order of 2/3 to 11/12.

It is a direct consequence of this theory that, in the author's words, "The main reason why some adults live shorter lives and others live longer is the difference in the number of faults they have inherited". This is the first consequence of the theory which is contradicted by observations on *Drosophila*. In so far as differences in adult longevity are genetically determined, by far the largest differences are those between inbred and outbred individuals.^{2,3} F_1 hybrids between inbred lines live for longer than do the parental lines (sometimes for twice as long). Outbred and genetically variable wild populations have approximately the same expectation of life as do F_1 hybrids. Now inbreeding increases the proportion of loci at which individuals are homozygous. An individual which survives for an appreciable time as an adult cannot, by definition, be homozygous for a fault. Therefore inbred individuals which survive to become adults, and which do not die immediately after emergence, are not homozygous for faults at any loci, and would be expected to be heterozygous for faults at fewer loci than are members of outbred wild populations. If two inbred lines are crossed, the F_1 hybrids would be expected to carry a load of faults intermediate between the loads carried by the parental lines. Thus according to Szilard's

theory, inbred lines should have a higher expectation of life than wild populations, and F_1 hybrids between inbred lines should be intermediate between their parents. Neither of these predictions is in fact true.

Further, since males have only a single X chromosome, any hit on that chromosome in a male would render the cell inviable, whereas in a female not heterozygous for a sex-linked fault both X chromosomes must be hit before a cell becomes inviable. Therefore females should live longer than males. This again is not the case in *D. subobscura*. In some strains females do live longer than males, but in other strains, both inbred and outbred, the reverse is true. This point is particularly telling since in *Drosophila* the sex chromosomes account for about one-fifth of the total chromosome material.

The other group of facts which are inconsistent with the theory concern the rate of ageing at different temperatures. Female *D. subobscura* of a particular strain have an expectation of life of about 56 days at 20° C and of 18 days at 30.5° C. The changes responsible for death at 30.5° C are not repaired or reversed in individuals kept for a time at 20° C. Consequently the changes responsible for death at both temperatures can properly be regarded as ageing processes. If these processes were, at each temperature, those postulated by Szilard, differing only in the rate at which hits occur, it follows that individuals kept for an appreciable time at 30.5° C should have, when returned to 20° C, an expectation of life at that temperature lower than that of individuals of the same chronological age not previously exposed to 30.5° C. In fact, exposure to 30.5° C for periods of the order of half the expectation of life at that temperature does not alter the further expectation of life at 20° C of males, and significantly increases that of females.

Hence, if, despite the genetic evidence to the contrary, we assume that ageing at 20° C is due to random hits on chromosomes, then ageing at 30.5° C cannot be explained by the same process proceeding at a higher rate. In other words, either at 20° C or at 30.5° C ageing must be due to a process different from that postulated by Szilard, it is possible, and in my view likely, that such a process is not primarily responsible for ageing at either temperature.

It is perhaps unreasonable to criticize a theory intended to explain ageing in mammals by quoting

observations on insects Unfortunately the temporal experiments cannot be repeated on a homoiotherm But there is some evidence¹ in mice, as well as in *Drosophila* that inbred individuals do not live as long as outbred ones In addition to this purely observational point, there is one more general reason why Szilard's work has made a theory of ageing by somatic mutation less, and not more, promising than it had previously appeared to be It is assumed that the 'target' is a whole chromosome, a 'hit' renders ineffective all the genes carried by that chromosome This assumption is made because, as Szilard shows if it were assumed that the target were an individual gene, it would be necessary also to assume that each individual carried a load of faults so high as to be inconsistent with the known fertility of consanguineous marriages There are events particularly mitotic errors and chromosome breakages, which would deprive cells of whole chromosomes or of large segments of chromosomes but they do not seem likely to be common enough to be the main cause of ageing Most biologists would be happier with a theory which assumed as the unit event a hit on a gene using the word gene here to refer to a functional unit or cistron Perhaps the most important thing Szilard has done is to show that such a theory, at least in its simplest form, would run into difficulties

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¹ Szilard L. *Proc U S Nat Acad Sci* 45 30 (1959)

² Clarke J M and Maynard Smith, J *J Genet* 53 172 (1959)

³ Maynard Smith J, *J Genet* 56 227 (1959)

⁴ Maynard Smith J, *J Exp Biol* 45 85 (1958)

⁵ Malthus O CIBA Colloquia on Aging 3 115 (1957)

ALL the observations quoted by Mr Smith in his interesting communication relate to fruit flies and they fall into two classes observations which we may expect to be able to duplicate in the case of mammals and those which we may not Since I do not propose to discuss here whether the theory might or might not be extended to insects I am primarily concerned with the former of the two classes

Smith states that a genetically variable 'wild' population of fruit flies has a substantially higher life expectancy than inbred fairly or wholly homozygous strains derived from it He also states that the F_1 hybrid, obtained by crossing two different inbred strains, has a substantially higher life expectancy than the two inbred strains themselves Smith holds that these findings are not compatible with the theory of ageing that I proposed

It is probably true that the observations quoted above could be duplicated with mammals and I am quite prepared to accept this thesis for the sake of argument As I shall presently show, however, my theory does not preclude that the homozygous inbred strains may have a substantially smaller life expectancy than the wild type strains Further, the theory demands that the life expectancy of the F_1 hybrid be appreciably higher than that of the wild type strain, if the wild type strain carries a substantial number of faults In order to see this, we may consider the following

At present there is no evidence that a gene may be responsible for anything except for the production of a specific protein molecule which might be endowed with a specific enzymatic activity In a wild popula-

tion, a given gene may be present in the form of a variety of alleles and the corresponding enzymes may differ in their turnover number For the purposes of discussion here I shall call an allele weak if the turnover number of the corresponding enzyme is small If this turnover number is very small the allele might be a recessive lethal A completely homozygous strain is of course, free of recessive lethals, but it may contain a number of 'weak' alleles

Again for the purposes of discussion here I shall adopt a somewhat over simplified picture and shall disregard the possibility that the enzyme levels in the somatic cells may be determined to some extent by the regulatory mechanisms of the cell through enzyme induction or otherwise On this over simplified basis, we may then say that the somatic cells of an inbred strain which is homozygous for a number of 'weak' alleles, are impoverished in the corresponding enzymes, so far as their biochemical activity is concerned

My theory assumes that only a small fraction of the enzymes, less than one fifth perhaps is important for the functioning of the somatic cells of the adult while practically all of the enzymes may be important for differentiation and morphogenesis during the embryonic life of the individual Accordingly we may then expect that an individual of the inbred strain (which is homozygous for a number of weak alleles) may be maldeveloped in the sense that it may have a much smaller reserve at birth than the wild type individual with respect to a number of physiological functions Thus it is conceivable that an individual belonging to an inbred strain may die at an age at which f the surviving fraction of its somatic cells has fallen to say $f^* = \frac{1}{2} \approx \frac{1}{2}$ whereas

an individual belonging to the wild type strain may die at an age at which f the surviving fraction of its somatic cells has fallen to about $f^* = \frac{1}{4} \approx \frac{1}{4}$

We may compute for this case the most probable age at death for man from formula (14) given on p 33 of my paper (*loc cit*) which reads

$$x_r + r = \sqrt{4m \ln \frac{1}{f^*}} + \ln \frac{1}{f^*}$$

where x_r is the number of hits at death r is the number of the inherited faults $m = 23$ is the number of chromosome pairs and f^* is the surviving fraction of the somatic cells at the age of death

The most probable age at death, t_r , is given by $t_r = 6 \times x_r$ years

For the inbred strain we obtain t_r , the most probable age at death by writing $r = 0$ and $\ln \frac{1}{f^*} \approx 1$ We thus obtain $t_r = 63$ years

For the wild type we obtain t_r , the most probable age at death, by writing $r = 2$ and $\ln \frac{1}{f^*} \approx 2$ We thus obtain $t_r = 81$ years The actual value for white females in the United States is $t_r = 80$ years

For the F_1 hybrid we obtain t_r , the most probable age at death by writing $r = 0$ and $\ln \frac{1}{f^*} \approx 2$ We thus obtain $t_r = 93$ years This is 12 years more than the value for the wild type

It may thus be seen that a substantially shortened life expectancy of the homozygous inbred strain is

compared with the wild type, need not be inconsistent with the theory. However, an increased life expectancy of the F_1 hybrid as compared with the wild type strain is a necessary consequence of the theory.

This consequence of the theory could be tested by experiments on short-lived mammals, say mice. In order to render the experiment more sensitive, one may first expose to ionizing radiation a population of wild type mice over several generations and may thereby increase the number of faults in the population. Starting with such a 'wild' population, enriched in faults, one would then select two unrelated families and derive from them two inbred homozygous strains. The theory demands that the F_1 hybrid of these two inbred strains should live appreciably longer than the population from which the two families were selected. Given a suitable opportunity, I propose to arrange for experiments of this sort. A negative result might well prove fatal for the theory.

I should perhaps add at this point that the observed differences in the life expectancy of the male and the female do not provide a usable criterion for the

validity of the theory because f^* , the 'surviving' fraction of the somatic cells at death, might differ appreciably for the male and the female.

Smith cites a rather peculiar effect of the temperature on the life expectancy of the male and the female in *D. subobscura*. It seems to me that any future theory of ageing that may be generally applicable to insects would be put to an unduly severe test, were one to demand that it account for this particular effect.

Because the theory of ageing that I proposed makes quantitative predictions, it is capable of being disproved by experiments and, sooner or later, such might be its fate. At present I am not aware, however, of any valid observations which contradict this theory. In these circumstances, I am not at present disposed to agree with the appraisal of the theory implied in the last paragraph of Mr Smith's communication.

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CROSS-LINKING OF DEOXYRIBONUCLEIC ACID IN SPERM HEADS BY IONIZING RADIATIONS

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IRRADIATION with X-rays of deoxyribonucleic acid in dilute aqueous solution leads to a reduction in the size of the molecule due to attack by hydroxyl radicals¹. Irradiation of the solid acid as the sodium salt was claimed by us to reduce the molecular weight² and we wrongly concluded (see below) that ionizing radiations, whether acting directly or indirectly via free radicals from water, produce breaks in the main chain. Since *in vivo* deoxyribonucleic acid is conjugated with protein, nucleoprotein obtained from the sperm of fish was irradiated and attempts were made to isolate the deoxyribonucleic acid so as to measure its molecular weight and to see if its radio-sensitivity was affected by the presence of proteins. Sperm heads were chosen for these experiments since they contain essentially only deoxyribonucleic acid and protamine. They can be prepared without denaturation as they take up only a few per cent of water and no break up of the native configuration occurs due to swelling. After the nucleoprotein complex has been dissociated in 2 *M* sodium chloride, deoxyribonucleic acid can be isolated in a very pure form (less than 0.1 per cent of protein contamination) by precipitating the protamine by the usual procedure³ with an anionic soap, sodium dodecyl sulphate. The detergent-protamine complex is removed by centrifugation at 20,000*g* for 30 min. If the sperm heads are obtained from viable sperm by cytolysis at temperatures below 4°C, the recovery of deoxyribonucleic acid is quantitative (better than 95 per cent).

Following irradiation by 20,000–1,000,000 rads with 1-MeV electrons from a Van de Graaff machine, the sperm heads dissolved apparently completely in 2 *M* sodium chloride, but after the removal of the

protamine complex it was found that a substantial fraction of the deoxyribonucleic acid had been lost. In this dosage, no deoxyribonucleic acid was lost if the solution in 2 *M* sodium chloride was centrifuged at 20,000*g* for 2 hr. It was found that the loss of deoxyribonucleic acid was related to the dose as shown in Fig. 1. No significant difference was found between sperm heads from salmon, trout and herring, and moreover, the same effect was obtained if viable whole sperm were irradiated in their seminal fluid and the nucleoprotein isolated after irradiation.

Evidence for Cross-linking

A possible reason for the loss of deoxyribonucleic acid on the addition of the detergent is that some of the protamine is chemically linked by the radiation to the deoxyribonucleic acid so that it, too, is involved in the detergent-complex⁴. But all attempts to demonstrate such a combination have failed. Thus the deoxyribonucleic acid was precipitated quantitatively from the dispersion of sperm heads in 2 *M* sodium chloride by the addition of a polyvalent cation, lanthanum chloride, and the precipitate analysed for protein by paper chromatography. No differences could be detected between the control and irradiated samples, though the latter 'lost' 30–50 per cent of their deoxyribonucleic acid on the addition of the detergent and neither contained more than 0.5 per cent protein. The best evidence that there was no combination with protein was obtained by isolating the deoxyribonucleic acid by ultracentrifugation. In a preparative 'Spinco' the deoxyribonucleic acid from a solution of sperm heads in 2 *M* salt (concentration of deoxyribonucleic acid 0.03 per cent)

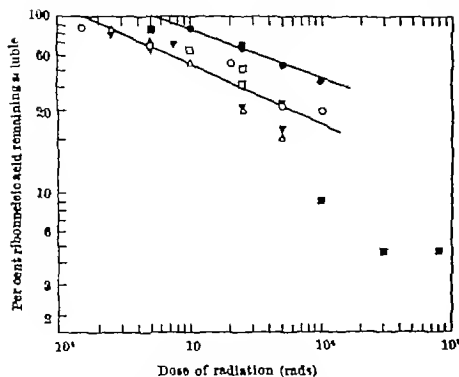


Fig. 1. Effect of 1.2 Mev electrons on the recovery of soluble deoxyribonucleic acid from nucleoproteins: (○) and (□) different preparations of salmon sperm heads; (△) nuclei from herring testes; (●) reconstituted nucleoprotamine fibres from trout sperm heads.

was completely spun down after 15 hr at 35 000g. The pellet of deoxyribonucleic acid was dissolved in water and then respun in 2 M salt under the same conditions. This was repeated twice and the final pellet of deoxyribonucleic acid contained less than 0.1 per cent protein according to the sensitive chromatographic technique of analysis developed by Kirby⁴. No difference in the protein content could be detected between deoxyribonucleic acid prepared in this way from irradiated and unirradiated sperm.

However, the solubility behaviour of the pellets of deoxyribonucleic acid obtained by ultracentrifugation is changed by irradiation and this provides evidence for the mechanism by which part of the deoxyribonucleic acid is removed by soaping after irradiation. While the control samples dispersed completely in 0.1 M sodium chloride, the deoxyribonucleic acid pellet from irradiated sperm heads contained some deoxyribonucleic acid in gel form which could be removed by spinning at 20,000g for 3 hr. The amount of deoxyribonucleic acid spun out under these conditions increases with radiation dose and is, within experimental error equal to the soaping loss. This gel component separated from irradiated sperm heads by centrifugation is not made soluble by the addition of trypsin which digests protamine very rapidly.

These results can be interpreted as showing that on irradiation some of the deoxyribonucleic acid has been cross linked to form a very loose gel like network which is so highly swollen in water that it is not spun out in a short time by centrifugation at 20,000g but is scavenged by the very flocculent precipitate produced by the addition of sodium dodecyl sulphate to 2 M sodium chloride. After very high speed centrifugation this material is compacted and can be removed by ordinary centrifugation at 20,000g. Irreversible behaviour of this type is to be expected from very lightly cross linked gels. This interpretation is further supported by the fact that after very large doses (that is, greater than 3×10^6 rads), deoxyribonucleic acid gel is removed by centrifugation at 20,000g presumably because the swelling has been reduced by additional cross links which tighten up the network. After 8×10^6 rads the sperm

heads no longer disperse at all in concentrated salt solutions.

The relationship between the amount of deoxyribonucleic acid removed by soaping (that is, the amount not behaving as gel) and radiation dose (see Fig. 1) is that found for cross linking of synthetic polymers⁵. The threshold, known as the gel point, arises from the fact that a minimum number of cross links have to be formed before any part of the material has been linked into an 'infinite' network required for it to behave as a gel. Charlesby⁶ demonstrated theoretically for linear polymers that at the gel point the number of cross links equals the number of molecules present. Since the cross links are distributed statistically, some molecules will be unchanged whereas others will be involved in several cross links, and it is these which form the gel fraction.

From the simple relationship of Charlesby it is possible to calculate the energy that has to be put into the system for a cross link to be produced from the threshold dose and the molecular weight of the polymer. The weight average molecular weight of the deoxyribonucleic acid was measured by light scattering and found to be between 9 and 11×10^6 though there was some variation from sample to sample. These high molecular weights, which are confirmed by viscosity measurements, can only be obtained by starting the preparation with viable sperm. If the sperm heads are stored, deoxyribonucleic acid of lower molecular weight is obtained. With a threshold of 2×10^5 rads and deoxyribonucleic acid having a weight average molecular weight of 10^7 (assumed to be twice the number average) a value of 40 eV per cross-link formed is obtained. This shows that the cross linking reaction is a very efficient process.

From the shape of the curve relating radiation dose and gel formed, it is possible⁷ in polymer systems to determine whether some breaking of chains occurred at the same time as cross linking. For this calculation the points at high doses are critical at the same time, experimentally these are the least reliable because they are biased by trapping non-cross linked material within the gel network. If applicable this calculation would show that there can not be more than one break for every four cross links but that there may be less. The average molecular weight of the residual deoxyribonucleic acid left after the removal of gel by centrifugation at 20,000g is less than that of the starting material and continues to decrease with increasing dose. This is in accord with cross linking theory⁸ since the deoxyribonucleic acid is polydisperse and the largest molecules will be the first to enter the gel fraction; the smaller molecules are left in the soluble fraction. This drop in the average molecular weight does not imply the occurrence of chain scission.

Mechanism of Cross-linking

No analytical work has been attempted to determine the nature of the cross link that is formed between deoxyribonucleic acid molecules. The possibility that they are an effect of aggregation by secondary valency forces (for example, hydrogen bonds) has been considered, but seems very unlikely in view of the general properties of the gel and the fact that it is not dispersed by the powerful hydrogen bond breaking solvent, 4 M urea. We do not know whether the gel like structure is formed by molecules that are joined together by a covalent bond or by a

chain-branching mechanism, involving breakage and reunion, which is called end-linking by Charlesby, which at the present time we use the term cross-linking loosely to denote a reaction that results in the formation of deoxyribonucleic acid with gel like properties

A degree of order seems to be necessary for efficient cross linking since the dose of radiation needed to produce gel in reconstituted nucleoprotein fibres, which were obtained by diluting solutions of sperm heads in 2 *M* sodium chloride, is three times greater than that needed to gel the sperm heads, which have the same overall composition. The reconstituted product is known to have an irregular structure and its composition is not stoichiometric.⁷ In recent experiments with Mr John Lett, evidence for cross-linking has been found even when pure deoxyribonucleic acid is irradiated as a solid. Although no gel is formed, except at very high doses, the results suggest that both cross-linking and main chain breaking occur simultaneously, but that the efficiency of the former depends very much on the nature of the sample. The great preponderance of main-chain breaks found in our earlier work² may probably be ascribed to the fact that the deoxyribonucleic acid used was of lower quality. The fact that our present samples have nearly twice the molecular weight of those used earlier supports this explanation. The exact factors determining the change over from cross-linking to degradation when the sodium salt of deoxyribonucleic acid is irradiated are now being studied, but it seems that the amount of cross-linking is very dependent upon the closeness of the packing of the deoxyribonucleic acid chains. The cross-linking is due to the direct action of the radiation, the free radicals produced in the water in which the sperm heads are suspended play no part, presumably because their range is too short. This was established by the fact that the cross-linking efficiency is independent of the amount of water in which the specimens are suspended and, moreover, alcohol-dried herring sperm give essentially the same result, though for experimental convenience we have preferred to irradiate suspensions.

The addition of 1 per cent cysteamine to a 10 per cent suspension of sperm heads provides powerful protection, reducing the amount of cross-linking to approximately half. This is not in conflict with the deduction that the action is largely direct, since protection under these conditions was first reported by Alexander and Charlesby⁸ for polymers and more recently by Markovitch⁹ for phage. If the irradiations are carried out under oxygen instead of air the amount of gel-like nucleic acid that is formed is greatly reduced. The importance of packing may arise from the fact that oxygen combines with the radiation-produced reactive centre and thereby prevents it from giving a cross-link. Competition by oxygen may explain why in preliminary experiments we have failed to find gel-like deoxyribonucleic acid in the nuclei of irradiated chicken erythrocytes in which the nucleoprotein is much less closely packed than in sperm heads.

Biological Implications

The production of a cross link by radiation provides a very effective way whereby one event can destroy the biological integrity of a macromolecule. Even if the part of the molecule involved in the formation of the cross-link is not essential to activity,

the joining of two molecules together will change the physical characteristics of the molecule profoundly. Since a dose of 1,000 rads produces a cross link in, approximately, 5 per cent of the deoxyribonucleic acid molecules present in the sperm cell, quantitatively this reaction is capable of explaining cellular effects of radiation which require doses of this order of magnitude. Such a theory would appear all the more attractive since one of the predominant chemical changes produced by the radioisotopic substances such as nitrogen mustards is the cross linking of deoxyribonucleic acid in the cell nucleus.¹⁰ The similarity of the end effects produced by radiation and the chemicals would then follow from the similarity of the chemical lesion. Against this mechanism is the fact that densely ionizing radiation such as polonium α -rays and 2-MeV neutrons are about ten times less efficient in cross-linking the deoxyribonucleic acid in sperm heads than are the sparsely ionizing radiations of X-, γ - and β rays. Yet the densely ionizing radiations are much the more effective in causing delay of mitosis and cell death—a *a priori* one would expect that the chemical reaction which initiates the sequence of events leading to cellular effects must also be more readily produced by the densely ionizing radiations. The possibility remains that there is a qualitative difference between sparsely and densely ionizing radiations in their effect on deoxyribonucleic acid, and the very low cross linking efficiency of the α rays could best be explained by the simultaneous production of a nearly equal number of main-chain breaks.

For the inactivation of viruses the relative effectiveness of the different radiations is in the reverse order from that found for cellular effects and in qualitative agreement with the cross linking reaction. Since the tightness of the packing of deoxyribonucleic acid appears to facilitate the formation of cross links, it is possible that this is the reaction responsible for the inactivation of bacteriophage by ionizing radiation.

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CARBONIC ANHYDRASE IN THE DECIDUOMA OF THE RAT

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ALTHOUGH extensive investigations have been made of various enzymes in placental tissue, relatively little attention has been paid to the enzymes of the experimentally induced decidual tissue that is, the deciduoma.

Deciduomata offer an excellent opportunity for research on the maternal components of the placenta, especially during the earliest phases of development, and also in embryo free uteri. Nevertheless, the only enzyme studied hitherto in detail in deciduomatous tissue is the histaminase¹, which has been demonstrated as characteristic of the maternal portion in the placenta of man, rabbit and rat. The presence of certain other enzymes in the deciduoma was indicated but results were only reported in summary.²

Carbonic anhydrase is another typical placental enzyme.³ Its presence was first detected in the mammalian female reproductive tract in the endometrium of the pro gravid rabbit.⁴ Investigations of its distribution showed that although the occurrence of carbonic anhydrase in the endometrial mucosa is limited to relatively few species, it is invariably associated with the placenta of mammals, it has been located in the maternal portion of the placenta of large domestic animals, carnivores, laboratory rodents and insectivores.⁵

Since experimentally induced deciduomata are structurally and functionally analogous to the decidual portion of the placenta proper, it was of interest to examine the induced decidual tissue for carbonic anhydrase. For several reasons the rat uterus is specially suitable for such a study. The rat endometrium contains negligible amounts of carbonic anhydrase during oestrus, and the content of this enzyme does not increase in response to progesterone treatment.⁶ This is in contrast to the rabbit endometrium where the response to progesterone as expressed by an increased content of carbonic anhydrase is so spectacularly characteristic that it forms the basis of an assay for luteal potency.⁷ Since the rat does not show a comparable progesterone-conditioned rise in carbonic anhydrase content, any increase in enzyme content found as the result of inducing decidualization can be safely ascribed to the presence of deciduomatous tissue. Further more recent studies⁸⁻¹¹ offer various techniques for induction as well as suppression of deciduoma in the rat.

This investigation was carried out to determine whether carbonic anhydrase is present in the deciduoma of the rat. If so, how early in the development of the deciduoma the enzyme becomes detectable, whether the enzyme activity, if present, is dependent upon the method of deciduoma induction, and

finally whether the suppression of the development by histamine antagonism or by disturbance of the hormonal equilibrium is reflected by the level of carbonic anhydrase activity.

The enzyme assay technique was essentially the same as described earlier.² No attempt was made to dissect the deciduoma from the uterine wall; the results were expressed as enzyme units (EU) per gram entire uterine horn fresh weight. Pseudo-pregnancy was induced in 3-4 months old female albino rats with regular oestrus cycles (stock colony, Anatomy Department, University of Birmingham) by faradic stimulation of the cervix on days of pro-oestrus and oestrus, of the cycle. On the fourth day of leucocytic vaginal smears certain procedures were applied in order to induce or to suppress deciduoma formation.

Four series of experimental animals were set up. Series I consisted of 20 females injected intraperitoneally with 20 mgm pyrazinazine (Pyrozolone, Upjohn), to evoke the decidual response by systemic means.¹² In series II there were 16 females which were laparotomized under ether anaesthesia on the fourth day of pseudopregnancy, the antimesometrial wall of the uterine lumen was scratched along its length with a burred needle to produce in these animals the typical deciduoma induced by trauma. Series III included 10 females laparotomized as above, the endometrium in both uterine horns was traumatized, but the lumen of one horn in each rat was instilled with 0.1 ml of saline solution containing 1 mgm of the antihistaminic diphenhydramine hydrochloride, to suppress the decidual development. Series IV consisted of 10 females which were given intraperitoneally 20 mgm pyrazinazine, this being followed immediately by a subcutaneous injection of 1 mgm ergotamine complex (made up of ergocristine, ergocoridine and ergocryptine methanesulphonate, 1:1:1 in 50 per cent ethanol), which has been previously shown¹³ to prevent the formation of deciduoma by disturbing the hormonal balance. In all four series the uterine weights were recorded, and the horns used for enzyme assay at 24, 48, 72 or 120 hr, respectively, after the termination of the procedure provoking deciduoma. Groups of 4 animals being used at each stage in series I, 3 in series II, and 2 each in series III and IV.

It was found that carbonic anhydrase is undoubtedly present in the rat deciduoma. The values established were low (ranging from 2 to 12 EU/gm) as compared with the progestational endometrium of the rabbit (up to 100 EU/gm.) but they were of the same order as those obtained for the rat maternal placenta (10 EU/gm).

The findings relating to the different experimental techniques used for induction (series I and II) and suppression (series III and IV) respectively of the decidual reaction can be summarized as follows:

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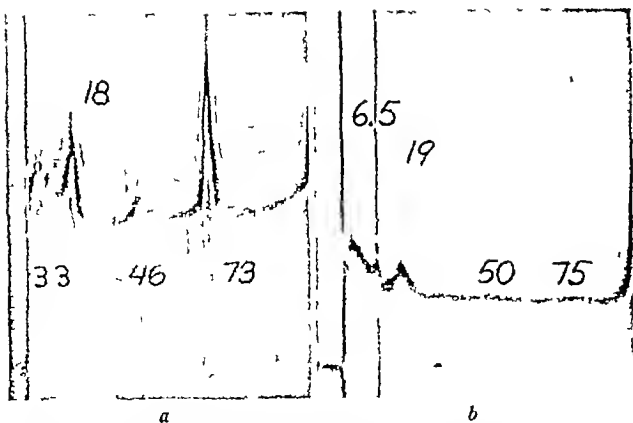


Fig 1 Ultracentrifuge patterns of macromolecular constituents of photosynthesizing *Chlorella pyrenoidosa*. Numbers on peaks are sedimentation coefficients corrected to water at 20° C. a, 2 hr 130,400g pellet from 4.4 gm of normally growing cells, after 8 min at 59,780 r.p.m., bar angle of 40°. b, 2-hr 130,400g pellet from 5.6 gm of 3-day nitrogen starved cells, after 20 min at 42,040 r.p.m., bar angle of 40°.

75 S The next slower peak, of sedimentation coefficient 46–50 S, probably corresponds to the 58 S dissociation product of the 75 S pea seedling particle. Only in preparations from stationary phase algal cultures, or when 'Carborundum' of grit smaller than 320 mesh was used as the grinding agent, did we observe another peak, 32–36 S, which may correspond to the second (38 S) dissociation product which Ts'o *et al.*¹³ found in the pea seedlings. The 18–20 S component appears to be the Fraction I protein which has been found in the extracts of all green plants^{10,11}. The 3.3 S component corresponds to a protein fraction that has been observed in various microbes.² Small amounts of a 105–110 S peak, though not evident in Fig 1a, were observed in our preparations from time to time. This appears to be analogous to the 105 S peak in the pea epicotyl preparations.¹⁴

Although the 75 S and 46–50 S components were degraded when incubated overnight in the cold with pancreatic ribonuclease in the magnesium sulphate/phosphate buffer, they were unaffected by pancreatic deoxyribonuclease. Overnight treatment with trypsin in the cold also largely degraded the 75 S organelles. In 0.01 M tris/0.005 M magnesium sulphate buffer, at pH 8.0, the 75 S component was stable for at least 3 days in the cold, but was completely degraded at the end of 5 days. In 0.01 M sodium ethylene-

diamine tetraacetate, at pH 7.0, it was completely degraded after 7 hr at room temperature. These properties are similar to those of the pea seedling¹ and yeast¹² 75 S organelles.

The high concentration of the slowly sedimenting component (5.6–9.2 S) in preparations from the chlorophyll-less mutant cells (Fig 2) is the most striking difference from the normal photosynthesizing cell preparations. In this respect the ultracentrifuge patterns of the mutant cell preparations resemble those obtained from yeast¹ and *E. coli*¹², which also require an organic source of carbon, like glucose, in their growth media.

Although Dagley and Sykes⁶ found that the 40 S organelles of *E. coli* disappeared almost completely after the bacteria were incubated for 2 hr on a nitrogen-free medium, Wolfe¹⁵ and Ashikawa¹ detected appreciable quantities of 80 S organelles in preparations from yeast even after two days of nitrogen starvation. We could detect no significant decrease in the relative amount of the 75 S organelle from *Chlorella* after 24 hr of nitrogen starvation, but after three days the size of the peak was drastically reduced (Figs 1b and 2b). Marked reductions were also observed in the sizes of the other protein-containing peaks. On a dry-weight or per cell basis, three day nitrogen deficient cells contain only one half as much nucleic acid and three fourths as much protein as do normally growing cells, and the base composition of the residual nucleic acid differs considerably from that of the normal cells.³ Since the greatest loss of nucleic acid is from the centrifugal fraction (1 hr at 130,400g) that is primarily composed of the 75 S component in normally growing cells, it appears that loss of this component from the ultracentrifuge patterns in nitrogen starved cells represents an actual loss of the functional 75 S organelles to the cells.

The sharp, slowly sedimenting (5.6–8.2 S) spike in the ultracentrifuge patterns of the nitrogen deficient cells (Figs 1b and 2b) most probably is deoxyribonucleic acid. It alone disappeared from the patterns after the preparations were incubated overnight in the cold with deoxyribonuclease, and it was resistant to trypsin. Sedimentation coefficients of the peaks remaining in the preparation after deoxyribonuclease digestion increased significantly because of the lowered viscosity of the solution.

After nitrogen starved photosynthesizing cells are returned to the complete medium for 18 hr, the protein content is restored, but the ribonucleic acid content on a dry-weight basis is greater than that of normal cells. The base composition of the total nucleic acids is once more the same as that of normal cells.³ Ultracentrifuge patterns from the 18-hr nitrogen-restored photosynthesizing cells closely resemble the patterns from normal cells (Fig 1a), but the ultracentrifuge patterns from the nitrogen-restored chlorophyll-less mutant cells again resemble those from proliferating yeast cells (Ashikawa, in ref 1) more closely than they resemble the patterns from photosynthesizing *Chlorella* cells. These differences between the two strains of cells probably reflect the metabolic changes produced by the loss of photosynthetic ability in the mutant cells, resulting in heterotrophic rather than autotrophic nutrition.

We may conclude that the number and kinds of macromolecular organelles in the *Chlorella* cell closely reflect the nutritive conditions under which the alga is grown, further, that the changes in the macromolecular architecture of the alga may be correlated with marked changes in its chemical composition.

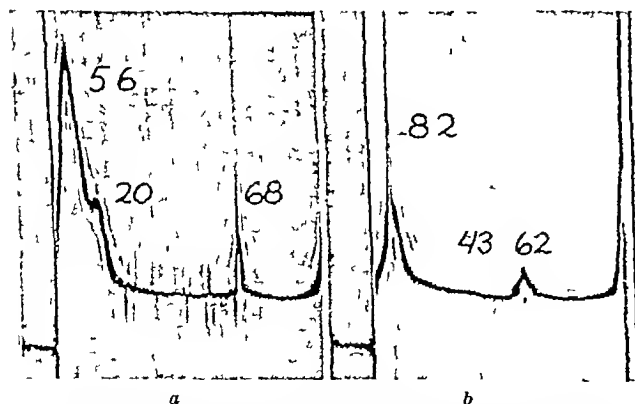


Fig 2 Ultracentrifuge patterns of macromolecular constituents of chlorophyll-less *Chlorella pyrenoidosa*, strain G 11. Numbers on peaks are sedimentation coefficients corrected to water at 20° C. a, 2 hr 130,400g pellet from 5.6 gm of normally growing cells, after 22 min at 42,040 r.p.m., bar angle of 50°. b, 2-hr 130,400g pellet from 6.8 gm of 3-day nitrogen starved cells, after 18 min at 42,040 r.p.m., bar angle of 50°.

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APPARENT OBSERVATION OF SOLAR CORPUSCULAR CLOUDS BY DIRECT CONTINUOUS-WAVE REFLEXION

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BEGINNING at about 1:31 a.m. E.S.T. on the morning of April 15, 1959, several unique Doppler signals were recorded at the Ohio State University Radio Observatory which may possibly be due to the reflexion of continuous wave signals from fast-moving solar corpuscular clouds passing in the vicinity of the Earth. The receiver in use at the time was a swept-frequency type with its centre frequency on 15 Mc/s for the reception of W W V (Washington, D.C.). The receiver had a 1 kc/s band width and was swept about twice a second over a frequency range of about 9 kc/s (4.5 kc/s above and below 15 Mc). The receiving antenna was a horizontally polarized corner reflector of 1,360 sq ft physical aperture rotating in azimuth about 6 r.p.m. The receiver output modulated the z axis of a cathode ray oscilloscope which was photographed on 35 mm film moving about 2 cm per min., giving a display of frequency versus time with fiducial marks along the time axis to indicate when the antenna was pointed in a reference direction (approximately south). Except for the swept-frequency receiver and rotating directional antenna, the technique was the same continuous wave reflexion method used at the Ohio State Radio Observatory since December 1957 for the detection of ionization induced by artificial Earth satellites.¹⁻³ The swept-frequency receiver had been added for the observations of any Doppler shifts of the reflected signals and the rotating antenna for the observation of the direction of signal arrival.

Fig. 1 is a photograph of the swept frequency record obtained with the above equipment between about 1:30 and 1:35 a.m. E.S.T. on April 15, 1959.

Frequency extends transversely with 15 Mc/s. at the centre and 15 Mc. minus 5 kc/s. at the top and 15 Mc. plus 4 kc/s. at the bottom. The row of dots at the top of the film are the direction fiducial marks. The central heavy trace is the 15 Mc/s. signal from W W V (and/or W W V H).

Of particular interest on this record are the two strong signals which sweep rapidly from high to low frequency through the band of reception at 1:31 and 1:34 a.m. The fact that they change from high to low frequency suggests that they might be Doppler shifted signals reflected from rapidly moving ionized clouds. Beginning about 1:45 a.m. many other apparent Doppler signals were recorded on the film until about 3:25 a.m., after which all such indications disappeared. All the signals after 1:45 a.m. differ from the two of Fig. 1 in that they persist much longer, have a periodic fluctuation of several kilocycles, and have a smaller maximum frequency deviation. Fig. 2 is a typical example of one of these signals recorded about 2:35 a.m.

The signal at 1:31 a.m. has a rate of frequency change of more than 400 c/s. per sec., and if it is a true Doppler reflexion of W W V must have a maximum frequency deviation of at least 20 kc. or several times as great as the receiver sweep range. The signal at 1:34 a.m. has a lower rate of change of frequency and also appears to be quite asymmetrical having the appearance of a segment of a Doppler curve at a considerable frequency deviation from the original frequency. Thus this signal might have been caused by a Doppler shift of another station transmitting on a frequency greater than 15 Mc/s.



Fig. 1. Swept frequency record of Doppler signals recorded between 1:30 and 1:35 a.m. (E.S.T.) on April 15, 1959. Frequency extends transversely with 15 Mc/s. at the centre and 15 Mc. minus 5 kc/s. at the top and 15 Mc. plus 4 kc/s. at the bottom. Time increases to the left. The dots along the top of the film are the direction fiducial marks.

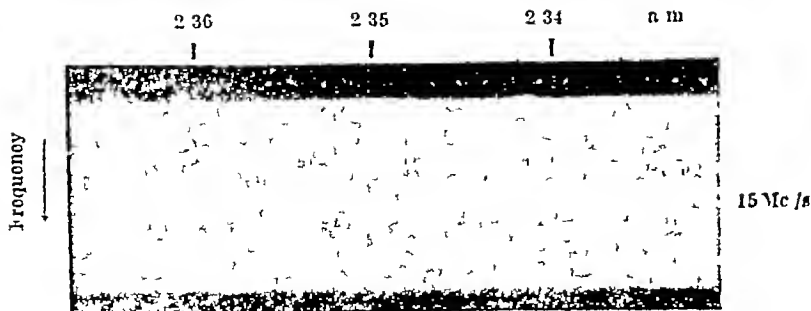


Fig 2 Swept-frequency record of Doppler signals recorded about 2 35 a m on April 15, 1959. These signals show less frequency deviation but have more frequency spread and a periodic fluctuation suggesting turbulence

The limited frequency-range of the sweep system (9 kc/s) prevents an accurate determination of the maximum frequency deviation. However, various considerations would place the maximum deviation between 20 and 80 kc/s. These values imply a velocity of the reflecting cloud of between 200 and 800 km per sec.

It may be significant that about two days earlier a large solar flare occurred near the central meridian of the Sun. This flare reached its maximum about 0900 UT on April 13, 1959, and was rated of importance 3 (highest rating) by the High Altitude Observatory of the University of Colorado⁴. Material ejected by this flare travelling at an average velocity of 900 km per sec would have reached the vicinity of the Earth at about 1 30 a m (EST) (0630 UT) on April 15, when the first Doppler signal was observed. An average velocity of 900 km per sec is not uncommon for flare-ejected material, terrestrial magnetic and other effects being observed typically about two days after large solar flares. Hence, the radio reflexions on April 15 could have occurred from ionized clouds forming part of corpuscular streams ejected from the Sun by the flare of April 13, the velocity at the time of the radio observations having decreased considerably below the average value.

All the signals recorded between 1 45 a m and 3 25 a m, such as shown in Fig 2, appear to have a Doppler spread of several kilocycles, with the later signals appearing to have a greater frequency dispersion than the earlier ones. The signal in Fig 2 has a frequency spread or dispersion of at least 4 kc/s. They also appear to possess a periodic fluctuation around a more slowly varying average frequency. This fluctuation amounts to a couple of kilocycles and is suggestive of turbulence in the clouds. The maximum deviation of the average frequency for these signals is about 4 kc/s, which corresponds to a velocity of 40 km per sec. Hence, these signals could be interpreted as due to reflexions from slower-moving turbulent clouds following in the wake of the high-velocity cloud recorded in Fig 1, and apparently trapped in the Earth's magnetic field.

A number of terrestrial phenomena occurred early on April 15 which also suggest the possible arrival of solar particles in the Earth's vicinity at that time. For example, the recordings of the Earth's magnetic field at the Magnetic Observatory at Agincourt, Ontario, Canada⁵, show fluctuations between 1 00 and 2 00 a m EST with little or no variations for the 3 hr preceding 1 00 a m and the 5 hr following 2 00 a m. The maximum increase in declination (east) amounts to about 22' with its highest values centred about 1 20 a m, or 11 min before the

first radio Doppler signal, compared to less than 6' maximum variation in the adjacent 8 hr. Of particular interest is the fact that the maximum declination variation is more than twice that of the other field components. It may be significant in this connexion that an ion cloud travelling radially away from the Sun and passing near the northern hemisphere of the Earth would produce a change in the approximately east-west component of the Earth's field (declination) which would be larger than the change in the other components (north and vertical) as observed at Agincourt. The fact that the de-

clination increase was eastward implies a cloud with a net positive charge.

The direction indications provided by the rotating receiving antenna indicate that the first Doppler signals (at 1 31 and 1 34 a m) were received from a generally north-western direction. This direction is consistent with that to be expected for clouds from the Sun passing by the Earth above the northern hemisphere, since as observed from Columbus clouds approaching from the Sun would be observed (in azimuth) to come from the north. The later Doppler signals (after 1 45 a m) show a direction of arrival which is also generally to the north with some appearing to begin toward the north-west and changing to a north-east or easterly bearing.

It is of interest to calculate the distance of the ionized clouds at their point of near approach and also their radar cross-section. Based on a frequency deviation of at least 20 kc/s (but not more than 80 kc/s) and a maximum rate of change of frequency of 410 c/s per sec, a distance of at least 10,000 km (but not more than 160,000 km) is obtained for the initial cloud (Fig 1). The calculated radar cross-section of this cloud is at least 100 sq km (but not more than about 5×10^4 times this value). For the later clouds, the maximum (average) frequency deviation is typically about 4 kc/s and the maximum rate of change of frequency about 75 c/s per sec. Hence, these clouds were about 2,000 km distant at near approach and had radar cross sections of about 0.2 sq km each. In order to reflect the 15 Mc/s signals electron densities in the clouds of the order of 10^{12} per cu m are required. From various considerations it appears that the clouds contained positive ions, electrons and perhaps neutral matter.

The above observations are suggestive of Doppler reflexions from solar corpuscular clouds. So far as we are aware, moving solar corpuscular clouds have not previously been detected by direct radio (or radar) techniques, so if the interpretation of the results is correct this marks the first observation of its kind.

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FLUCTUATIONS IN PHOTON STREAMS

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BRIEF mention was made in a previous communication¹ of the way in which photon fluctuations have been studied in connexion with the performance of detectors of radiation, particularly for the infra-red region. The ability to detect small radiation signals despite the inevitable presence of noise in the device is called detectivity. Milatz and van de Velden² were the first to recognize that a limit to the detectivity of a thermal detector is set by the spontaneous fluctuations in temperature as given by the Einstein-Fowler formula³

$$\overline{\Delta E^2} = kT^2 \frac{\partial E}{\partial T} \quad (1)$$

where E is the energy in the receiver, T the absolute temperature and k the Boltzmann constant.

The mean square fluctuation $\overline{\Delta n^2}$ in the density of photons in a temperature enclosure is (see ref. 3)

$$\overline{\Delta n^2} = n + \frac{n^2}{N} \quad (2)$$

where n is the mean density of photons, and N the density of Bose cells. The first term in equation 2 is equal to the fluctuation $\overline{\Delta n^2} = n$ in a random set of classical particles having mean density n . The second term is similarly identifiable with the fluctuation $\overline{\Delta n^2} = n^2/N$ in the squared amplitude in a random set of classical waves. The total fluctuation can therefore be regarded as comprising a 'classical particle' part, n , and a 'classical wave' part, n^2/N .

Lewis⁴ used equation 2 to calculate the fluctuation in the energy exchanged by a black receiver with an isothermal cavity, and found the same limit to the detectivity as had been derived by Milatz and van de Velden. Clark Jones⁵ showed that this agreement provides a means of using equation 1 to calculate the limiting detectivity of any radiation receiver in equilibrium with an isothermal enclosure, whatever may be its spectral responsibility and whether or not its mechanism is thermal. The result may be summarized by saying that in each small frequency range the mean square fluctuation in the number m of photons affecting a detector having quantum efficiency ϵ is

$$\overline{\Delta m^2} = m \left(1 + \frac{n}{N} \right) \quad (3)$$

where

$$m = \frac{1}{2} \epsilon n A \quad (4)$$

$$n = N / (\exp h\nu/kT - 1) \quad (5)$$

$$N = 8\pi\nu^2 dv/c^3 \quad (6)$$

A is the effective surface area of the receiver, c the velocity of light, ν the wave frequency, and h the Planck constant.

These developments have led to an understanding that the detectivity of radiation receivers is subject to limitations which do not essentially depend on the particular mechanism (whether photo emissive, photoconductive, thermal or phase coherent) but are determined by the extent to which its wave length responsivity causes the detector to be susceptible to the fluctuations in the ambient thermal radiation. These photon fluctuations became of practical interest when it was found^{6,7} that some of the best actual detectors of infra red radiation had detectivities close to the limit set by equation 3. In the Rayleigh-Jeans approximation $\nu \rightarrow 0$, equation 3 also represents the ordinary Johnson noise in the radiation resistance of an antenna⁸.

Photon fluctuations have acquired renewed interest with the demonstration⁹ that partial coherence of visible light can be measured by means of the correlation between fluctuations in the photocurrents in two photocells. The experiments have occasioned some surprise, and it has even been suggested that non zero correlation would be contrary to fundamental quantum notions. On general correspondence principle grounds, however, the properties of radiation which admittedly make fluctuation interferometry possible in the radio region¹⁰ cannot just disappear at optical wave-lengths: there must be some gradual transition through the infra red. Correlation between the signals from two coherently illuminated cells arises from the 'wave' fluctuations, and provides the only means so far known of investigating this component experimentally for visible light. The 'particle' fluctuations at the two cells are mutually uncorrelated, and act as noise tending to mask the effect which it is desired to measure. The familiar transition (equation 3) in the infra red from the predominance of 'wave' noise to that of 'particle' noise as the wave length shortens makes it clear that the 'wave' component is indeed always present, but that it becomes increasingly smothered by the 'particle' noise as the optical region is approached, so that a refined method is needed to measure it.

A difficulty remained, however.¹¹ Hanbury Brown and Twiss developed a theory of the fluctuation in the output of a photocell which was based on the analysis of the detailed interaction between the photoelectrons and the radiation field. It gives results consistent with the picture that photons 'arrive' at random, subject to the probability of 'arrival' being proportional to the instantaneous value of the square of the classical electric vector of the incident radiation. A statistical approach of this kind had been abandoned in earlier work on fluctuations affecting radiation detectors because of the apparent difficulty of making the argument¹²

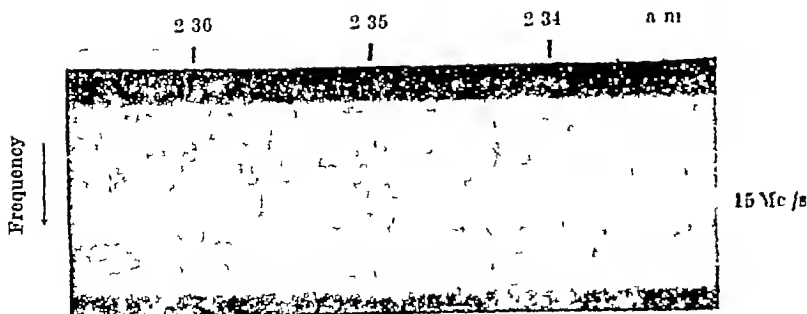


Fig. 2 Swept-frequency record of Doppler signals recorded about 2 35 a m on April 15, 1959. These signals show less frequency deviation but have more frequency spread and a periodic fluctuation suggesting turbulence.

The limited frequency range of the sweep system (9 kc/s) prevents an accurate determination of the maximum frequency deviation. However, various considerations would place the maximum deviation between 20 and 80 kc/s. These values imply a velocity of the reflecting cloud of between 200 and 800 km per sec.

It may be significant that about two days earlier a large solar flare occurred near the central meridian of the Sun. This flare reached its maximum about 0900 UT on April 13, 1959, and was rated of importance 3 (highest rating) by the High Altitude Observatory of the University of Colorado⁴. Material ejected by this flare travelling at an average velocity of 900 km per sec would have reached the vicinity of the Earth at about 1 30 a m (EST) (0630 UT) on April 15, when the first Doppler signal was observed. An average velocity of 900 km per sec is not uncommon for flare-ejected material, terrestrial magnetic and other effects being observed typically about two days after large solar flares. Hence, the radio reflexions on April 15 could have occurred from ionized clouds forming part of corpuscular streams ejected from the Sun by the flare of April 13, the velocity at the time of the radio observations having decreased considerably below the average value.

All the signals recorded between 1 45 a m and 3 25 a m, such as shown in Fig. 2, appear to have a Doppler spread of several kilocycles, with the later signals appearing to have a greater frequency dispersion than the earlier ones. The signal in Fig. 2 has a frequency spread or dispersion of at least 4 kc/s. They also appear to possess a periodic fluctuation around a more slowly varying average frequency. This fluctuation amounts to a couple of kilocycles and is suggestive of turbulence in the clouds. The maximum deviation of the average frequency for these signals is about 4 kc/s, which corresponds to a velocity of 40 km per sec. Hence, these signals could be interpreted as due to reflexions from slower-moving turbulent clouds following in the wake of the high-velocity cloud recorded in Fig. 1, and apparently trapped in the Earth's magnetic field.

A number of terrestrial phenomena occurred early on April 15 which also suggest the possible arrival of solar particles in the Earth's vicinity at that time. For example, the recordings of the Earth's magnetic field at the Magnetic Observatory at Agincourt, Ontario, Canada⁵, show fluctuations between 1 00 and 2 00 a m EST with little or no variations for the 3 hr preceding 1 00 a m and the 5 hr following 2 00 a m. The maximum increase in declination (east) amounts to about 22γ with its highest values centred about 1 20 a m, or 11 min before the

first radio Doppler signal, compared to less than 6γ maximum variation in the adjacent 8 hr. Of particular interest is the fact that the maximum declination variation is more than twice that of the other field components. It may be significant in this connexion that an ion cloud travelling radially away from the Sun and passing near the northern hemisphere of the Earth would produce a change in the approximately east-west component of the Earth's field (declination) which would be larger than the change in the other components (north and vertical) as observed at Agincourt. The fact that the declination increase was eastward implies a cloud with a net positive charge.

The direction indications provided by the rotating receiving antenna indicate that the first Doppler signals (at 1 31 and 1 34 a m) were received from a generally north-western direction. This direction is consistent with that to be expected for clouds from the Sun passing by the Earth above the northern hemisphere, since as observed from Columbus clouds approaching from the Sun would be observed (in azimuth) to come from the north. The later Doppler signals (after 1 45 a m) show a direction of arrival which is also generally to the north with some appearing to begin toward the north-west and changing to a north-east or easterly bearing.

It is of interest to calculate the distance of the ionized clouds at their point of near approach and also their radar cross-section. Based on a frequency deviation of at least 20 kc/s (but not more than 80 kc/s) and a maximum rate of change of frequency of 410 c/s per sec, a distance of at least 10,000 km (but not more than 160,000 km) is obtained for the initial cloud (Fig. 1). The calculated radar cross-section of this cloud is at least 100 sq km (but not more than about 5×10^4 times this value). For the later clouds, the maximum (average) frequency deviation is typically about 4 kc/s and the maximum rate of change of frequency about 75 c/s per sec. Hence, these clouds were about 2,000 km distant at near approach and had radar cross-sections of about 0.2 sq km each. In order to reflect the 15 Mc/s signals electron densities in the clouds of the order of 10^{12} per cu m are required. From various considerations it appears that the clouds contained positive ions, electrons and perhaps neutral matter.

The above observations are suggestive of Doppler reflexions from solar corpuscular clouds. So far as we are aware, moving solar corpuscular clouds have not previously been detected by direct radio (or radar) techniques, so if the interpretation of the results is correct this marks the first observation of its kind.

The work reported here was supported in part by the Army Rocket and Guided Missile Agency, US Army Ordnance Missile Command, under Contract DA-33-019-ORD-2867 with the Ohio State University Research Foundation.

¹ Kraus, J. D., *Proc. Inst. Rad. Eng.*, 40, 610 (1958).

² Kraus, J. D., Hagg, R. C., and Albus, J. S., *Proc. Inst. Rad. Eng.*, 40, 1534 (1958).

³ Kraus, J. D., and Drees, E. E., *Proc. Inst. Rad. Eng.*, 40, 1580 (1958).

⁴ Preliminary Reports of Solar Activity, Report TR 398 for week ending April 17, 1959, High Altitude Observatory, Boulder, Colorado.

⁵ Indices of Geomagnetic Activity for Agincourt, Ontario, Division of Terrestrial Magnetism, Dominion Observatory, Ottawa, Ontario, Canada.

exchanging radiation with the T_1 region. For example, it may represent a detector made of a material which absorbs all the radiation entering its substance but which has a dielectric constant differing from that of its surroundings so that partial reflexion occurs at its surface. If $T_1 = T_2$, the average energies I_1 and I_2 radiated by the T_1 and T_2 regions are equal, and the expression 7 reduces to $4\epsilon I^2$. The mean square fluctuation is therefore proportional to ϵ , and this accords with the form of the wave noise term $\Delta m^2 = mn/N$ in equation 3 (since m contains ϵ as a factor, see equation 4). By contrast, if $T_1 \gg T_2$, I_2 can be neglected and expression 7 tends to $2\epsilon I^2$. This shows that the mean square fluctuation now varies as ϵ^2 in accordance with the wave term $\Delta m^2 = \epsilon mn/N$ in equation 3a.

For a detector conforming to this model, the previous difficulties have now been resolved. Equation 3a is seen to be correct under the conditions of the experiments made by Hanbury Brown and Twiss, namely, when the emitted radiation field is effectively zero, but not for detectors which are hot enough to radiate appreciably. Equation 3 is correct when applied to the exchange of radiation between a cavity and a detector in equilibrium, but not with the extended interpretation ascribed to it by Jones and Fellgett. In reaching these conclusions, it has been necessary to consider not only interaction between the absorbed and the emitted radiation but also interactions involving both the reflected radiation and that radiation which is regarded as 'virtually emitted' if we consider the detector as an assembly of classical or quantized oscillators.

It is not certain that the model is completely general. The discussion given above is purely classical wave and a quantum mechanical approach is needed in which stimulated emission replaces the classical wave-interference effects. This method will automatically include a 'particle' term as well as the 'wave' term, and may show what happens when there are competing mechanisms of absorption of radiation, one of which is 'active' in producing output from the cell whereas the others are not.

Despite these limitations, it seems very plausible (to put it no higher) that equation 3 is correct generally when the detector is at the temperature of the radiation field in which it is placed, and that equation 3a becomes true in the limit when the detector is too cool to radiate appreciably. The effect of these conclusions on the calculation of the limiting detectivity of radiation detectors remains to be investigated in detail.

It now appears, therefore, that the discrepancy which was pointed out in earlier publications between the fluctuation formula derived by Jones and Fellgett on one hand and by Hanbury Brown and Twiss on the other, was real and that it showed limitations in both methods of calculation as they were then conceived. The two formulae have now been reconciled, and each found to be correct in the circumstances for which it was originally derived, by taking account of the interaction between the incident, emitted and reflected radiation streams, the relevance of which had not previously been appreciated.

- * Hanbury Brown B. and Twiss R. Q. *Nature* 177 27 (1958)
- 178 1046 (1958)
- * Hanbury Brown R. and Twiss R. Q. *Phil Mag* 45 663 (1954)
- * Hanbury Brown R., Jemison R. C. and Das Gupta M. K. *Nature* 170 1061 (1950)
- * Hanbury Brown R. and Twiss, R. Q. *Nature* 179 1125 (1957)
- Proc. Roy. Soc. A* 242 309 (1957)
- * Fellgett P. B. thesis Univ Camb (1951)
- * Fellgett P. B. "Visitas in Astronomy" 478 edit. A Beer (Pergamon Press London 1955)

By Dr C W McCOMBIE

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Two contradictory views on the fluctuations in the absorption and emission of photons by matter have been discussed in recent papers.¹⁻² Both views agree that the mean square fluctuation, ΔN^2 , in the number N of photons in a small frequency range absorbed or emitted in unit time by a black body will exceed the value N , appropriate to Poisson fluctuations, by a factor $1 + \epsilon$ here ϵ is the mean number of photons in one of the electromagnetic modes concerned and is given by $\{\exp(h\nu/kT) - 1\}^{-1}$. The disagreement arises when the body absorbs imperfectly. According to one view^{1,4} the fluctuations in the number of photons absorbed (or emitted) will exceed Poisson fluctuations by the factor $1 + \epsilon$, no matter how small the fraction of incident photons absorbed. This opinion claims support from the quasithermodynamic type of argument, given by Clark Jones¹ and by Fellgett⁴, and generally used to establish the ultimate sensitivity limits for radiation detectors. The other view² maintains that the random selection of photons for absorption tends to make the fluctuations approach a Poisson distribution: more precisely, the factor $1 + \epsilon$ is reduced to $1 + \epsilon\epsilon$, where ϵ is the absorptivity. This second view is supported by detailed calculations² concerned primarily with the photon correlation experiments of Hanbury Brown and Twiss.³

In this communication the quasithermodynamic approach will be applied to a particular model. The results agree with the detailed calculations in supporting the second point of view, and for this model at least the conflict is resolved. The agreement depends on taking account of the fact that, because of stimulated emission, the radiation emitted by matter depends in general on the radiation field into which it radiates the mean rate at which an atom radiates into an electromagnetic mode is proportional to $1 + \epsilon$ (cf. Heitler⁵). This effect must be allowed for whenever, as in the disagreement under discussion, $1 + \epsilon$ is distinguished from unity. The results also agree with the standard formula for the ultimate sensitivity limit of radiation detectors derived by Clark Jones and Fellgett, although, as mentioned, it has been claimed that this formula supports the first view. This claim depends on the assumption that the mean rate at which the detector absorbs radiation from a black body radiation field with which it is in equilibrium can be equated to the absorptivity multiplied by the rate of incidence of the black body radiation on the detector: it will emerge that, because of stimulated emission effects, this equality does not hold for the model to be considered here.

In the quasithermodynamic approach the system concerned is characterized by the coefficient α where $\alpha\Delta T$ is the ratio of loss of heat from the system when its temperature exceeds that of the surround

¹ Fellgett P. B. *Nature* 179 956 (1957)

² Mollat J. M. W. and van de Velden H. A. *Physica* 10 549 (1943)

³ Fowler B. H. "Statistical Mechanics" (Camb Univ Press 1929)

⁴ Lewis W. B. *Proc. Phys. Soc.* 59 31 (1947)

⁵ Jones R. O. *J. Opt. Soc. Amer.* 37 870 (1947)

⁶ Fellgett P. B. *J. Opt. Soc. Amer.* 39 970 (1949)

⁷ Moss T. S. *J. Opt. Soc. Amer.* 40 903 (1950)

ings by ΔT . The basic result used is the following analogue of Nyquist's theorem when the system and its surroundings are both at temperature T , the mean square fluctuation in the energy absorbed or emitted in unit time by the system in thermal exchange with its surroundings is $\alpha k T^2$. This result reduces the calculation of the magnitude of the fluctuations to the calculation of α .

The importance of considering stimulated emission can be seen very simply by considering the fluctuations for a set of very weakly absorbing and emitting atoms. The photon absorption-rate will equal a constant θ_T , depending on the number, nature and temperature of the atoms, multiplied by \bar{n} , the mean number of photons in an electromagnetic mode in the (small) range of frequencies absorbed by the atom. To determine α , we suppose the surroundings at temperature T and the atoms at temperature $T + \Delta T$. Since the atoms radiate and absorb weakly, \bar{n} will have the value \bar{n}_T appropriate to the temperature of the surroundings. The rate of absorption of photons will be $\theta_T + \Delta T \bar{n}_T$ and, with neglect of stimulated emission effects, the rate of emission would equal that of atoms in equilibrium with radiation at $T + \Delta T$, which must equal the rate of absorption from this radiation, that is, $\theta_T + \Delta T \bar{n}_T + \Delta T$. But because the atoms are actually radiating into radiation at temperature T , not $T + \Delta T$, and for a given state of the emitter the radiation is proportional to $1 + \bar{n}$, the rate of emission must be modified to $\theta_T + \Delta T \bar{n}_T + \Delta T (1 + \bar{n}_T)/(1 + \bar{n}_T + \Delta T)$. Substitution of the resulting value (note that $d\bar{n}/dT$ can be written $\bar{n} (1 + \bar{n}) h\nu/kT^2$) of α in the quasi-thermodynamic result gives $\theta_T \bar{n}_T$ for ΔN^2 . This represents Poisson fluctuations, in agreement with the second view, since the absorption is small. Neglect of stimulated emission introduces an extra factor $1 + \bar{n}$, lending spurious support to the first view.

The main model to be considered here consists of a large cavity filled with a tenuous gas of atoms which absorb only in a small frequency-range around ν at a rate again specified by θ_T . The walls are perfectly reflecting apart from a small opening, of area A , to the outside. Radiation, which enters the cavity from the outside and re-emerges after being reflected around but not absorbed by an atom, is to be regarded as scattered. Thus the model can be adjusted to represent arbitrary ε .

To determine α and ε for the model, it is necessary to consider non-equilibrium situations in which \bar{n}_{inc} , the number of photons per mode in the radiation incident on the aperture from the outside, differs from the value \bar{n}_T appropriate to the temperature of the atoms. The number of photons per mode in the cavity will then differ from \bar{n}_T , it will be supposed, however, that \bar{n} has the same value, denoted by \bar{n}_c , for all modes of frequency ν in the cavity. The value of \bar{n}_c is fixed by the energy balance requirement that the net rate of emission of photons through the aperture, $(\bar{n}_c - \bar{n}_{inc})\varphi$, where φ is a constant fixed by A and ν , must equal the net rate of emission of photons by the atoms, so that

$$(\bar{n}_c - \bar{n}_{inc})\varphi = \theta_T \bar{n}_T (1 + \bar{n}_c)/(1 + \bar{n}_T) - \theta_T \bar{n}_c \quad (1)$$

where stimulated emission effects have been treated as before.

In order to determine α the surroundings are supposed at temperature T , so that \bar{n}_{inc} is \bar{n}_T , and the atoms at temperature $T + \Delta T$. The net rate of energy loss $\varphi(\bar{n}_c - \bar{n}_T)$, evaluated to the first order in ΔT , gives α . The preliminary determination of

\bar{n}_c follows from (1) with \bar{n}_{inc} and T replaced by \bar{n}_T and $T + \Delta T$. The quasithermodynamic result then gives

$$\Delta N^2 = \frac{\alpha k T^2}{(h\nu)^2} = \frac{\theta_T \varphi (1 + \bar{n}_T) \bar{n}_T}{\theta_T + \varphi (1 + \bar{n}_T)} \quad (2)$$

Because of stimulated emission, ε_T , which can be regarded either as the emissivity or the absorptivity, must be defined rather precisely, but the appropriate operational definitions are clear. As the emissivity, ε_T would be determined by letting the system, with the atoms at temperature T , radiate in the absence of incident radiation, and taking the ratio of the emitted radiation $\varphi \bar{n}_c$ to that from a black body of the same area and temperature, namely, $\varphi \bar{n}_T$. As the absorptivity, ε_T , would be found by increasing the incident radiation slightly above its equilibrium value, so that \bar{n}_{inc} exceeds \bar{n}_T , and taking the ratio of the net rate of absorption of radiation, $(\bar{n}_{inc} - \bar{n}_c)\varphi$, to the extra rate of incidence, $(\bar{n}_{inc} - \bar{n}_T)\varphi$, the values of ε_T in the two cases are easily determined from equation 1. The results for ε_T agree, being given by

$$\varepsilon_T = \frac{\theta_T}{\theta_T + \varphi (1 + \bar{n}_T)} \quad (3)$$

\bar{N}_T is the mean flux of photons which, when system and surroundings are at temperature T , proceed from atoms of the gas to the outside without intervening absorption, as distinct from (a) photons which enter and leave without absorption, or (b) those which are emitted by an atom and absorbed by an atom without leaving the cavity. Only a fraction $\varphi/(\theta_T + \varphi)$ of the radiation emitted by an atom will escape, the rest being re-absorbed. The atoms will radiate at the rate $\theta_T \bar{n}_T$. Consequently

$$\bar{N}_T = \frac{\varphi \theta_T \bar{n}_T}{\theta_T + \varphi} \quad (4)$$

It may be noted that \bar{N}_T exceeds $\varepsilon \varphi \bar{n}_T$, the rate of emission in the absence of incident radiation. The ratio of the two, $(1 + \bar{n}_T)/(1 + \varepsilon \bar{n}_T)$, is just the stimulated emission factor corresponding to the different values of \bar{n}_c .

According to equations 2, 3 and 4, ΔN^2 can be expressed in two algebraically equivalent forms

$$\Delta N^2 = \varepsilon \varphi \bar{n}_T (1 + \bar{n}_T) = \bar{N}_T (1 + \varepsilon \bar{n}_T) \quad (5)$$

The first form reproduces the result used in the theory of the ultimate limit of radiation detectors. The second exhibits for this model the complete agreement between the results of the quasithermodynamic discussion and the results of the detailed approach of Hanbury Brown and Twiss.

I am indebted to my colleagues, Drs E W Elcock and P T Landsberg, for their comments on this communication, and to Dr P B Fellgett for correspondence on preliminary versions of this and the preceding communication by Fellgett, Clark Jones and Twiss.

¹ Fellgett, P B, *Nature*, **170**, 950 (1957)

² Twiss, R W, and Hanbury Brown, R., *Nature* **170**, 1120 (1957)

³ Hanbury Brown, R, and Twiss, R Q, *Proc Roy Soc, A*, **242**, 309 (1957)

⁴ Fellgett, P B, *J Opt Soc Amer*, **30**, 970 (1940)

⁵ McCombie, C W, "Rep Progr Phys", **16**, 266 (1953)

⁶ Jones, R Clark, *J Opt Soc Amer*, **37**, 879 (1947)

⁷ Purcell E M., *Nature*, **178**, 1449 (1956). Silittio R M., *ibid*, **170**, 1127 (1957). Mandel, L., *Proc Phys Soc*, **72**, 1037 (1958). Kahn, F D., *Optica Acta*, **5**, 93 (1958). Hanbury Brown, R, and Twiss, R. Q., *Proc Roy Soc, A*, **243**, 201 (1958)

⁸ Heitler, W., "The Quantum Theory of Radiation", 3rd edit (Clarendon Press, Oxford, 1954)

FORTHCOMING EVENTS

(Meetings marked with an asterisk * are open to the public)

Monday November 16

SOCIETY OF CHEMICAL INDUSTRY PESTICIDES GROUP (at 14 Belgrave Square London W.1) at 9.30 a.m.—Symposium on "Pyrethrum"

Tuesday November 17

UNIVERSITY OF LONDON (at Queen Mary College, Mile End Road London E.1) at 1.30 p.m.—Prof G P Whittingham "The Challenge of Biology"

INSTITUTION OF ELECTRICAL ENGINEERS, MANAGEMENT AND CONTROL SECTION (at Savoy Place London W.C.2) at 5.30 p.m.—Discussion on Sequence Networks versus Summation Transformers for the Derivation of Single Quantities for Protective Relaying opened by Mr C. Adamson and Dr E. A. Talkhan

RESEARCH DEFENSE SOCIETY (in the Physiology Lecture Theatre University College Gower Street, London W.C.1) at 5.30 p.m.—Prof Sirbols Zuckerman, O.B.E., F.R.S., "The Inevitability of Science" (Twenty-eighth Stephen Paget Memorial Lecture)

UNIVERSITY OF LONDON (at the London School of Hygiene and Tropical Medicine, Keppel Street, London W.C.1) at 5.30 p.m.—Dr C. E. Balglish, "Biochemical Aspects of Disorders of Aminoacid Metabolism" (Tenth of fifteen lectures on "The Science Basis of Medicine" organized by the British Postgraduate Medical Federation. Further lectures on November 19 December 1 3 8 10, 12)

INSTITUTE OF PHYSICS (at 47 Belgrave Square London S.W.1) at 6 p.m.—Dr R. L. F. Noyd "Some Techniques and Results of Space Exploration"

ROYAL AERONAUTICAL SOCIETY (at 4 Hamilton Place London W.1) at 7 p.m.—Dr J. A. Sherriff "Magnetohydrodynamics"

Wednesday November 18

INSTITUTE OF METAL FINISHING (in the Lecture Room of the Royal Festival Hall London S.E.1) at 9.30 a.m.—Symposium on "Progress in Polishing"

BRITISH INSTITUTION OF RADIO ENGINEERS (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street London W.C.1) at 3 p.m. and 6 p.m.—Half-day symposium on "Electronic Lighting Techniques"

ROYAL GEOGRAPHICAL SOCIETY (at 1 Kensington Gore, London S.W.7) at 5 p.m.—Prof M. E. L. Mallowan and Mr David Oates "Pre-Salinaceous Nile"

ROYAL METEOROLOGICAL SOCIETY (at 40 Cromwell Road London S.W.7) at 5 p.m.—Dr O. K. Tock, "Mean Meridional Circulations in the Atmosphere" Prof H. Riehl, "Exchange of Heat Moisture and Momentum between Hurricane Ella (1958) and its Environment"

INSTITUTION OF ELECTRICAL ENGINEERS SUPPLY SECTION (at Savoy Place, London W.C.2) at 5.30 p.m.—Dr J. S. Forrest, Mr P. J. Lambeth and Mr D. F. Oskoshott "Research on the Performance of High Voltage Insulators in Polluted Atmospheres"

INSTITUTION OF MECHANICAL ENGINEERS NUCLEAR PANEL (at 1 Birlingside Walk Westminster, London W.1) at 6 p.m.—Discussion on "To What Extent Should Design Wait on Research for Nuclear Power Plant?"

Wednesday November 18—Wednesday December 2

BUTLIN EXHIBITION (at Olympia London)*

Thursday November 19

UNIVERSITY COLLEGE (in the Anatomy Theatre Gower Street London W.C.1) at 1.15 p.m.—Dr M. Mary Dargatzis "The Anatomical Foundations of Lissencephaly" (An Anthropological Interpretation)"

ROYAL SOCIETY (at Burlington House Piccadilly London W.1) at 4.30 p.m.—Special General Meeting to consider the Annual Report of the Council followed by Scientific Papers

INSTITUTION OF NAVAL ARCHITECTS (at 10 Upper Belgrave Street London W.1) at 4.45 p.m.—Mr J. R. Crewe and Mr W. J. Layton "The Hoverscraft—a New Concept in Maritime Transport"

INSTITUTION OF MINING AND METALLURGY (at the Geological Society Burlington House Piccadilly London W.1) at 5 p.m.—Mr F. A. Williams "Use of High Tension Separation in Dressing Jig Concentrate from Decomposed Columbite-bearing Granite Nigeria" Mr M. L. Fitzgerald "Metallurgical Accounting and Control"

LONDON METEOROLOGICAL SOCIETY (at the Royal Astronomical Society Burlington House Piccadilly London W.1) at 5 p.m.—Annual General Meeting Prof H. Davenport "Some Recent Progress in Analytic Number Theory" (Presidential Address)

ROYAL AERONAUTICAL SOCIETY (at 4 Hamilton Place London W.1) at 6 p.m.—Mr W. P. Smith "Some Recent Progress in Air Survey with special reference to Newly Developed Territories" (Fifteenth British Commonwealth Lecture)

SOCIETY OF CHEMICAL INDUSTRY, ROAD AND BUILDING MATERIALS GROUP (at 14 Belgrave Square London S.W.1) at 6 p.m.—Dr H. W. Taylor "Aspects of the Crystal Structures of Calcium Silicates and Aluminates"

Thursday November 19—Friday November 20

PLASTICS INSTITUTE (at the Royal Institute of British Architects 66 Portland Place London W.1)—Conference on "The Influence of Plastics in Building"

Friday November 20

BRITISH PSYCHOLOGICAL SOCIETY OCCUPATIONAL PSYCHOLOGY SECTION (in the Department of Psychology, Birkbeck College Malet Street London W.C.1) at 1 p.m.—Dr John C. Webster (U.S.A.) "Making Yourself Heard"

INSTITUTE OF NAVIGATION (at the Royal Geographical Society 1 Kensington Gore London S.W.7) at 5.15 p.m.—Mr C. M. Code "Radiometry Radio-Astronomy and Infra-red Techniques"

INSTITUTION OF ELECTRICAL ENGINEERS EDUCATION DISCUSSION CIRCLE (at Savoy Place London W.C.2) at 8 p.m.—Discussion on "The Ordinary National Certificate—a New Look" opened by Mr T. Siklos

INSTITUTION OF ELECTRICAL ENGINEERS LONDON GRADUATE AND STUDENT SECTION (at Savoy Place London W.C.2) at 6.30 p.m.—Mr G. J. Waddon "Plastic Cables in the Telecommunications Industry"

ROYAL INSTITUTE (at 21 Albemarle Street London W.1) at 9 p.m.—Sir Lawrence Bragg F.R.S. "Atoms and Molecules"

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates indicated

ASSISTANT LECTURER or LECTURER IN THE DEPARTMENT OF PHILOSOPHY—The Registrar University College of Wales Aberystwyth (November 14)

LECTURER (with a good degree in biochemistry) in ENDOCRINE BIOCHEMISTRY to undertake research into the endocrine aspects of carcinoma in human patients in the University Endocrine Unit at the Liverpool Radium Institute—The Registrar The University Liverpool 8 (November 14)

LECTURER (preferably with a veterinary qualification) in PHARMACOLOGY OF THE SCHOOL OF VETERINARY MEDICINE—The Registrar Trinity College Dublin (November 16)

JOSEPH LUCAS STURTEVANT (with a good honours degree in some branch of engineering physics or chemistry and prepared to work for a higher degree) for research into the initiation of explosion in gases—The Registrar, King's College (University of London) Strand London W.C.2 (November 20)

HEAD (with ample experience and superior attainments in chemical research and analysis and the ability to organize, lead and inspire a large scientific staff) also responsible for the research laboratory—The Civil Service Commission 17 North Audley Street London W.1, quoting Ref No. S.6041/59 (November 21)

GRANADA RESEARCH GRANT IN COMMUNICATION—The Registrar University College of North Staffordshire Keele, Staffs (November 20)

LECTURER IN ORGANO CHEMISTRY at the University of Melbourne Australia—The Secretary Association of Universities of the British Commonwealth 36 Gordon Square London W.C.1 (November 20)

LECTURER IN PHYSICAL METALLURGY at the University of Queensland Australia—The Secretary Association of Universities of the British Commonwealth 36 Gordon Square London W.C.1 (November 20)

ASSISTANT LECTURER or LECTURER IN MATHEMATICS—The Registrar University College of South Wales and Monmouthshire Cathays Park Cardiff (December 1)

LECTURER (preferably with an interest in algae and fungi) in THE DEPARTMENT OF BOTANY University of Natal, South Africa—The Secretary Association of Universities of the British Commonwealth 36 Gordon Square London W.C.1 (December 4)

SENIOR LECTURER IN PURE MATHEMATICS—The Secretary The Queen's University Belfast (December 5)

SENIOR LECTURER or READER (senior theoretical astrophysical) IN PHYSICS in the Theoretical Group of the School of Physics, University of Sydney Australia—The Secretary Association of Universities of the British Commonwealth 36 Gordon Square London W.C.1 (December 5)

LECTURER and a SENIOR LECTURER IN APPLIED MATHEMATICS at the University of Sydney, Australia—The Secretary Association of Universities of the British Commonwealth 36 Gordon Square London W.C.1 (December 5)

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LECTURER in PHYSICAL CHEMISTRY at the University of Natal South Africa—The Secretary Association of Universities of the British Commonwealth 36 Gordon Square London W.C.1 (December 11)

CHIEF OF MECHANICAL ENGINEERING—The Registrar, University College of South Wales and Monmouthshire Cathays Park Cardiff (December 12)

GRADUATE to carry out a field and laboratory research programme IN CROP PHYSIOLOGY—Professor of Agricultural Botany The University Reading Berks (December 15)

LECTURER IN PHYSIOLOGY at the University of Queensland Australia—The Secretary Association of Universities of the British Commonwealth 36 Gordon Square London W.C.1 (December 15)

RESEARCH FELLOW IN THE DEPARTMENT OF RADIOBIOLOGY—The Registrar, The University Leeds 2 (December 18)

ASSOCIATE PROFESSOR (university grade) with qualifications and considerable experience in some branch of the technology of wool production or wool commerce or rural extension and interested in the application of science to the practical problems of the sheep and wool

industry) IN WOOL TECHNOLOGY at the University of New South Wales, Australia—The Agent-General for New South Wales, 56-57 Strand London, W.C.2, and the Bursar The University of New South Wales, Box 1, Post Office, Kensington, New South Wales, Australia marking envelope "University Appointment" (December 21)

SAVILLIA PROFESSOR OF ASTRONOMY—The Registrar, University Registry, Oxford (December 24)

ENTOMOLOGIST Grade C (with a good honours degree in entomology (zoology) and with a particular interest in biological control work)—The Director Commonwealth Institute of Biological Control, Science Building, Carling Avenue, Ottawa Ontario, Canada (December 31)

AGRICULTURAL DEVELOPMENT OFFICER (aged 25-40, with considerable experience in arid/tropical agriculture based on well and flood irrigation) with the Aden Government—The Crown Agents, 4 Millbank London, S.W.1 quoting Ref M 3A 5357/T A

BIOCHEMIST, Basic Grade (graduate in chemistry, or Associate or Graduate Member of the Royal Institute) IN THE DEPARTMENT OF PATHOLOGY—The Group Secretary, Queen Elizabeth Hospital for Children, Hackett Road, London E.2

SENIOR SCIENTIFIC OFFICER (with an honours degree in zoology with postgraduate experience in entomology) at the West African Stored Products Research Unit, Federation of Nigeria to undertake original investigations into problems associated with stored food-stuffs in Nigeria, and evolve methods of improving quality and reducing losses with particular reference to losses caused by insect infestation—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD 153/14/012/T

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LETTERS TO THE EDITORS.

PHYSICS

The D Region of the Ionosphere

At KJELLER near Oslo, measurements of ionospheric cross modulation were made in the period March, 1957—May, 1958, by means of the pulse technique introduced by Fejer.¹ In this communication we shall present some typical results from these observations.

In connexion with a research project undertaken by the Norwegian Defence Research Establishment in order to study the polar radio black-out phenomenon, a number of *ad hoc* experiments were planned in order to study the D region during disturbed conditions. Some results obtained from a first short series of observations carried out near Tromsø during November 1958 will be presented in this note.

Quiet conditions, observations at Kjeller. In the experiments at Kjeller a frequency of 2.05 Mc/s was used for the wanted wave, and a frequency of 1.7 Mc/s. was used for the disturbing wave. The pulse duration was of the order of 100 μ sec in both cases and the transmitted peak powers of the wanted and disturbing waves were 5 and 75 kW respectively.

Fig. 1 shows a typical record sample from observations at Kjeller obtained on June 2, 1957, between 0200 and 0225 M.E.T.

Although reliable observations could only be made at Kjeller during periods when the man made noise level was low, it has been possible to establish typical night and day time profiles for the different seasons. In Fig. 2 we have shown as an example the results from the winter observations. The standard deviations which are given are the means of the standard deviations deduced for single days.

In order to convert the cross modulation curves to electron-density profiles, we have assumed a certain curve for the values of the collision frequency

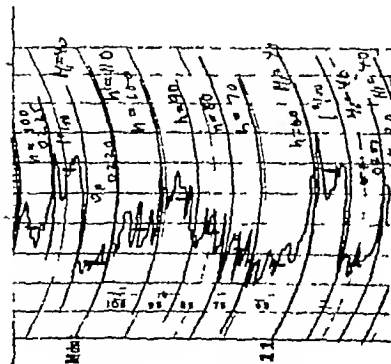


Fig. 1. Typical record sample.

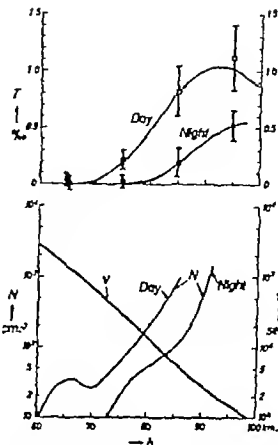


Fig. 2. Results from winter observations at Kjeller.

ν as a function of height. We have also assumed a value of 3×10^7 for the cooling constant G . The final duration of both the wanted and disturbing waves was taken into account. In Fig. 2 the resultant electron-density curves are also shown together with the assumed ν curve.

Disturbed conditions, observations near Tromsø. For the cross modulation experiment a frequency of 2.7 Mc/s was used for the wanted wave and a frequency of 2.3 Mc/s was used for the disturbing wave. The duration was again of the order of 100 μ sec for both pulses, and the transmitted peak powers of the wanted and disturbing wave were 2 kW and 50 kW respectively.

Observations were made simultaneously of partial reflections from the D region using the same transmitter as for the disturbing wave in the cross modulation experiment.

The observations of partial reflections require an observing site with a low noise level. Noise measurement made near Tromsø during the summer 1955 showed that it was possible to find an observing site where the noise level was of the order of 260 $^{\circ}$ K during day time, in agreement with the results of Gardner.²

During the observations in November 1958 we found that when high absorption occurred it was normally possible to obtain weak partial reflections down to a height of the order of 60 km. Observations were made of the strength of both the ordinary and extraordinary waves as a function of height and the method introduced by Gardner and Pawsey³ was used in order to convert the results into electron density curves.

A detailed analysis of even the first short series of observations has not yet been completed. In this communication we shall only indicate the types of

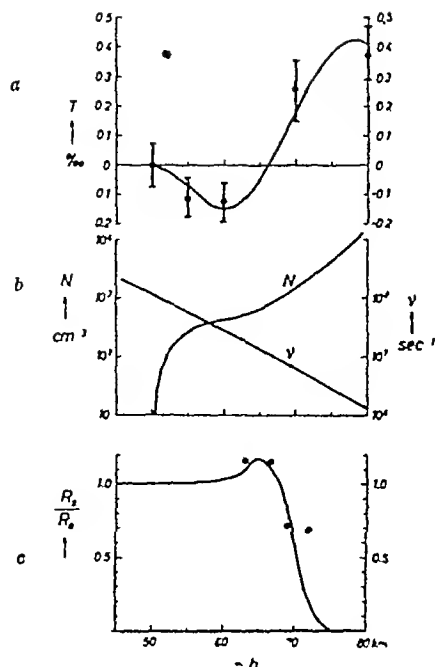


Fig 3 Results obtained during a disturbed period near Tromsø. The results obtained, by showing some results from a selected period when weak, but still quite stable echoes were observed. In Fig 3a the observed values of cross modulation are shown. The observations were obtained as mean values during the period 2000–2200 MET on November 20. The ionosonde recordings in Tromsø (20 km from the observing station), showed no echoes at 2000h, and only faint indications of echoes at 2100h and 2200h. The strength of the echoes on 2.7 Mc/s was of the order of 40 db below the strength obtained during quiet conditions.

In Fig 3b we have shown the electron density profile deduced from the smooth curve of Fig 3a, together with the ν curve. In Fig 3c the measured values of the ratio between the amplitudes of extraordinary and ordinary waves are shown. The smooth curve is deduced from the electron-density profile of Fig 3b. The partial reflexion measurements were made in a short period round 2130 MET.

Fig 3 showed that consistent results were obtained by the two different methods. Rather low frequencies were used in this first short series of observations both for the disturbing and wanted waves, and it was therefore only possible to make deductions with any certainty about the very low part of the D region. New series of observations have been undertaken or planned in which higher frequencies have also been used for the disturbing wave.

In order to be able to convert the observed results into electron density profiles, two assumptions were made, and these will now be briefly discussed.

A value of 3×10^{-3} was assumed for the cooling constant G . This value was chosen because it gave the best overall consistency of the cross-modulation results.

Finally a curve was assumed for the collision frequency ν . Our measurements have however provided us with two independent checks of this curve.

(a) The measurements of cross-modulation from Tromsø show a transition from negative to positive cross-modulation round 65 km., and the level where this transition should occur is

critically dependent on the assumed ν curve. (b) In some cases, no significant differential absorption occurred below the height of the lowest partial reflexions observed, and the measured ratio of the amplitude of the extraordinary and ordinary waves is then determined by ν .

The work reported here has been sponsored in part by the Electronics Research Directorate of the Cambridge Research Center, Air Research and Development Command, US Air Force, through its European Office, under contract AF 61(052)-08.

B BJELLAND
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¹ Fejer, J. A., *J. Atmos. Terr. Phys.* 7, 322 (1955).

² Gardner, F. F., *ibid.* 5, 293 (1954).

³ Gardner, F. F. and Pawsey, J. L., *ibid.* 3, 321 (1953).

A Comparison of Charges on the Electron, Proton and Neutron

WE are gratified that attempts to test the charge-excess hypothesis have begun so soon, but we find the meaning of Hillas and Cranshaw's experiment extremely obscure and we are not able to see that the conclusion claimed follows validly¹.

For example, the ion-trap is well inside the nozzle of the bottle, and any residual charge of the atoms and the gas could readily be compensated by the acquisition of free charges in the nozzle. Although the field produced by any such residual charge would probably itself be insufficient to liberate charges from the material of the nozzle, it would be amply sufficient to drag along charges already liberated. Surface interactions in the nozzle between the fast-moving gas and adsorbed material would very likely lead to production of free charges, and their general presence seems to be confirmed by the drift in potential actually noted. Again, it is not clear what happens to the free charges assumed to be collected by the ion-trap. They would presumably travel to the battery, and this is outside the bottle, the potential of which it is required to measure. The effect of these unbalanced charges is not clear. Furthermore, a potential of the same order as would be expected in the absence of balancing electrons is actually applied to the very box the potential of which it is wished to measure.

The meaning of the observed large ionization current in the air, the fluctuations of the measured current, and the sudden changes of potential, as described, remains quite obscure to us, and it would seem necessary, in view of the minute difference of charge concerned, that much fuller consideration be given to these concomitant effects to establish how they influence the results.

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¹ Hillas, A. M., and Cranshaw, T. E., *Nature*, 184, 892 (1959).

Influence of the Thomson Effect on the θ - φ Relationship for a Constrictive Resistance in Thermal Equilibrium

THE relationship between the temperature θ and the electrical potential φ at any point within a current carrying constrictive resistance in thermal equilibrium can be expressed in the form¹

$$\int_0^{\theta_1} \frac{\lambda}{\chi} d\theta = \frac{1}{2}\varphi^2 - \int_0^{\varphi} \int_0^{\theta_1} \sigma d\theta d\varphi \quad (1)$$

provided that the material is both homogeneous and isotropic

In this equation λ and χ are the thermal and electrical conductivities respectively, and σ is the Thomson coefficient. At the warmest section in the constriction the temperature is θ_1 and the potential φ is arbitrarily taken to be zero.

For most metals the ratio of the thermal and electrical conductivities is roughly proportional to the absolute temperature T , and we have the Wiedemann-Franz-Lorentz equation²:

$$\frac{\lambda}{\chi} = AT$$

The Thomson coefficient σ is likewise approximately proportional to the temperature³, except at temperatures near the melting point, and we can write

$$\begin{aligned} \sigma &= BT \\ &= \frac{\tau\lambda}{\chi} \end{aligned}$$

where A , B and τ are constants.

The θ φ relationship can then be written in the form

$$\int_0^{\theta_1} \frac{\lambda}{\chi} d\theta = \frac{1}{2}\varphi^2 - \tau \int_0^{\varphi} d\varphi \int_0^{\theta_1} \frac{\lambda}{\chi} d\theta$$

If we define an operator Q to be such that $Qf(\varphi)$ is

$$\int_0^{\varphi} f(\varphi) d\varphi$$

then the foregoing equation becomes

$$[1 + \tau Q] \int_0^{\theta_1} \frac{\lambda}{\chi} d\theta = \frac{1}{2}\varphi^2$$

so that:

$$\begin{aligned} \int_0^{\theta_1} \frac{\lambda}{\chi} d\theta &= \frac{1}{[1 + \tau Q]} \frac{1}{2}\varphi^2 \\ &= \frac{1}{2} [1 - \tau Q + \frac{1}{2}\tau^2 Q^2 - \frac{1}{6}\tau^3 Q^3 + \dots] \frac{1}{2}\varphi^2 \\ &= \frac{1}{2} \varphi^2 - \frac{\tau}{2} \varphi^2 + \frac{\tau^2}{4} \varphi^4 + \dots \\ &= \frac{1}{2} [\exp(-\tau\varphi) + \tau\varphi - 1] \quad (2) \end{aligned}$$

Thus:

$$\begin{aligned} \int_0^{\theta_1} \frac{\lambda}{\chi} d\theta &= \int_{\theta_0}^{\theta_1} AT dT = \frac{1}{2} A [T_{\theta_1}^2 - T_{\theta_0}^2] \\ &= \frac{1}{2} A [\exp(-\tau\varphi) + \tau\varphi - 1] \quad (3) \end{aligned}$$

If the product $\tau\varphi$ is small, this result becomes to a close approximation

$$A [T_{\theta_1}^2 - T_{\theta_0}^2] = \varphi \left[1 - \frac{\tau\varphi}{3} \right] \quad (4)$$

Equation (1) corresponds with that part of the constriction in which the electric current flows in the direction of decreasing temperature. In that part where the current flows in the direction of increasing temperature, the algebraic sign of the Thomson coefficient is reversed, and in this part of the constriction the θ φ relationship is

$$\frac{1}{2} A (T_{\theta_1}^2 - T_{\theta_0}^2) = \frac{1}{2} A [\exp(\tau\varphi) - \tau\varphi - 1] \quad (5)$$

$$\text{so that } A (T_{\theta_1}^2 - T_{\theta_0}^2) = \varphi^2 \left[1 + \frac{\tau\varphi}{3} \right] \quad (6)$$

if $\tau\varphi$ is small

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¹ Jones F L. "Fundamental Processes of Electrical Contact Phenomena" (H.J.L.S.O., 1955).

² Sommerfeld A and Bethe H. "Elektronentheorie der Metalle" in "Handbuch der Physik" (Springer, 1933).

³ Fowler R H. "Statistical Mechanics".

Resolution of Wide-range Grating Spectrometers

WHILE it is common experience that the wave number resolution of grating spectrometers tends to be constant over a wide wavelength range¹, the theoretical basis for this observation does not appear to have been clearly formulated. The reason for this omission is doubtless due to concentration of interest on a particular grating or set of gratings and to the diversity of sources of radiation and detectors used for different spectral regions. However, if an unlimited range of gratings be assumed so that maximum diffracted energy can always be assured, and attention is confined to a black body source, some simple relationships may readily be deduced.

From the general form of the grating equation

$$d(\sin \theta_1 + \sin \theta_2) = n\lambda \quad (1)$$

where d is the grating spacing, θ_1 the angle of incidence, θ_2 the angle of diffraction, λ the wave-length and n the order of the spectrum, it is obvious that for a given geometrical configuration λ in the first order is proportional to d . Only the first order need be considered since a grating in the n th order is for our present purpose, equivalent to a grating with spacing d/n in the first order. The spectral interval obtained with a grating in a given spectrometer is proportional both to d , as can be seen by differentiating equation (1), and to the slit width, s .

Now a frequency N in wave-numbers $\propto 1/\lambda$ and, on differentiation, $\delta N \propto \delta\lambda/\lambda^2$, so that for a given spectrometer $\delta N \propto s/\lambda$, since $\delta\lambda$ and λ are both proportional to d . Thus for δN to be constant s must be proportional to λ .

The energy reaching the detector of a grating spectrometer is proportional to $sJ_\lambda \delta\lambda$, where $J_\lambda \delta\lambda$ represents the quantity of radiation between λ and $\lambda + \delta\lambda$, and after substituting for $\delta\lambda$ this is proportional to $s^2 \lambda J_\lambda$. Fortunately, for a black-body at 2000° K the variation of J_λ with wave-length is such that for constant energy on the detector s is nearly proportional to λ from 2 to 20 μ and consequently δN is almost constant over this range. More detailed information is given in Table 1 and it will be seen that at wave-lengths beyond 20 μ the energy falling on the detector cannot be maintained without sacrificing resolution. At 125 μ the maximum slit-width of 15 mm (5:1 reduction on 3-mm aperture of a Golay cell) has been reached in the example given.

As the wave-length increases beyond 20 μ , J_λ becomes proportional to λ^{-4} with over increasing accuracy (Rayleigh-Jeans law) and the energy reaching the detector therefore tends to be proportional to $s^2 \lambda^{-3}$. If this quantity is maintained constant, $s^2 \propto \lambda^3$ and $\delta N \propto s/\lambda \propto \lambda^{1/2}$, approximately in accordance with values of δN given in Table 1.

Table 1

| λ (μ) | J_λ | λJ_λ | s (mm.) | Spectral Interval δN (arbitrary units) | Energy on detector $s^2 J_\lambda$ |
|------------------------|-------------|---------------------|--------------|--|--|
| 2 | 82 | 164 | 0.1 | 1 | 0.164 |
| 10 | 0.088 | 0.88 | 0.5 | 1 | 0.220 |
| 20 | 0.0067 | 0.134 | 1 | 1 | 0.134 |
| 50 | 0.0101 | 0.0090 | 4 | 1.6 | 0.154 |
| 125 | 0.0051 | 0.0041 | 15 | 2.4 | 0.144 |

In the corresponding case when resolution is limited by diffraction rather than by energy, δN is of course independent of wave-length.

A. E. MARTIN

Sir Howard Grubb, Parsons and Co., Ltd.,
Optical Works,
Walkergate,
Newcastle upon Tyne, 6

¹ Lord, E. C., and McCubbin, T. K., *J. Opt. Soc. Amer.*, 47, 689 (1957)

Strength Impairment Mechanism of Glass in Aqueous Systems

RECENTLY we conducted a precision tension ('Instron') strength study of two glass fibre fabrics exposed to several different environments. The resulting data are summarized in Fig 1. When one considers a logical basis for the experimental data, it appears that the water deterioration of glass is a chemical solution process. There is a two-fold evidence for this view. First, the higher pH exposures of the glass fibres give rise to a greater weakening than with a simple water exposure. This agrees well with the observed solubility versus pH relations of typical glasses, and it implies that the molal activation energies for glass fracture in a glass system with microcracks present therein are lower in the high pH solutions^{1,2}. Such high pH solutions might be found useful to accelerate or expedite glass fractures where this slight solution effect can be tolerated. Second, the drying out of the glass fibres after exposure did not serve to restore the full original strength of the glass fibres. If only a physical adsorption were involved a full reversibility could be expected.

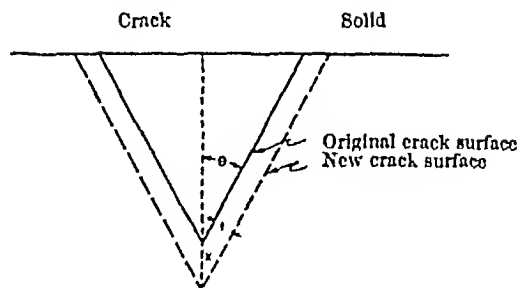


Fig. 1 Relationship of crack angle and rate of attack (chemical). The effect of stresses superimposed is to make λ larger than the theoretical maximum 0. Crack angle, λ , increase of crack depth $= t \cos \theta$, r , rate of attack $\propto t$.

Table of values ($t=1$) from $\lambda = t \cos \theta$

| | |
|-----|------|
| 1° | 57.3 |
| 5° | 23.6 |
| 10° | 11.5 |
| 15° | 8.20 |
| 20° | 5.76 |
| 25° | 3.86 |
| 30° | 2.92 |
| 35° | 2.00 |

Shows rate of change. The high values for sharp cracks in 'constant' geometry case as $dx/d\theta = -t \cos \theta$ at 0.

The literature shows considerable evidence of aqueous (both vapour and liquid) weakening, but this appears to be the first indication of the effects of pH therein and of the probable strength-impairment mechanism implied thereby^{3,4}. The subject glass fibres were of commercial grade, hence they may be expected to have contained numerous microcracks. If the chemical solution were vigorous enough, then presumably the defective surface layers could be removed and the unit glass fibre strength would be significantly increased ($\times 2-4$) over the original

Table 1 SUMMARY OF INSTRON TENSION TEST DATA*

| | Fabric A | Fabric B |
|--------------------------------------|--------------|--------------|
| 1 Air strength (Av. of 20) | 4.82 lb | 6.40 lb |
| 2 Wet strength (3.4 hr exposure) | 4.11 | 3.08 |
| 3 Wet and dried | 4.58 | 6.44 |
| 4 Wet cement strength (average of 5) | | |
| | pH 11 Cement | pH 13 Cement |
| 1-2 hr | 3.02 | 2.85 |
| 3-3 1/2 hr | 4.18 | 2.03 |
| 5-5 1/2 hr | 4.23 | 2.08 |
| 8-8 1/2 hr | 4.30 | 3.11 |
| 24-24 1/2 hr | 4.08 | 3.08 |
| 120 hr (10) | 4.23 | 4.00 |
| | | pH 11 Cement |
| | | 3.64 |
| | | 3.60 |
| | | 3.05 |
| | | 3.77 |
| | | 3.79 |
| | | 3.00 |
| | | 5.23 |

* All are averages of ten specimens unless otherwise noted.

levels⁵. Our results (Table 1), suggest that aqueous chemical solution or film formation is the basic mechanism of the glass fibre deterioration which we have observed. From the literature, it is of interest to note that the water reaction impairment of glass is evidently operative even under ordinary laboratory atmosphere circumstances, for otherwise the paraffin oil (sodium dried) case would not have conferred the reported 20 per cent strength increase⁶. We believe that our finding helps to correlate many apparently unconnected empirical results in the literature and affords predictions of glass fibre and other glass behaviours in various engineering environments.

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METALLURGY

Reversion of Nodules Formed by the Grain Boundary Reaction in Aluminium-Zinc Alloys

The grain boundary reaction is a phenomenon by which nodules with large lamellar precipitates grow from grain boundaries during artificial ageing of super-saturated solid solution alloys. It is called discontinuous or cellular precipitation by some workers. There have been many studies on the grain boundary reaction in aluminium-zinc alloys (Fig 1). We have recently shown that the crystallographic orientation of nodules formed by the reaction is identical with that of the adjoining crystal grain, from which the nodules grow.¹ However, the reversion process, which dissolves the lamellar precipitates in the nodules into matrix and reduces the nodules to the homogeneous solid solution, has not yet been reported.

Optical microscopic observations were made on the reversion process of the nodules in aged aluminium-zinc alloys containing 30 and 40 per cent zinc. Specimens with nodules were solution heat-treated for a short time in a salt-bath regulated at a uniform solid solution temperature. As the heating went on, the lamellar precipitates gradually dissolved into matrix. The surface of the nodules became wavy by electrolytic polishing (Fig 2) on account of the varying zinc concentration, but it became flat by chemical polishing. By further heating all precipitates were dissolved into matrix, though the advancing boundaries of the nodules scarcely changed their positions. A polygonization-like structure was

volume changes of nodules owing to the rapid dissolution of precipitates.

We wish to thank Dr. Z. Takamura for his helpful discussions and Mr. S. Yamaya for his assistance.

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CHEMISTRY

A Paper-Chromatographic Method for the Determination of Suitable Buffer Systems for Countercurrent Distribution

BETINA recently described¹ a method for the determination of suitable pH values for the extraction of antibiotics. He used air-dried buffered paper, which is absorbent and tends to lead to the formation of 'comets', and he did not take into account the ratio of the volumes of the moving and stationary phases r , which also influences the R_F value. Thus the accuracy of his method is rather limited. Using a relatively moist paper and taking into account some quantitative relationships involved, it is possible to make this method more precise.

The distribution of a solute between an organic solvent and a buffer solution is given by

$$\left. \begin{aligned} K &= \frac{l}{1 + K_B/[OH^-]} \text{ (bases)} \\ &= \frac{l}{1 + K_A/[H^+]} \text{ (acids)} \end{aligned} \right\} \quad (1)$$

where K = partition ratio (ratio of overall concentrations of solute in organic and water phase), l = partition coefficient (ratio of concentrations of unionized solute in organic and water phase), K_B , K_A = ionization constant of base or acid.

Assuming that paper chromatography is a continuous extraction process, the R_F is expressed² by

$$\left. \begin{aligned} R_F &= \frac{Kr}{Kr + 1} = \frac{kr}{kr + 1 + K_B/[OH^-]} \text{ (bases)} \\ &= \frac{kr}{kr + 1 + K_A/[H^+]} \text{ (acids)} \end{aligned} \right\} \quad (2)$$

where r is the ratio of the volumes of the moving and stationary phases $r = V_{org}/V_{aq}$.

Plotting of R_F against pH gives S-shaped curve whose shape and position depends on

(a) The partition number kr . The higher kr the higher and further to the left is the curve. At kr values higher than 50 the shape of $R_F = f(pH)$ curves is independent of kr and only their position depends on kr . Thus an α fold increase of kr shifts the curve to the left by $\log \alpha$ pH units.

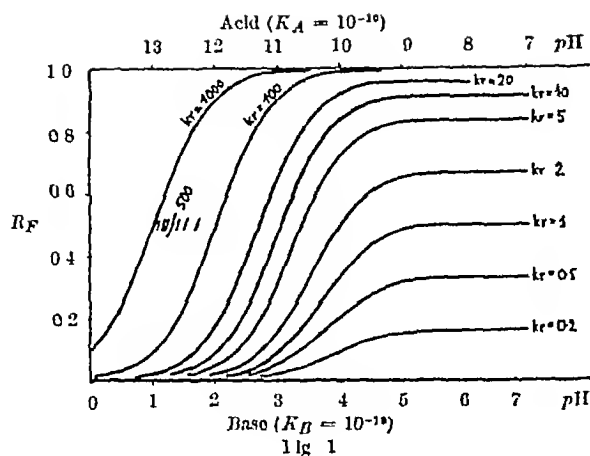
(b) The ionization constant K_B (K_A). The smaller the constant the further to the left is the curve. An α fold decrease in K_B (K_A) shifts the curve by $\log \alpha$ pH units to the left (higher pH values for acids and lower pH values for bases).



Fig. 1. 22 per cent zinc, aged for 16 hr at 100°C. (×40). Fig. 2. 20 per cent zinc, aged for 40 hr at 100°C, and heat-treated for 40 sec. at 300°C. (×400). Fig. 3. 30 per cent zinc, aged for 40 hr at 100°C, and heat-treated for 100 sec. at 800°C. (×400). Fig. 4. 40 per cent zinc, aged for 10 hr at 100°C, and heat-treated for 20 sec. at 400°C. (×80). Fig. 5. 40 per cent zinc, aged for 16 hr at 100°C and heat-treated for 20 sec. at 400°C, then re-aged for 12 hr at 100°C. (×80).

observed in them (Fig 3). When the specimens were chemically polished and etched with a solution of 2 parts nitric acid, 2 parts hydrochloric acid, 1 part of hydrofluoric acid, and 30 parts of ethanol, etch pits were formed within the nodules (Fig 4). The density of these etch pits is greater than that of matrix grains, and moreover they lie on lines nearly perpendicular to the advancing boundaries. The same specimens were re-aged and etched with Wassermann's reagent, when a network structure was clearly observed, caused by preferential precipitation (Fig 5). The nodules in Fig 5 are those which were newly formed by re ageing.

It is presumed that this phenomenon may be a kind of polygonization, that is, a formation of sub boundaries composed of an array of dislocations. These dislocations may be due to the misfitting boundaries formed by a union of the minute nodules grown at the same grain boundary, as was shown in dendritic growth³, or the incomplete annealing of localized plastic deformation produced from the rapid



It can be seen from (2) that the ratio r of the volumes of the mobile and stationary phases must be taken into account when interpreting paper chromatography data for batchwise extraction. For example, in the same system, a tenfold decrease or increase of r changes the pH of the non-mobile phase which is necessary to stop the migration of the substance, by 1 unit. Partition ratio of a solute at a given pH can be calculated from

$$K = \frac{1}{r} \left(\frac{R_F}{1 - R_F} \right) \quad (3)$$

In order to decrease the adsorption of the paper, the use of moist buffered paper, with $W_z = 1.5$, where $W_z = (\text{wt of humid paper})/(\text{wt of dry paper})$ is recommended^{4,6}. For organic solvents slightly soluble in water (hexane, benzene, chloroform), a value of r of about 2 is obtained³. Thus we have

$$K = \frac{1}{2} \left(\frac{R_F}{1 - R_F} \right) \quad (4)$$

The formula (4) permits the determination of the optimal pH value when mixtures are separated by countercurrent distribution. The best separation for a binary mixture is obtained when

$$r\sqrt{(K' \cdot K'')} = 1 \quad (5)$$

Where K' and K'' are the partition ratios of the substances to be separated. Calculating these ratios from (4) at various pH values it is easy to find the value at which the condition (5) is satisfied.

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The method is based on the circular gas chromatograph already described¹. The apparatus consisted of two 5-ft copper columns of $\frac{1}{4}$ -in. outside diameter connected through a circulating pump at one end and a thermal conductivity detector and injection system at the other. Each column contained 12.25 gm of 20-40 mesh size insulating brick. The apparatus was evacuated, and 3.43 gm of partitioning liquid was injected using a hypodermic syringe. After about an hour of pumping, the recorder base-line became constant indicating an even distribution of the liquid. Separations were made at ambient temperature and at vapour pressure of the partitioning liquid. Sample sizes were 20-50 μ l.

Fig. 1 shows, as an example, the detector record for the separation of (A) methyl formate and (B) diethyl ether using furan as the partitioning liquid. The subscripts on the chromatogram for A and B denote the number of times each compound has passed the detector. The amplitude of each peak decreased with the number of cycles. After five to ten cycles the sample became evenly distributed. A new sample can then be injected. The addition of a number of samples made a negligible contribution to column characteristics.

Table 1

| Partitioning liquid | Components in binary mixtures | Cycle retention times (min) | | |
|---------------------|-------------------------------|--------------------------------|-----------------|--------------|
| | | With partitioning liquid alone | Support mixture | Support only |
| Furan | Methyl ether | 5.7 | 5.5 | 4.0 |
| | Methyl formate | 4.1 | 3.9 | 3.5 |
| Furan | 4 Methyl-1 pentene | 12.3 | 12.3 | 5.6 |
| | n pentane | 6.3 | 5.4 | 4.7 |
| Methyl formate | 4 Methyl-1 pentene | 11.7 | 11.9 | 5.6 |
| | n pentane | 5.0 | 4.8 | 4.7 |
| Methyl formate | Methyl ethyl ketone | 22.0 | 22.5 | 12.0 |
| | 2,2,3 Trimethylbutane | 12.0 | 12.3 | 5.0 |

Table 1 shows retention times for the separation of two binary liquid solutions on each of the two partitioning liquids, furan and methyl formate. Retention times are given for the compounds injected individually and as binary solutions. Retention times are also listed for the compounds injected on the same column support but prior to the addition of partitioning liquid and using helium as a carrier gas. Pressures were adjusted to the vapour pressure of the partitioning liquid. Agreement between retention

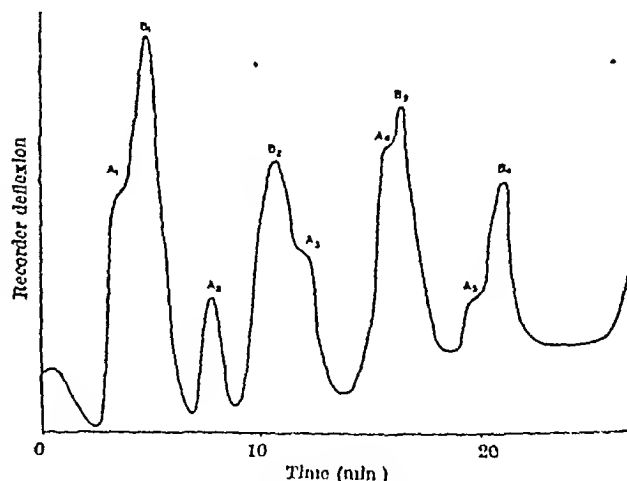


Fig. 1 Mixture injected: A, methyl formate; B, diethyl ether. Furan column.

Volatile Liquid Partition Chromatography

Gas chromatographic separations have been made using the gas phase of the partitioning liquid as the eluting gas instead of the conventional inert carrier gas. This eliminates an essential component in conventional gas chromatography.

tunes for compounds injected singly and in solutions permitted unambiguous identification. Ratios of retention times show that the partitioning liquid is affecting separation although the brick support itself exhibits some selectivity.

Elimination of the inert carrier gas is potentially useful in non analytical applications of gas chromatography. The method is a unique way of using relatively high molecular weight carrier gases.

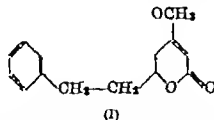
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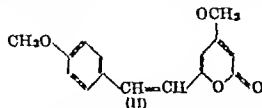
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A New Carbonyl Compound from *Piper methysticum* Forst.

THE rhizomes of *Piper methysticum* Forst. are the raw material from which the Polynesians and other Pacific island peoples prepare their ceremonial (and soporific) beverage 'ava' (also known as *kava* or *kava kava*). The chemical constituents of 'ava root' were first studied over a hundred years ago, but the most extensive investigation was carried out by Borsche and co-workers¹ some thirty years ago. While Borsche established the structure of several constituents, none of these compounds, curiously enough, was found to possess physiological activity. This negative result led to the surmise that activity is perhaps introduced during the preparation of the drink which involved chewing of the root². Van Veen³ in 1938 showed that a substance, marindinin, was responsible for the drug action of *ava*. Marindinin, however, was later shown to be identical with Borsche's dihydrokawaifol⁴ (I), a substance previously found to have no physiological activity⁵.

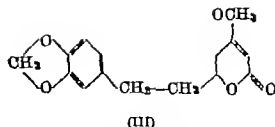


The unresolved state in which this problem had remained for many years induced us some time ago to initiate a chemical re-investigation. The recent upsurge of interest in *ava* originating from several laboratories⁶⁻⁸ prompts us to report our preliminary findings at this time. The Polish workers⁶ re-investigated one of Borsche's compounds, yangonin and corrected its structure from a γ pyrone to an α pyrone (II). The German workers⁷ established for the first



time beyond doubt that the 'ava' constituent dihydro-methystein (III) possesses sedative activity. The Riker group⁸ substantiated this finding and in addition isolated a new substance designated 'compound A'⁸ of empirical composition $C_{14}H_{12}O_3$.

In our work 'ava root' was dried, milled and extracted in a Soxhlet with ethanol for 31 hours



(The material was collected by Dr C. E. Swanholm of this Laboratory at Waialeale Island of Oahu and its identity was established by comparison with an authentic specimen in the Bernice P. Bishop Museum collection.) The solid residue after evaporation of the solvent *in vacuo* was refluxed with ether and filtered while warm to remove insoluble material. Upon cooling of the ethereal solution a yellow solid separated. This solid after two recrystallizations from ethanol melted at 115–118° C and was found to be identical with dihydromethystein (III) by comparison with the published information on this compound and by elemental analysis (performed by Dr A. Bernhardt, Mülheim Germany). The infra red spectrum (Nujol mull) of (III) exhibited the bands reported by the Riker group⁸ as well as a series of bands at 8–11 μ characteristic for the dioxymethylene grouping⁹.

The ethereal mother liquor from which dihydromethystein had been removed was washed successively with acid and base and the ether was removed *in vacuo*. The resulting residue was dissolved in methanol and treated with Girard's reagent T according to Vogel's¹⁰ procedure. The resulting carbonyl components were distilled, yielding as the major fraction a yellow oil, b.p. 104° C/0.4 mm. From spectral considerations this oil appeared to contain a dioxymethylene grouping and a carbonyl function conjugated with olefinic unsaturation. A crystalline 2,4-dinitrophenylhydrazone of this oil melted at 204–207° C (from ethyl acetate). Its infra red spectrum agreed with previously made assignments of functional groups. The combustion analysis of the derivative supported an empirical composition of $C_{14}H_{12}O_3$, although this formulation cannot be considered entirely established.

Further work on this and other minor constituents of *P. methysticum* is in progress. In this connexion it is worth noting that recent work in this laboratory¹ established the presence of alkaloids in this plant to the extent of 0.012 per cent (based on dry root). This finding is in fair agreement with an earlier alkaloid report.¹²

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Structure of Bituminous Coals: Evidence from Distribution of Hydrogen

STUDIES of the structure of vitrinite bituminous coals by X-ray diffraction¹ and infra-red spectroscopic^{2,3} techniques have led to the paradoxical conclusion that although the greater part of the carbon (75 per cent) is ordered in aromatic systems, most of the hydrogen (for example, up to 80 per cent) in a coal containing 83 per cent carbon is attached to the few carbon atoms not in aromatic systems. This paradox cannot be resolved by supposing the aromatic systems to be very large, or if small that they are heavily substituted by alkyl groups: the X-ray evidence denies the first supposition, and the second is inadmissible since the infra-red work shows that long alkyl chains are absent and the ratio of methyl to methylene groups is small. The average molecular weight⁴ is such that one molecule must contain a considerable number of these aromatic systems. Thus a molecule in coal apparently consists of a number of rather small aromatic systems, say 1-3 fused rings, highly substituted by aliphatic groupings that serve mainly to link together the ordered regions and mostly do not terminate in methyl groups.

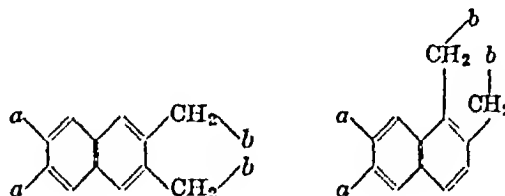
Attempts to construct suitable molecules on paper, and with atomic models—in the first instance with a medium-rank coal of 83 per cent carbon content—show that it is difficult to find any structure that answers the above requirements and at the same time has an elementary composition near that of coals. These experiments lead to the following conclusions:

1 The structure must be built on a more or less regular repetitive pattern, like a polymer, one cannot achieve a high enough degree of substitution if one starts with a random assortment of aromatic systems randomly linked together by short chains and aliphatic rings.

2 Even if some regular pattern is adopted, one can still not attain high substitution if any one aromatic nucleus is linked to any other by only one linkage.

3 It has been possible to find one (and so far only one) type of structure that fits the requirements of the X-ray and infra-red studies and also the elementary

analysis. In this, any one aromatic nucleus is linked to any other by two aliphatic linkages. The prototype of such molecules is 9,10-dihydroanthracene, which can be regarded as composed of two (non coplanar) benzene rings linked by two methylene bridges. In view of the X-ray evidence concerning the size of the aromatic nuclei it is reasonable to consider molecules built up of naphthalene rather than benzene residues; the structure envisaged has for hydrocarbon skeleton a copolymer of units like



where all bonds *a* are linked to CH_2 groups and all *b* to ortho positions in aromatic rings. In addition a third aromatic residue can be attached to any pair of methylene groups yielding a triptycene derivative.

It can be seen that a molecule built to this pattern will be somewhat flexible, but much less so than a chain polymer, it will be far from planar, and, in view of the variety of ways in which units can be linked together, of such extended and irregular shape that it is unlikely to pack regularly with others in a crystal. The greater part of the oxygen in coals can be accounted for as phenolic hydroxyl^{5,6} and strongly conjugated carbonyl chelated to hydroxyl⁵⁻⁸. The structure in Fig. 1 illustrates one way in which units of the type described above can be built together into a molecule. The elementary composition of the molecule shown is that of a typical low-rank coal (82 per cent carbon). The content of hydroxyl and carbonyl groups is close to that found by direct determination on the coal (for refs. see above), and the environment of the carbonyl groups is such that their vibration frequency would be close to 1600 cm^{-1} (the only band in the spectra of coals that can be ascribed to carbonyl¹ is at 1600 cm^{-1}). The molecular weight is 1490, which is somewhat higher than that found experimentally for solvent extracts of the coal, but may well be too low as

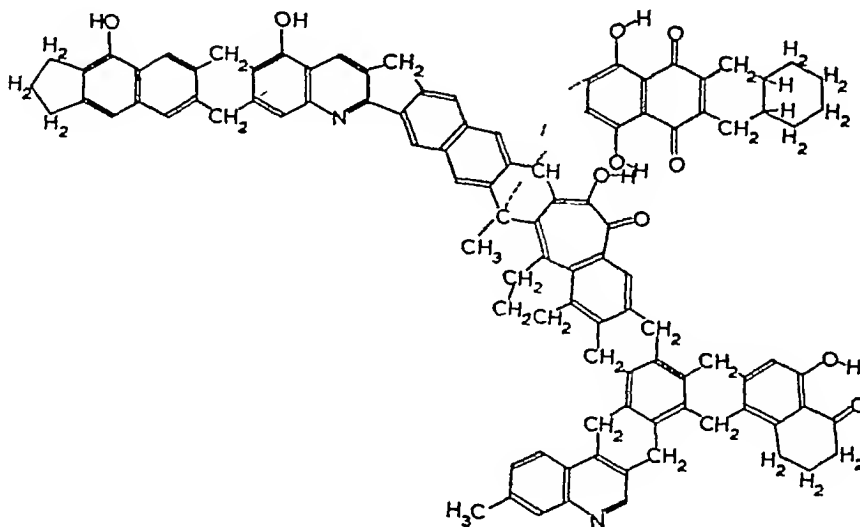


Fig. 1. $\text{C}_{149}\text{H}_{100}\text{O}_{10}\text{N}_2$, molecular weight 1490. Analysis (per cent): 82.1 C, 5.2 H, 1.0 N, 10.7 O (cf. D III coal, 82.3 C, 5.0 H, 1.8 N, 10.9 O, D.M.F. Parr's basis). Ratio $\text{C-H}_{\text{ar}}/\text{C-H}_{\text{al}} = 0.26$. Hydroxyl content, 6.25 per cent O as OH, carbonyl, 4.15 per cent O as $\text{C}=\text{O}$. Ratios, carbon as CH_3/CH_2 , $\text{CH}:\text{C} = 2.23:3.1$. Average composition of non aromatic portion $\text{CH}_{1.5}$. Overall average number of intercluster linkages 3.5 per cluster. Number of atoms per aromatic cluster (including coplanar substituent atoms and assuming oxygen to have the same X-ray scattering factor as carbon), in the range 12-19. Vibration frequency of all carbonyl groups about $1610\text{--}1620\text{ cm}^{-1}$. Fraction of total carbon in aromatic combination

a weight average for the whole coal. The ratio $C-H_{ar}/C-H_{al}$ for the model is 0.26 for the molecular weight chosen, or 0.22 if the weight is doubled. A short extrapolation of the curve given by Brown³ gives a value of 0.18-0.2 for the ratio for a coal of this carbon content. By varying appropriately the oxygen content and the state of reduction of some of the ring systems the composition and functional group analysis of other coals of carbon content in the range 78-80 per cent can be satisfactorily represented, with ratios $C-H_{ar}/C-H_{al}$ equal to or slightly higher than those deduced by Brown³ from the infra red spectra.

Thus there is at least one pattern of structure that can resolve the paradox set by X ray and infra red studies of coal structure. In fact this type of structure can also give a plausible account of a number of other physical and chemical properties of coals, such as reactivity to various reagents, behaviour on pyrolysis, and the thermodynamic non ideality of solvent extracts of coals in solution. The model may therefore be a sufficiently good approximation to serve as a working hypothesis. Its properties in relation to those of coals will be examined in more detail in a paper to be submitted to *Fuel*.

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BIOCHEMISTRY

A New Crystalline Salt of Oxytocin

A CRYSTALLINE salt of oxytocin, its flavanate, was reported several years ago from this Laboratory.¹ The flavanate crystallized in long silky needles and, as was reported, was rather difficult to handle. Therefore a search was made for other crystalline salts of the hormone in the hope of obtaining crystals with more convenient properties.

Formation of precipitates was observed on the addition of various acids and salts (for example, naphthalene- β -sulphonic acid, picric acid, ammonium raneckate, ammonium sulphate sodium hellantate, and *p*-hydroxyazobenzene-*p*'-sulphonic acid) to aqueous (5 per cent) solutions of oxytocin. The precipitates formed by the addition of the last two reagents went into solution on addition of ethanol and on slow evaporation crystals were obtained (Fig. 1). The salt of oxytocin formed with *p*-hydroxyazobenzene-*p*'-sulphonic acid showed the more convenient properties and was studied further. This salt separates from a aqueous ethanol at 22° in orange-coloured crystals (rectangular plates and well formed prisms) with marked birefringence. Crystals were also obtained from only partially purified oxytocin, and the product had a considerably higher potency than the starting material. The avian depressor test is not influenced by the presence of *p*-hydroxyazobenzene-*p*'-sulphonic acid. A loss of



Fig. 1

weight of about 5 per cent was observed on drying the salt at 100° *in vacuo* over phosphorus pentoxide for 6 hr. but the dried substance showed about the same total amount of activity as before drying.

Solutions of *p*'-hydroxyazobenzene-*p*'-sulphonic acid or its salt with oxytocin in 0.1 N hydrochloric acid exhibit a strong absorption band with a maximum at 33 mμ. From the optical densities measured at this wave length the acid content of the salt was determined. Several batches of the crystalline salt were investigated and it was found that they contain 24 per cent of the acid whereas the calculated value is 21.6 per cent. However, after recrystallization of the salt from aqueous ethanol, an acid content of 21 per cent was found. Analytical values were also close to the calculated ones. The new crystalline salt of oxytocin has no well-defined melting point. It sinters at 190-200°, decomposes at 240-250°. The recrystallized salt has a potency of about 400-450 units per mgm (ref. 2).

The salt migrates as a single substance both on paper chromatograms and in countercurrent distribution ($k=2.8$) in a solvent of *n*-butanol water. However, if 0.1 per cent acetic acid is added to this solvent system, *p*'-hydroxyazobenzene-*p*'-sulphonic acid exhibits a distribution coefficient $K=2.8$, whereas oxytocin has a K value about ten times less and so they can be easily separated. Another method for the separation of the hormone from the sulphonic acid is by passing a solution of the salt through a column of the carboxylic anion exchange resin 'Amberlite IRC 50 (H cycle)'. The coloured acid component is practically unadsorbed and is readily removed by washing the column with dilute acetic acid. On the other hand, oxytocin stays on the column and can be eluted afterwards with a mixture of acetic acid / pyridine / water. A still more convenient procedure for the conversion of the new oxytocin salt into salts of the hormone with other acids consists of passing a solution of the coloured salt through a column of a weak anion exchange resin (for example, 'Dowex 3') which was treated previously with an acid, such as acetic acid.

The properties of this salt of the hormone known so far suggest that it may serve, instead of the dried pituitary powder as a working standard preparation in the biological assay for oxytocic activity as well as being useful in the purification of oxytocin.

We wish to thank Dr. William H. Stein and Dr. Stanford Moore for the sample of highly purified *p*-hydroxyazobenzene-*p*'-sulphonic acid used in this

work. Knowing that Bergmann and associates^{3,4} found various sulphonic acids to be useful reagents for forming crystalline salts of amino-acids and peptides, we were fortunate in obtaining from Drs W H Stein and S Moore a group of such compounds which they felt would be worth trying. We are also indebted to Mr Joseph Albert for the microanalyses, to Mr David N. Reifsnyder for his assistance in the experiments, to Miss Dade Tull and Miss Maureen O'Connell for the biological assays.

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Complex Formation of Chlorpromazine with Flavins

In previous reports^{1,2} concerning the mechanism of inhibition of D-amino-acid oxidase, the formation of a complex of the inhibitor and the coenzyme, flavin adenine dinucleotide, was described. Experiments with chlorpromazine, however, indicated a different mechanism of inhibition.

Chlorpromazine concentrations ranged from 4×10^{-6} – 2×10^{-5} M, nearly the maximum solubility at pH 8.3. Complex formation of chlorpromazine and flavin adenine dinucleotide was tested by fluorimetry and spectrophotometry. As chlorpromazine did not quench the fluorescence of flavin adenine dinucleotide or shift its spectrum, complex formation of chlorpromazine with flavin adenine dinucleotide was excluded as the mechanism of inhibition of D-amino acid oxidase by chlorpromazine. From these results and kinetic analysis of enzymic reactions, the inhibition was attributed to the competition of chlorpromazine with flavin adenine dinucleotide³.

However, it has been suggested recently⁴ that the phosphorescence of riboflavin is quenched by chlorpromazine, so this was re-examined using higher concentrations of chlorpromazine than 10^{-5} M. Tests were carried out at pH 6.5–7.0, where chlorpromazine is more soluble than at pH 8.3.

In the preliminary experiments, the addition of excess chlorpromazine to flavin adenine dinucleotide solution at pH 6.5 changed the colour of the latter from yellow to brownish yellow and diminished its fluorescence.

The absorption spectrum of the mixture of flavin adenine dinucleotide (9×10^{-6} M) and chlorpromazine (2×10^{-3} M) in phosphate buffer (M/10, pH 6.5) was measured. As shown in Fig 1, it was lower than the theoretical curve obtained by adding the spectra of flavin adenine dinucleotide and chlorpromazine.

The quenching action of chlorpromazine on the fluorescence of flavin adenine dinucleotide was then analysed. The relation between the fluorescence intensity of flavin adenine dinucleotide and the concentration of chlorpromazine (C) is

$$f/f^1 = 1 + C/k$$

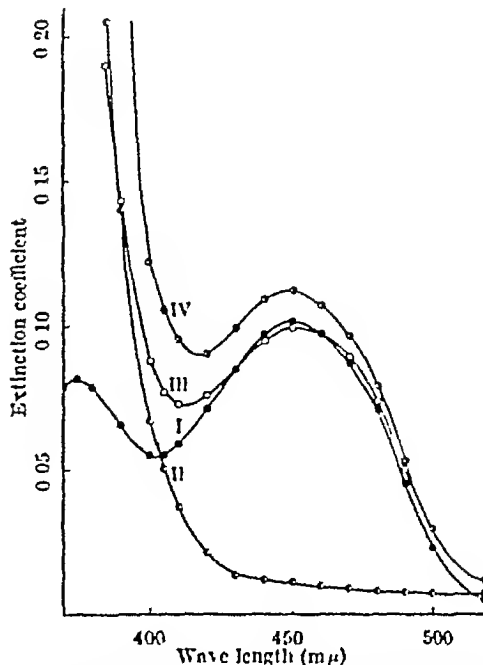


Fig 1 Spectra of flavin adenine dinucleotide and chlorpromazine. I, flavin adenine dinucleotide (9×10^{-6} M) in phosphate buffer (M/10, pH 6.5), II chlorpromazine (2×10^{-3} M) in the same buffer, III, mixture of chlorpromazine (2×10^{-3} M) and flavin adenine dinucleotide (9×10^{-6} M) in the same buffer, IV, theoretical spectrum of flavin adenine dinucleotide + chlorpromazine.

where f and f^1 are the fluorescence intensities of flavin adenine dinucleotide in the absence and in the presence of chlorpromazine, and K is the dissociation constant of chlorpromazine from its complex with flavin adenine dinucleotide. By plotting f/f^1 against C , a straight line, with intercept 1, can be obtained, and K can be calculated from the slope of this line.

The plots of f/f^1 obtained by experiment gave a straight line as shown in Fig 2. K was calculated to be 1×10^{-3} M.

Fluorimetric and spectrophotometric analyses were also applied to the interaction between chlorpromazine and riboflavin or flavin monophosphate. Nearly the same results were obtained as with flavin adenine dinucleotide, and the dissociation constant of

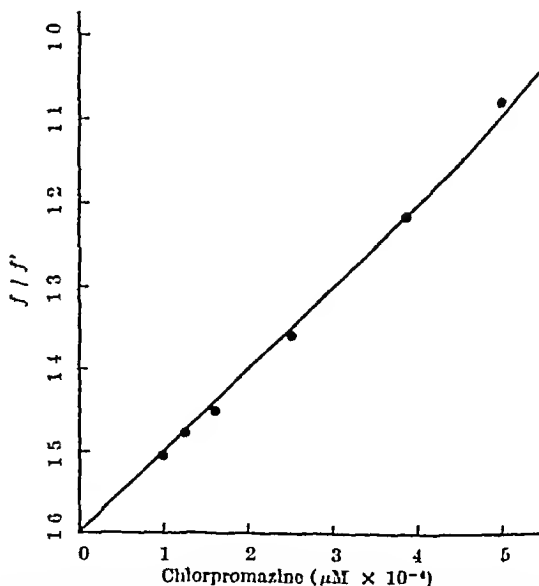


Fig 2 Quenching action of chlorpromazine on the fluorescence of flavin adenine dinucleotide. f and f^1 correspond to the fluorescence intensities of flavin adenine dinucleotide (1×10^{-6} M) in the absence and in the presence of chlorpromazine in phosphate buffer (M/10, pH 7.0).

chlorpromazine from its complex with riboflavin or flavin monophosphate was also calculated to be $1 \cdot 10^{-3} M$ from fluorimetry.

From these results, it may be concluded that chlorpromazine forms a complex with the isoalloxazine part of flavins at a concentration of $10^{-3} M$. Considering the order of the dissociation constants of the complexes calculated from fluorimetry it is clear that complex formation can be excluded from the mechanism of inhibition of D amino acid oxidase by chlorpromazine. However the complex formation of chlorpromazine with flavins could be significant *in vivo* if higher concentrations of chlorpromazine than $10^{-3} M$ were reached. For example, the fact that the injection of flavin adenine dinucleotide can reverse the effects of chlorpromazine on an electroencephalogram can be partly explained by the formation of a complex of these two compounds in the living body.⁸

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The preparation thus obtained reveals a strong activity in the test on the gain of weight of the uterus of immature mice.²

Table 1 shows the increase in purity at the different stages (2 experiments).

The glycoprotein nature of the preparation was demonstrated by the determination of the hexoses (13 per cent) hexosamines (11 per cent) and the high percentage of sialic acid (8 per cent). Electrophoresis in the liquid phase according to Tiselius³ at pH = 8, 6, 4, $\mu = 0.1$, revealed the non homogeneous quality of the product. Finally, the product was tested histologically on the ovaries of immature rats hypophysectomized 2 months before. A distinct follicular maturation was observed together with a protoplasmic hypertrophy of the interstitial cells.

Thus even at this degree of purity the preparation possesses both follicle-stimulatory and luteinizing stimulatory properties.

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Preparation of a Highly Purified Sample of the Urinary Gonadotrophin

The difficulty encountered in the determination of the physical and chemical properties of the urinary gonadotrophin is closely related to its small concentration in urine. It is also the reason why so many studies concerning this hormone refer mainly to its biological properties. Nevertheless it would be of considerable interest to obtain gonadotrophin of high purity. That is why we attempted to isolate it from the urine of sterilized women or women at the menopause. We report here our preliminary results.

The urine is adjusted to pH 4.5 and 3 parts of 95 per cent alcohol are added. The precipitate is extracted 3 times with 50 per cent alcohol. The residue is separated by centrifugation and the remaining liquid is concentrated to a 75 per cent alcoholic solution. The precipitate is washed, dried and dissolved in a buffered acetate solution (pH 4.5). The resulting solution is adsorbed on kaolin.¹ The ammoniacal eluate is adjusted to pH 5.1 then 3 parts of acetone are added. The precipitate which is formed is centrifuged, washed and dried. It is then passed through an ion exchange resin ('Permutit' or 'Dowex'). The product is purified without appreciable loss. The association of two ion exchange resins brings no improvement.

Biosynthesis of Carotenes in Carrot Extracts

Using methyl and carbonyl labelled acetate Grob and Butler^{1,2} have shown that both carbon atoms of acetate are extensively incorporated into β -carotene synthesized by *Mucor hemalis*. They also found that pantothenic acid and pantothenic stimulate β -carotene synthesis, on the basis of this fact they have suggested that coenzyme A is involved in carotenogenesis. Studies have therefore been made to investigate the role of coenzyme A in the biosynthesis of carotenoids. The present study details the results of the experiments on carotene biosynthesis using extracts prepared from carrots (*Daucus carota*).

The carrots after removal from the soil were cooled in crushed ice and in the frozen condition they were cut into small pieces 10 gm (fresh wt.) were ground with 100 ml phosphate buffer (0.2 M pH 5.8) at 0°C for about 10 min and the fine debris removed by centrifugation at 500g for 5 min. The supernatant solution of the carrot extract (containing protein concentration of about 6 mg/ml) were incubated at 28°C in 250 ml Erlenmeyer flasks on a rotary shaker for 18 hr with the desired substrates in phosphate buffer (pH 5.8 0.2 M). Carotenes were extracted in freshly distilled ether. The etheral extract was freed of moisture by treating with anhydrous sodium sulphate. The carotenes were transferred in 5 ml petroleum ether (b.p. 80–100°C) and were determined as β -carotene

Table 1

| | Experiment 1 | | Experiment 2 | |
|---------------------|---|--|---|--|
| | Weight of the final product (mg/ml urine) | Weight of the uterus/weight of the product | Weight of the final product (mg/ml urine) | Weight of the uterus/weight of the product |
| Alcohol precipitate | 571 | 22 mg/ml | 230 | 25 mg/ml |
| Kaolin extract | 4 | 218 mg/ml | 16 | 80 mg/ml |
| Permutit eluate | 0.4 | 33 mg/ml | 3 | 84.9 mg/ml |
| | | 0.0033 mg/ml | | 0.001 mg/ml |

by measuring E_{450} m μ . ($E_{1\text{cm}}^{1\%} = 2500$) in a Beckman photo-electric spectrophotometer. Co-enzyme A and yeast extract used during the experiment were commercial preparations from Nutritional Biochemicals Corporation and Difco Laboratories respectively. Adenosine triphosphate was prepared in the laboratory by Lepage's method³.

Table 1 CAROTENE SYNTHESIS BY CARROT EXTRACT INCUBATED WITH VARIOUS SUBSTRATES

The test system contained final concentrations of 0.2 M phosphate buffer pH 5.8, substrates in amount listed below and 5 ml of carrot extract in a total volume of 30 ml in each 250 ml Erlenmeyer flask, incubated 18 hr at 28° C

| Substrate | Amount added (mgm) | Carotene amount in μ moles | | |
|-----------------|--------------------|--------------------------------|------------------|------------|
| | | Zero time | After incubation | Net change |
| Glucose | 0.25 | 0.148 | 0.101 | +0.013 |
| Glucose | 0.25 | 0.148 | 0.200 | +0.052 |
| + yeast extract | 50 | | | |
| Acetate | 250 | 0.148 | 0.168 | +0.020 |
| Acetate | 250 | 0.148 | 0.217 | +0.069 |
| + yeast extract | 50 | | | |
| None (control) | — | 0.148 | 0.123 | —0.025 |

Table 2 COFACTORS REQUIREMENTS FOR INCORPORATION OF ACETATE INTO CAROTENE BY CARROT EXTRACTS. THE CONDITIONS WERE EXACTLY AS IN TABLE 1

| Substrate added* | Net change in amount of carotene (in μ mole) |
|---|--|
| Acetate | +0.0225 |
| Acetate + yeast extract | +0.0600 |
| Acetate + coenzyme A + adenosine triphosphate | +0.0039 |
| Acetate + coenzyme A | +0.035 |
| Acetate + adenosine triphosphate | +0.0425 |
| None (Control) | —0.0192 |

*The amounts of acetate and yeast extract added were same as given in Table 1 whereas coenzyme A and adenosine triphosphate added were 0.1 and 5.0 mgm respectively.

Table 1 lists the results of an experiment showing that carrot extracts can form significant amounts of carotene from glucose as well as from acetate. It seems that acetate is superior to glucose in synthesizing carotenes in carrot extracts. From the results of control experiments it can be seen that some amounts of carotene originally present in the experiment (at zero time) disappears during the incubation. For this reason it appears that the true amount of carotene synthesized in the experiment may be considerably greater than the net accumulation determines. Because of the magnitude of the rate of destruction of carotenes in such control experiments, they are usually performed as a routine check in all tests of carotene synthesis.

Also included in Table 1 are results of experiments which show that yeast extract stimulates carotene synthesis both in acetate as well as in glucose containing media. Friend *et al.*⁴ observed that yeast extract stimulates growth and carotenogenesis in *Phycomyces blakesleeanus* in acetate medium. They also observed that none of the B vitamins present in the yeast extract is responsible for the stimulation.

The results of an experiment recorded in Table 2 indicate that coenzyme A and adenosine triphosphate present in the yeast extract might be the stimulating factors.

With this information at hand, it appeared necessary to approach experimentally the detailed mechanism with the use of cell-free preparations. Preliminary experiments have shown that most of the

synthesis in carrots is localized in the supernatant fraction obtained by centrifuging the carrot extract at approximately 18,500 *g* for 30 min at 0° C.

We wish to thank Dr C V Ramakrishnan for his interest in this work and the M S University Research Foundation for a grant towards laboratory expenses.

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Ribonucleases of Mouse Tissues and of the Ehrlich Ascites Tumour

DURING investigations of the infectivity for the Ehrlich mouse ascites tumour of ribonucleic acid isolated from tissues infected with Mengo encephalitis virus¹, it was found that some factor in the ascitic plasma, the fluid in which the tumour cells are suspended *in vivo*, prevented the production of virus by the tumour cells. Since ribonuclease is known to destroy the infectivity of 'Mengo-RNA' preparations, the ascitic plasma was examined for the presence of this enzyme. It was found to have a significant level of activity, releasing 600 ± 90 μ gm ribonucleic acid-phosphorus/hr/ml (average of 8 determinations) from $\frac{1}{2}$ per cent ribonucleic acid at 37°C and pH 7.4 (veronal-acetate buffer).

Careful construction of a pH-activity curve revealed that the ascitic plasma ribonuclease is optimally active at pH 7.3. Since this differed from the reported pH optima of the alkaline ribonucleases of liver and pancreas, and preliminary estimations showed that the Ehrlich tumour cells were almost devoid of activity at neutral pH, it raised a question as to the origin of the ascitic plasma enzyme. In an effort to provide an answer, ribonuclease activities (both acid and alkaline) were determined for a number of normal mouse organs, and for cells of the Ehrlich ascites tumour.

The ribonuclease assay procedure depended on the formation, from yeast ribonucleic acid, of perchloric acid-soluble substances absorbing at 260 m μ . Incubations were carried out at 37°C. in veronal-acetate buffers of constant ionic strength (0.06) at 15 pH values between 5.0 and 8.5. Tissue homogenates were prepared in distilled water and were diluted so that all contained similar levels of activity per unit volume.

All normal organs with significant ribonuclease activity had an acid maximum between pH's 5.6 and 5.8, with the exception of brain (6.0) and pancreas. Skeletal and cardiac muscle, and the combined formed elements of the blood had negligible ribonuclease activity. In the alkaline range, the tissues could be classified into four groups (Table 1) on the basis of their pH optima and activity levels.

(1) Pancreas had a vastly greater activity than any other tissue. It, alone, had a sharp optimum at pH 7.3. No acid peak could be demonstrated, probably because of the significant activity of the alkaline pancreatic enzyme in the acid region.

(2) The lymphoid tissues spleen, thymus and lymph nodes, had similar patterns of activity. The pH activity curves of all three were characterized by broad plateaux between the limits indicated in Table 1. The thymus curve had no differentiable peaks while the lymph nodes and spleen showed somewhat more activity in the region of pH 7.3. Lung and intestinal mucosa gave similar curves with more definite differentiation of peaks at pH 7.3.

(3) The parenchymatous organs, kidney, liver and submaxillary salivary gland, formed a distinct group with pH optima in the region of 7.8.

(4) Brain, muscle (skeletal and cardiac) and the combined formed elements of the blood had minimal levels of activity with no clearly defined maxima in their pH-activity curves.

Mouse blood serum and ascitic plasma had similar levels of activity, and the pH-activity curves of both showed single, well-defined maxima at pH 7.3.

Compared with the normal tissues the ascites tumour cell appeared to be quite novel. It had little activity at physiological pH's but showed pH optima at 4.8 and 8.4. In the presence of $4 \times 10^{-4} M$ *p*-chloromercuribenzoate, a compound which has been shown to reverse the inhibition of ribonuclease by a naturally occurring ribonuclease inhibitor of rat liver¹, the picture changed completely. As illustrated in Fig 1 the acid and alkaline peaks disappeared and were replaced by a broad maximum between pH's 6.5 and 7.2, with a ten fold increase of enzyme activity at pH 7.0. The ascites tumour cells thus appear to contain a potent inhibitor of ribonuclease, and the two optima seen in the pH activity curve in the absence of *p*-chloromercuribenzoate may be a reflexion of dissociation of the enzyme inhibitor complex at acid and alkaline pH's.

The pancreas is the only tissue with a sharp pH optimum at 7.3, and the shapes of the pH-activity curves of the serum and ascitic plasma are identical with that of the pancreas. The localization of pancreatic ribonuclease in the zymogen granules² and the demonstration of carbamylcholine induced liberation of ribonuclease from pancreas slices³ suggest that this enzyme is part of the digestive secretion of this organ. In support of this conclusion is the fact that the intestinal juices were found to have a relatively high level of activity (Table 1) with a well-defined optimum at pH 7.3.

The similarities between the curves obtained with lung and small intestine and those of the lymphoid

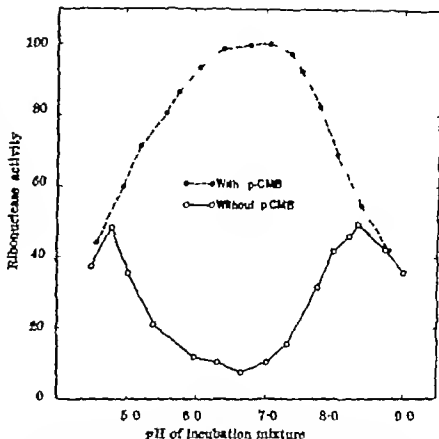


Fig. 1. pH activity curve of Ehrlich tetraploid ascites tumour cells measured \bigcirc in the presence of $3 \times 10^{-4} M$ magnesium ion and \bullet with $3 \times 10^{-4} M$ magnesium ion and $4 \times 10^{-4} M$ *p*-chloromercuribenzoate. Ribonuclease activity is expressed as the percentage of the activity obtained at the optimum pH with inhibitor immobilized by *p*-chloromercuribenzoate.

tissue may be due to the relatively large accumulations of lymphoid elements in both tissues and the tendency to show peaks at pH 7.3 to the large blood content of the lung and to adsorbed pancreatic enzyme by intestinal mucosa. The broad maxima characteristic of the lymphoid tissue curves may be due to the presence in these tissues of several ribonucleases with pH optima between pH's 6.5 and 7.3. To consider these tissues as the source of the serum enzyme would require the assumption that a ribonuclease optimally active at pH 7.3 was released preferentially therefrom.

The most probable source of the serum and ascites plasma ribonuclease, therefore, appears to be the pancreas, on the basis of the striking similarities in the shapes of the pH activity curves and of the physiological peculiarities of the pancreatic enzyme. The exocrine nature of this enzyme suggests two possible routes for its entry into the blood stream. It could be absorbed during its secretion by the pancreas, or it could be absorbed by the intestine after discharge into the gut lumen.

The apparent grouping of the tissues according to the level and pH optimum of the alkaline ribonuclease may represent functional alliances within each group with respect to their nucleic acid metabolism. Investigations are in progress to ascertain whether the unique pattern of activity found in the Ehrlich (tetraploid) ascites tumour cells is characteristic of other malignant and free living cell types as well.

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Table 1. ALKALINE RIBONUCLEASE OF MOUSE TISSUES.

| Tissue | Mean activity* | pH maximum |
|--|----------------|------------|
| (1) Pancreas | 9,000 | 7.3 |
| (2) Spleen | 153 | 6.7 → 7.4 |
| Thymus | 90.0 | 5.4 → 7.1 |
| Peripheral lymph nodes | 84.4 | 6.8 → 7.4 |
| Intestinal mucosa | 100 | 6.8 → 7.4 |
| Lung | 28.8 | 6.8 → 7.5 |
| (3) Kidney | 34.4 | 7.9 |
| Salivary gland | 16.8 | 7.8 |
| Liver | 12.8 | 7.8 |
| (4) Brain | 3.2 | Indefinite |
| Muscle | 0.9 | Indefinite |
| Heart | 0.4 | Indefinite |
| Blood cells | 0.2 | Indefinite |
| Normal serum | 4.0 | 7.3 |
| Ascitic plasma | 3.8 | 7.3 |
| Intestinal contents | 144 | 7.3 |
| Ehrlich ascites tumour cells | 5.6 | 8.3 |
| Ehrlich ascites tumour cells + <i>p</i> -chloromercuribenzoate | 8.5 | 6.6 → 7.2 |

* Ribonuclease activity is expressed as the change in optical density at 260 mμ in the acid-alkaline experiment divided by 1 gm. (wet weight) of tissue in 50 ml. under the conditions of assay. Values are the means of several estimations.

Paper Electrophoresis of Trypanosomal Extracts

ELECTROPHORESIS has been of value in determining the physico-chemical constitution of cell-free extracts of micro-organisms^{1,2}. These studies have been confined mainly to the bacteria and no such investigation of trypanosomal extracts has been made. Moving-boundary electrophoresis has been the method most frequently employed to analyse microbial extracts although the simplicity of paper electrophoresis would be of obvious advantage. The purpose of this communication is to describe the technique for paper electrophoresis and the resultant electrophoretic patterns of trypanosomal extracts.

Trypanosomes were obtained from citrated heart-blood of heavily-infected rats by differential centrifugation. After the third washing with physiological saline in a graduated centrifuge tube, the trypanosomes were re-suspended in distilled water to the proportion of 0.5 ml water to every 0.1 ml packed trypanosomes. This suspension was shaken with ballotin beads in a Mickle disintegrator for half an hour. The extract contained approximately 20 mgm protein/ml. The type of buffer used appears to be a critical factor in electrophoresis of the extracts. Longworth's veronal buffer at pH 8.6, Sorensen's phosphate buffer at a pH range of 6.0-8.2 and McIlvaine's phosphate-citric acid buffer all failed to effect adequate migration and demarcation of the several fractions. The buffer described by Bodman³ gave excellent results. This buffer of pH 8.7 is composed of barbitone soluble 40 gm, sodium acetate 26 gm, magnesium sulphate 2 gm, N/10 sulphuric acid 256 ml, and distilled water to make a final volume of 5 litres. The buffer is always discarded after use. The extracts were applied to strips of Whatman 3 MM paper (no separation occurred on bacterial-membrane filters) with a Pastour pipette using a ruler as a guide across the horizontal electrophoresis tank. A potential difference of 130 V was applied for 20 hr after which the strips were fixed in a solution of 9 parts methanol and 1 part glacial acetic acid and then stained with bromophenol blue. Electrophoretograms of the patterns were constructed with an 'EEL' scanning unit.

Fig 1 shows a typical electrophoretogram of an extract of *Trypanosoma rhodesiense*. It will be seen

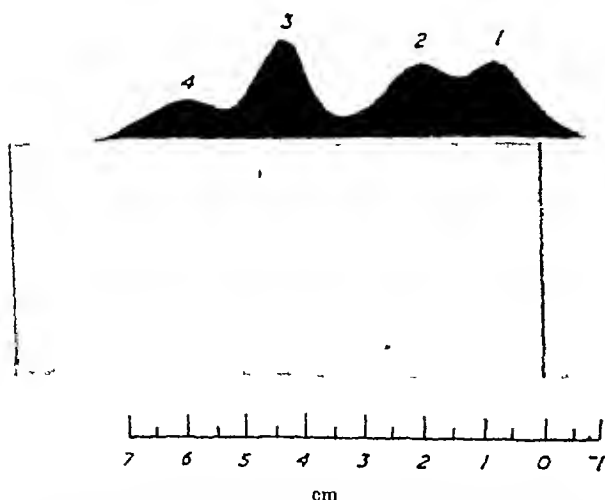


Fig 1 Paper electrophoretic analysis of a cell free extract of *Trypanosoma rhodesiense*. Electrophoresis performed in Bodman's veronal acetate buffer of pH 8.7 at 130 V for 20 hr.

that the extract is composed of four fractions. Fraction 1 and the closely associated fraction 2, both of low mobilities, are 28.75 per cent and 23 per cent of the total respectively. Fraction 3 which appears as a distinct band of greater mobility contains 26.65 per cent of the total. Fraction 4 which appears as a 'tail' is present in most, but not all samples, in this instance it amounts to 16.6 per cent of the total. There is a slight variation in the proportion of fractions from sample to sample but the number of fractions, except for fraction 4, and their respective mobilities seem to be constant.

Work is now in progress to determine the chemical nature of the individual fractions and to compare the electrophoretograms derived from various species of pathogenic African trypanosomes. It is also foreseen that the isolation of the trypanosome's antigens and the application of immuno-electrophoretic techniques may shed some light on the perplexing problem of the apparent antigenic variation occurring during the course of some trypanosome infections.

This work will be published in detail elsewhere.

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Hydrolysis of 'Heated' Haemoglobin

A DIMINISHED rate of alkaline denaturation of haemoglobin is not confined to foetal haemoglobin only, as was already found by Singer *et al.*¹ Künzer² in a survey on the occurrence of 'foetal' haemoglobin in various blood disorders found an alkali-resistant fraction in the anaemia developing after burns. Our observations have confirmed Künzer's and it has been found that this minor haemoglobin abnormality develops during the first few hours after the burn and persists for some time. This abnormality develops before that of clinical anaemia and involves the patients' own and transfused cells. The detailed results of this work will be published elsewhere.

Heating to 52°C for four minutes followed by incubation at 37°C in glucose acid citrate in an atmosphere of nitrogen did *in vitro* produce a similar lesion.

Hemolysates were rendered stroma free and concentrated by ultra-filtration.

Aliquots were hydrolysed with 1.5 N hydrochloric acid at 110°C for periods of 5, 10, 15, 20, 25 and 30 minutes. The hydrolysis products in the supernatant were separated by drying measured aliquots in polythene caps *in vacuo* over phosphorus pentoxide and potassium hydroxide at approximately 4°C. The dried residues were quantitatively applied to Whatman 3 MM filter paper squares and the peptides separated by combined electrophoresis and chromatography³. Parallel experiments were run simultaneously. Fifteen spots could be located after 30 minutes hydrolysis and these were arbitrarily numbered. To investigate the rate of liberation of the peptides, the colour intensities of the spots 1, 2, 3, 9 and 10 were determined according to the method described by Meyer⁴. The readings were expressed as

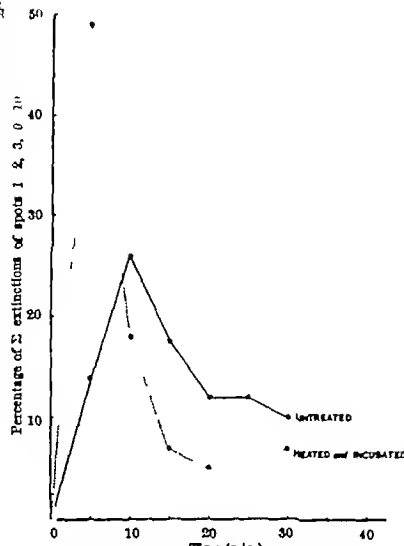


Fig 1 The rate of liberation of spot 10 by acid hydrolysis

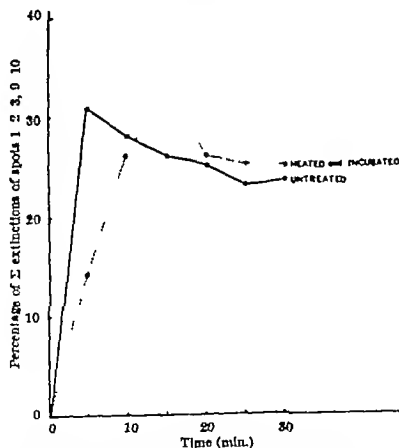


Fig 2 The rate of liberation of spot 1 by acid hydrolysis.

a percentage of the sum of the extinctions of all the spots investigated. Fig 1 shows the rates of liberation of spot 10 and Fig 2 the same for spot 1 as averages of duplicate experiments. Spot 10 was liberated more rapidly from heated blood than normal blood while the rate of liberation of spot 1 was somewhat delayed in the heated sample. The intensity of the areas 2, 3 and 9 remained almost constant throughout the period investigated. The other areas showed little intensity change. The area 1 derived from normal blood shows a hydrolysis rate closely corresponding to a first-order reaction, while spot 10 derived from heated blood approximates to a first order reaction. Complete hydrolysis of the peptides 1 and 10 gave rise to 12

amino-acids—lysine, valine and leucine being the predominant. Both peptides 1 and 10 show similar electrophoretic mobility but 10 migrates much faster on chromatography. It is reasonable therefore to suppose that 10 is derived from the degradation of 1.

The differing behaviour of the two hemoglobin samples on hydrolysis could be due to the differing rates of exhaustion of some of the enzymes of the glycolytic cycle, which could be the reflection of an accelerated general ageing process causing an early accumulation of lactate and pyruvate. This causes a decrease in internal cell pH which could affect the secondary configurational structure of the globin and therefore its rate of acid hydrolysis.

The primary defect responsible for these findings may be the irreversible inactivation of glucose 6 phosphate dehydrogenase or of phosphoglycerate dehydrogenase or both. The early decrease of activity of these enzymes *in vivo* and *in vitro* in the ageing erythrocytes was observed by Lohr *et al.*⁴ A primary developing deficiency in glucose 6 phosphate dehydrogenase might give rise to a similar behaviour on acid hydrolysis of the erythrocytes of familial idiopathic hemoglobinemia.

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Interaction of Streptomycin and Dihydrostreptomycin with Apo- and Co-dehydrogenases

It is well known that streptomycin reacts with nucleoproteins and highly polymerized nucleic acids¹ to form precipitates *in vitro*.

Attempts to discover whether streptomycin can also react with unpolymerized nucleotide compounds such as mono-, di- or oligo nucleotides, have shown that no precipitate is formed with the compounds tried hitherto.²

Nevertheless it is possible that streptomycin reacts with these nucleotides without forming a visible precipitate. In order to test this last possibility experiments were carried on the interaction between streptomycin and enzymes with nucleotide like coenzymes or prosthetic groups.

The diphosphopyridine nucleotide linked yeast alcohol dehydrogenase was used for this purpose. The dehydrogenase was prepared in a crystalline state from baker's yeast according to Racker.³ 500 and 5 000 μ gm streptomycin (Pfizer streptomycin sulphate) or dihydrostreptomycin (Poulenc sulphate) were added and the diphosphopyridine nucleotide reduction rate when coupled with oxidation of the ethanol was determined with a quartz spectrophotometer SF 4 at 340 m μ .

Streptomycin had no effect on the oxidation of ethanol by the dehydrogenase-diphosphopyridine nucleotide mixture, whereas monododecanoic acid stopped the process immediately (Fig 1).

Streptomycin and dihydrostreptomycin, incubated for 24 and 48 hours with

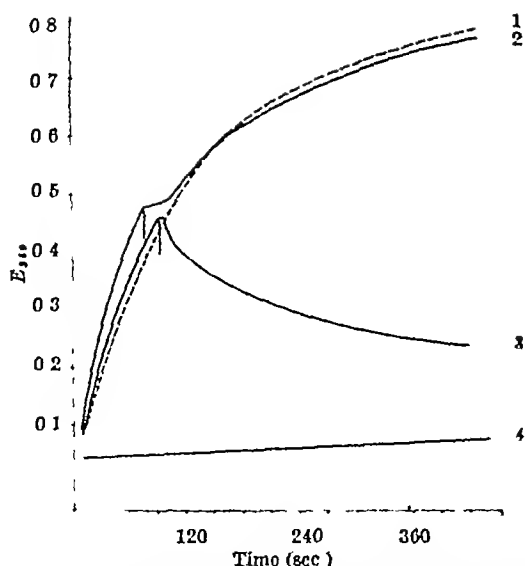


Fig 1 Reduction of diphosphopyridine nucleotide (0.06 μ mole) by crystalline alcohol dehydrogenase (0.018 mgm) with ethanol as substrate (0.6 μ mole). (1) Control curve without any inhibitor (2) Streptomycin sulphate 500 μ gm (3) Iodoacetate acid, as a specific inhibitor (4) All components as in the main test except the specific substrate (ethanol)

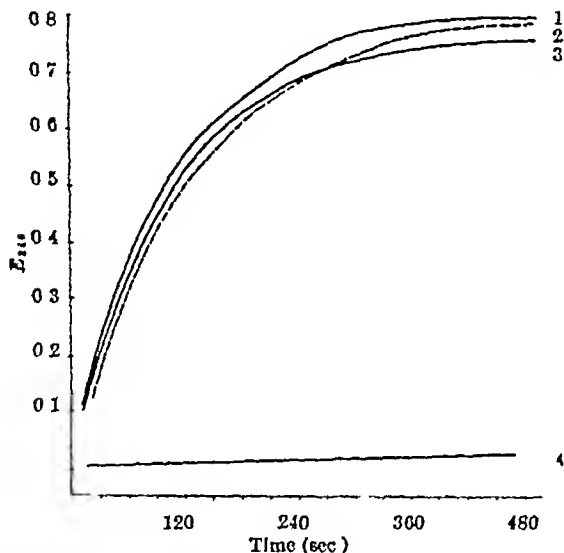


Fig 2 Influence of preincubation of diphosphopyridine nucleotide with streptomycin or dihydrostreptomycin on the reduction of diphosphopyridine nucleotide in the presence of alcohol dehydrogenase and ethanol. All concentrations the same as in Fig 1. (1) Diphosphopyridine nucleotide incubated with streptomycin for 50 hr (2) Diphosphopyridine nucleotide incubated without antibiotics for 50 hr (3) Diphosphopyridine nucleotide preincubated with dihydrostreptomycin at 0°C for 50 hr (4) Same components as in the main test without the substrate

diphosphopyridine nucleotide to test for a possible interaction with the nucleotides, but the reduction curve was identical with that for unincubated diphosphopyridine nucleotide (Fig 2).

We then examined whether incubation at 0°C of the apodehydrogenase itself influenced its activity. As Fig 3 shows there is a remarkable diminution in the reduction rate of diphosphopyridine nucleotide when the apodehydrogenase previously incubated with streptomycin was used. The extent of inhibition depends upon the contact time of the enzyme protein with the antibiotic.

It seems that the frequently observed inhibition of dehydrogenase activities by streptomycin is due probably not to its reaction with the coenzyme but rather to that with the protein moiety of the enzyme.

To what extent this phenomenon is responsible

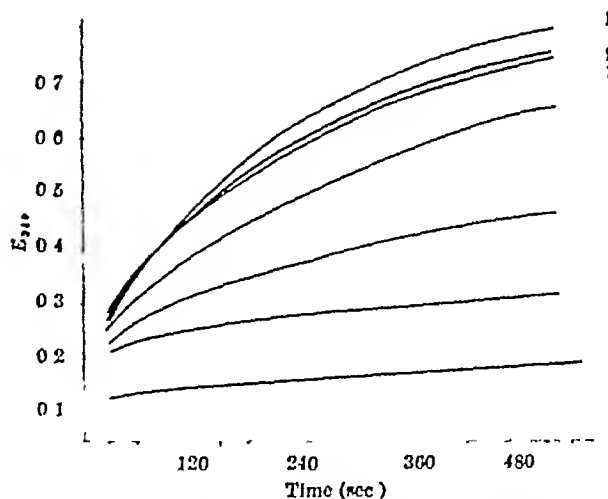


Fig 3 The inhibition of diphosphopyridine nucleotide reduction by streptomycin when preincubated with alcohol dehydrogenase for various times. (1, 2, 3) Controls for 24, 48 and 60 hours respectively, preincubation without antibiotic; streptomycin being added at the start of the reaction. (4, 5, 6) Apodehydrogenase preincubated with streptomycin at 0°C for 24, 48 and 60 hr respectively. (7) Without substrate. Experimental conditions as in Fig 1.

for the anti-bacterial action of streptomycin remains in doubt, probably it is not very important since the inhibition is slow. As far as we know no such experiments have hitherto been carried out with the streptomycin group of antibiotics. Streptomycin has even been used to remove impurities from some purification procedures for enzyme proteins⁴ with little loss of their activity.

A more detailed report of these experiments will be published elsewhere⁵.

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Colorimetric Estimation of Citric Acid

A NUMBER of analyses have been developed^{1, 2, 3} whereby citric acid can be estimated with varying degrees of sensitivity. Some¹ are usable for only small quantities of citric acid in solution, while others^{2, 3} possess a considerably wider range but are complicated either by reagents or by the sensitivity of the determination at the higher levels. For the most part these methods are difficult to handle and vary in their sensitivity from day to day. The method of Cartier and Pin, for example, can be used to determine reasonably wide ranges (100–1200 μ gm) of citric acid, but the reagent used for the development of the colour reaction is light-sensitive and may interfere with the estimation. The methods of Natanson *et al.* and Buffa and Peters, on the other hand, are complicated by the fact that the reagent used to decolorize the permanganate (hydrogen peroxide) interferes with the colour reaction, and considerable care must be taken to remove all traces of it.

ANIMAL PHYSIOLOGY

Mechanism of the Antidiuretic Effect of Vasopressin

It has been said that the antidiuretic effect of vasopressin, one of the posterior pituitary hormones is based on accelerated reabsorption of water in the renal tubules.

S. Itoh reported that the intracellular concentration of chloride is reduced when Pitressin (posterior pituitary extracts) is added to a suspension of red blood cells.¹ This chloride shift of course, depends on the carbonic anhydrase activity in red blood cells.

I have examined manometrically the effect of posterior pituitary extracts (Pharm Japonica) on the enzyme activity. Enzymes were extracted by chloroform and ethanol from cow's red blood cells by Roughton's method.² M/5 sodium bicarbonate which was dissolved in N/50 sodium hydroxide and diluted 4 times with physiological saline was used as substrate. As inhibitor of the enzyme 1.0 mgm/ml solution of acetazolamide was used. Conditions of the experiment are given in Table 1.

| TABLE 1 | | A | B | C | D |
|-------------------------------------|--------|-----|-----|-----|-----|
| Main compartment of Warburg's flask | | | | | |
| Enzyme | (mgm.) | 10 | 10 | 10 | 10 |
| M/5-Phosphate buffer (pH 6.8) | (ml.) | 1.4 | 1.4 | 1.4 | 1.4 |
| Inhibitor | (ml.) | — | 0.2 | — | 0.2 |
| Posterior pituitary extract | (ml.) | — | — | 0.2 | 0.2 |
| Distilled water | (ml.) | 0.4 | 0.2 | 0.2 | — |
| Sklearn | | | | | |
| Substrate | (ml.) | 0.2 | 0.2 | 0.2 | 0.2 |

Experiments were performed in air at 10°C

Results are shown in Figs 1 and 2. Fig 2 shows each reaction speed by the finite difference method. It was noted that there was marked activation of the reaction caused by posterior pituitary extract.

The activators of the enzyme, however, are not yet definitely known.³ Certain amino acids, peptides

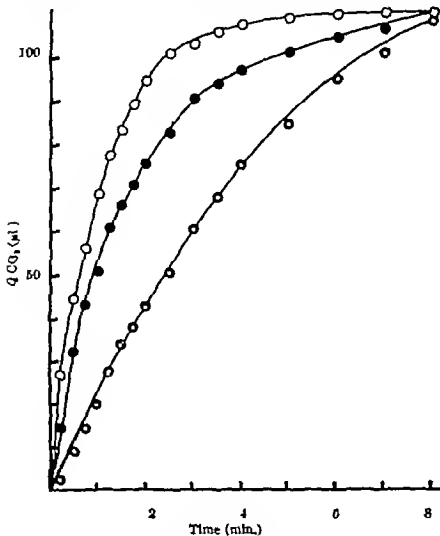


Fig 1 ○—○ Posterior pituitary extract added
●—● basic reaction ○—● inhibition.

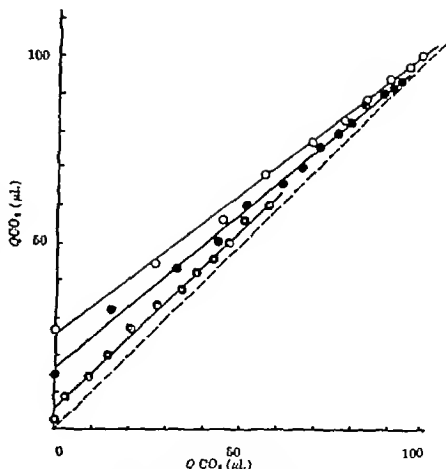


Fig. 2 ○—○ Posterior pituitary extract added
●—● basic reaction ○—● inhibition.

and various tissue extracts are listed⁴ but there are many objections to these activators.⁵

The results do not indicate clearly whether the activation of carbonic anhydrase strictly speaking is due to vasopressin or some impurities, but in my opinion the net mechanism of acceleration of reabsorption of water in renal tubules by vasopressin can be ascribed to the activation of this enzyme occurring in the tubule cells.

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Intravascular and Intracardiac Blood Velocity Patterns recorded by means of NTC Resistors

NTC resistors (thermistors) can be used for measuring intravascular blood flow.^{1,2} The thermistor is heated by an electric current and cooled by the flowing blood. So its temperature is a function of the blood flow rate in its immediate environment, and since the thermistor's electric resistance increases some 5 per cent for a temperature drop of 1°C, resistance measurement provides a fairly sensitive method for the determination of flow. Mounting very small NTC beads in a cardiac catheter (Delaunoy's³ succeeded in recording the blood flow in the large vessels without opening the thorax. An NTC bead having a diameter of 0.5 mm was placed in a small cavity made in the side wall of a catheter near the tip and fixed with a plastic cement. The quantitative determination of flow rates by this method has not yet been entirely successful because of several difficulties, such as the large influence of small blood temperature variations and the complicated calibration procedure.

We used thermistor catheters of the Delaunoy type for recording velocity patterns rather than for

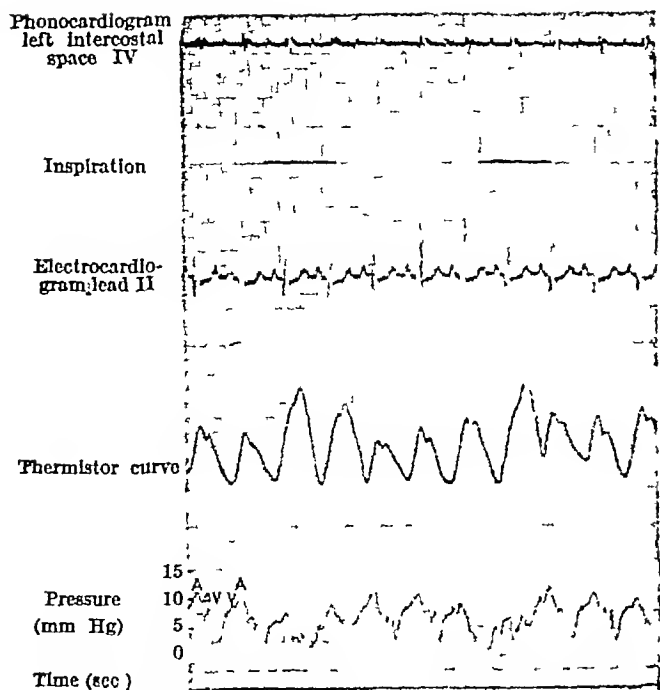


Fig 1 Simultaneously recorded pressure and thermistor curves of the right atrium

measuring flow rates in the heart and large vessels. The dynamic response characteristics of the thermistor catheter had to be considerably improved in order to make it suitable for recording the rapid changes in flow occurring during the cardiac cycle.

A vitreous-enamel-covered NTC bead (Philips B 8 320 02P/1K) with platinum alloy terminals was embedded in a special type of nitrocellulose lacquer in a small lateral cavity about 5 mm from the (occluded) catheter tip. After hardening of the lacquer, the catheter was placed under a metallurgical microscope and lacquer was removed from the bead with a dental drill, as far as this was compatible with adequate insulation of the terminals. Insulated copper wires connected the thermistor terminals through the catheter lumen to the recording apparatus. By this method we obtained thermistor catheters with very small thermal inertia and time lag.

The thermistor (resistance about 1000 ohms at 25°C) was connected as one arm in a Wheatstone bridge with an applied voltage of 8 V (d.c.). The bridge output was fed into a Sanborn 150-1600 general purpose pre-amplifier connected to a 150 M four-channel recording system. Together with the thermistor curve were recorded the electrocardiogram, the phonocardiogram or respiratory movements and the intravascular pressure by means of a Statham P23Db transducer. Simultaneous pressure and thermistor curves were thus obtained from the venae cavae, the cardiac chambers, the pulmonary artery and the aorta of anesthetized dogs. Fig 1 shows curves recorded with the pressure and thermistor catheters in the right atrium near the atrioventricular valve. The thermistor curve shows a rather steep rise beginning about 0.02 sec. after the top of the V wave of the pressure curve. At this moment the tricuspid valve opens and passive filling of the right ventricle starts. The corresponding increase in flow velocity is followed by a further rise due to the atrial systole. Early in the ventricular systole the thermistor curve reaches its maximum. A notch is usually observed in the descending limb, synchronous with the AV notch

of the pressure tracing, indicating the closure of the tricuspid valve. During inspiration the increase of the negative intrathoracic pressure causes an increased flow, which is reflected in an upward displacement of the thermistor curve. Moreover the ascending limb then extends further into the ventricular systole, so that the notch, which remains synchronous with the AV peak of the pressure curve, is then located on this part of the curve.

In the latest experiments a double lumen catheter has been successfully used, one lumen contained the thermistor wires, whereas the other was used for pressure measurement and cuvette oximetry. A series of experiments is now in progress to establish the normal velocity patterns at different sites in the cardiovascular system and to get some insight into the changes which may occur in disease. Especially in valvular incompetence and intracardiac shunts characteristic blood velocity patterns may be expected. In our opinion thermistor catheters of the construction described may become a valuable tool in physiological research and in the diagnosis of heart disease.

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Assessment of the Phagocytic Activity of the Macrophage System

In 1953 Biozzi, Benacerraf and Halpern reported a technique for assessment of the phagocytic activity of the macrophage (reticulo-endothelial) system involving the introduction of a known quantity of particulate carbon into the circulation and the recording of its disappearance over a period of time. Serial samples of blood were removed from the retro-orbital plexus of the experimental animal as previously described by Halpern and Pacaud², and the concentration of carbon in each sample was measured by means of an absorptiometer. The logarithmic value of each of the absorptiometer readings was plotted against the time of removal of the sample, and the slope of the line in closest relationship to these successive points was taken to indicate the rate of uptake of particulate carbon by the cells of the macrophage system.

The method we now report is a modification of the technique described above. The retro-orbital plexus puncture² has been discarded, and the measurement of the concentration of carbon in serial blood samples has been replaced by a direct continuous recording of the variations in concentration of circulating carbon. The experimental animal is immobilized either in a close-fitting cage, harness or by anaesthesia. A relatively translucent but vascular part of the animal is maintained in the pathway of a specially constructed light absorptiometer (Fig 1). A sensitive meter or recording instrument is brought to zero reading after which a specific amount of particulate carbon suspension is injected intravenously. Changes in the meter reading are then observed and recorded.

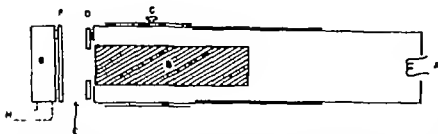


Fig. 1 Apparatus for measuring concentration of circulating carbon. A 12-V lamp, B quartz rod, C locking nut, D iris diaphragm, E, adjustable space for holding animal part, F spectrum filter, G sealed photoelectric cell, H sensitive microammeter.

during the presence of carbon in the circulation of the animal.

The apparatus consists of a light absorptometer so designed as to hold a small and relatively translucent part of an animal (ear, tongue, skin web, tail, omentum). Modification of this system to suit variations in size and shape of the part to be exposed can be made without difficulty. The light source is adjustable for distance and intensity by means of a sliding-sleeve mechanism and a variable transformer. The diameter of the beam is regulated by means of a camera iris diaphragm. A quartz rod is introduced so as to channel the beam of light and to maintain the lamp at a distance from the animal in order to avoid direct heating effects. A sensitive microammeter is connected to a sealed photoelectric cell shielded by a spectrum filter.

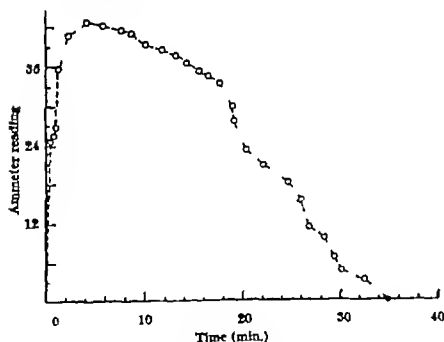


Fig. 2. Density recording of variations in blood carbon concentration.

Fig. 2 shows a typical recording obtained following the introduction of particulate carbon into the circulation of a rabbit via an ear vein. The opposite ear was connected into the light absorptometer system and recordings made at timed intervals.

We are indebted to Prof J W A Duckworth for giving us facilities to carry out this work, and to Mr T F A. Brock for technical assistance. We gratefully acknowledge support from the National Research Council of Canada.

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Thermoregulatory Heat Production in the Brain

THE increase in the metabolic rate elicited in homeothermal animals by exposure to cold is attributed by many investigators exclusively to striated muscle. According to others the liver and intestine have also to be considered as a source of extra heat, but only a few stress the importance of these viscera^{1,2}. The participation of the brain in chemical thermoregulation has apparently not been investigated.

Copper-constantan thermocouples were introduced into rats under light urethane anaesthesia (0.06 gm per 100 gm. body weight). (1) Into the brain just behind the coronary suture in the direction of the diencephalon at depths of 7 mm (Brain₁) and 1 mm (Brain₂) respectively, (2) into the colon 6 cm from the anus, (3) into the lumbar musculature, (4) into the subcutaneous tissue above the cranium and in most cases also into the subcutaneous tissue of the back. The rats were placed into a copper chamber the temperature of which was maintained by a water bath at about 31°C. The experiment proper was begun about an hour and a half later oxygen consumption and body temperatures being recorded every minute³. The environmental temperature was changed abruptly by transferring the respiratory chamber to a water bath at 18–20°C, and vice versa several times in the course of the experiment.

Fig. 1, representing a typical response to cold was taken from an experiment in which a total of six similar responses were obtained in the course of 12 hours. The stabilization of brain temperature coincides with the rise in oxygen consumption, whereas temperatures at other sites still continue to decline: colonic temperature falling well below brain temperature. The temperature of arterial blood being always lower than colonic temperature, an increase in blood flow could only decrease and never increase the temperature difference between the arterial blood and the brain if heat production in the

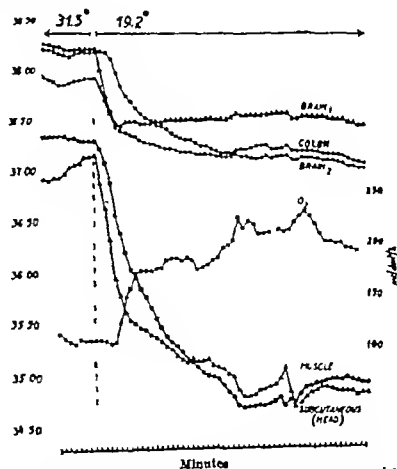


Fig. 1 Effect of exposure to cold on oxygen consumption and on temperatures at various sites in the body of the rat.

latter remained unaltered. The crossing of the brain and the colonic temperature curves therefore indicates a local increase in heat production, originating most probably in the neuroglia.

A detailed account of this work will be published elsewhere.

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Thiosulphate Metabolism in the Animal Organism

THE occurrence of thiosulphate in animal urine was demonstrated by Schmiedeberg¹ long ago, and Nyiri² and Pirio³ showed that this substance is capable of being oxidized into sulphate by animal tissues. So far there has been a lack of more accurate details on the endogenic synthesis and the mechanism of oxidation of thiosulphate in the animal organism, but recently some light seems to have been thrown on the subject by the work of Sörbo.⁴

In the course of work on the process of oxidation of thiosulphate by the autotrophic micro-organism *Thiobacillus thio-parus*,⁵ we came to the conclusion that only the outer sulphur atom of thiosulphate is directly metabolized and oxidized. It reacts with some unknown receptor forming a compound of the type $X-S-SO_3$. The hydrolysis of the binding between the two sulphur atoms in this compound leads in turn to the formation of sulphate from the inner sulphur, while the outer sulphur atom undergoes further metabolism.

In the light of these facts we considered whether thiosulphate in the animal body may not be similarly metabolized. In order to examine this, rats were injected subcutaneously or intraperitoneally with thiosulphate labelled with sulphur-35 in the outer or inner position. The urine and faeces of the animals were collected quantitatively at determined intervals of time. The total amount of sulphur, the sulphur in the thiosulphate and the sulphate in the urine were determined, and the specific activity of these three forms of sulphur was estimated. It should be mentioned that the radioactive sulphur excreted with the faeces under these conditions was insignificant and we therefore neglected it in our calculations.

Table 1 shows the percentage of radioactivity introduced in the form of isotopic sulphur excreted in the urine. If the radioactivity represented an inner atom of thiosulphate, the quantity of radioactivity excreted after 24 hr reached a value of 98 per cent. When thiosulphate was labelled in the outer position, only about 60 per cent of the activity was excreted during the first 24 hr, and even after 120 hr had elapsed a considerable percentage of activity still remained in the organism. We have therefore ascertained that the biological half-life time of both atoms of sulphur in thiosulphate in the animal organism is different and that it is markedly longer for the outer atom of sulphur.

Table 1 THE EXCRETION OF RADIOACTIVE SULPHUR FROM THIOSULPHATE IN RAT URINE AFTER SUBCUTANEOUS INJECTION OF 100 MG% $Na_2S_2O_3 \cdot 5H_2O/100$ GM BODY-WEIGHT

| Time after injection (hr) | Percentage of the dose | | | |
|---------------------------|------------------------|---------|----------------------|---------|
| | $(^{35}S-SO_3)^{==}$ | | $(S-^{35}SO_3)^{==}$ | |
| | Range | Average | Range | Average |
| 0-6 | 36.2-67.5 | 48.2 | 61.0-67.5 | 85 |
| 6-24 | 4.6-10.7 | 10.1 | 5.0-34.6 | 13 |
| 24-48 | 0.4-2.8 | 1.1 | 0.6-2.1 | 1.5 |
| 48-72 | 0.3-1.3 | 0.7 | 0.3-1.4 | 0.8 |
| 72-96 | 0.3-1.2 | 0.6 | 0.2-0.7 | 0.4 |
| 96-120 | 0.2-1.1 | 0.4 | 0.01-0.0 | 0.3 |

Table 2 THE EXCRETION OF THIOSULPHATE IN RAT URINE AFTER SUBCUTANEOUS INJECTION OF 100 MG% $Na_2S_2O_3 \cdot 5H_2O/100$ GM BODY-WEIGHT

| Time (hr) | mgm Range | mgm Average | Percent of the dose range | Percent of the dose average |
|-----------|-----------|-------------|---------------------------|-----------------------------|
| 0-6 | 36.8-63.5 | 48.8 | 18.4-31.7 | 24.4 |
| 6-24 | 2.3-6.5 | 4.2 | 1.1-3.2 | 2.1 |
| 24-48 | 0.2-0.4 | 0.3 | normal | normal |

Table 3 PERCENTAGE OF METABOLIZED LABELLED SULPHUR (THE AMOUNT INJECTED MINUS EXCRETED AS UNCHANGED THIOSULPHATE) IN EXCRETED SULPHATE

| Time (hr) | ^{35}S outer $(^{35}S-SO_3)^{==}$ Range | Average | ^{35}S inner $(S-^{35}SO_3)^{==}$ Range | Average |
|-----------|---|---------|---|---------|
| 0-6 | 7.3-10.2 | 14.7 | 53.1-67.5 | 81.7 |
| 6-24 | 4.2-22.2 | 11.4 | 3.0-42.5 | 16.8 |
| Total | | 26.1 | | 98.5 |

Table 2 shows the quantity of thiosulphate excreted with the urine during the experiments already mentioned. The increased quantity of thiosulphate appears in the urine only during the first 24 hr after the preparation has been administered. This is interpreted to mean that these are molecules of thiosulphate, which in general do not enter into the metabolic process. During the first 24 hr, 20-28 per cent of the thiosulphate is excreted with the urine, while the rest is metabolized. Sulphates are formed from the metabolized sulphur, but at rates different from the two sulphur atoms of thiosulphate.

Table 3 gives the percentage of radioactivity of metabolized sulphur in the sulphate excreted in the urine. It follows from this that during the first 6 hr, only about 17 per cent of metabolized outer sulphur is oxidized to sulphate, but about 85 per cent of the inner sulphur. After 24 hr, about 98 per cent of the metabolized inner sulphur, but only 40 per cent of the outer sulphur of the thiosulphate has been excreted in the form of sulphate.

As may be seen from these data, the fates of the two sulphur atoms in the processes of thiosulphate metabolism in the animal organism take different paths. In principle, only the outer sulphur atom enters into tissue metabolism. There is therefore an analogy with the observations which we carried out using *Th. thio-parus* to oxidize thiosulphate. The ability of the animal organism to transform a considerable quantity of thiosulphate and the high rate at which this substance is metabolized suggest that thiosulphate may be an important metabolite and therefore the mechanism proposed by Sörbo⁴ may play a significant part in sulphur metabolism.

It follows from our investigations that the sulphite group of thiosulphate is very quickly and completely

excreted as sulphate. This would at the same time indicate a mechanism of sulphate formation via a thiosulphate stage.

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PLANT PHYSIOLOGY

Role of the Anion in Magnesium Uptake from Foliar Applications of its Salts on Apple

DURING recent work on uptake of magnesium from foliar applications of its salts the findings of Fisher and Walker¹ that apple leaves take up magnesium more rapidly from the nitrate and chloride than from the sulphate were confirmed, and an explanation of this differential behaviour is proposed as follows.

Table 1 shows the results of an experiment in which leaves were momentarily dipped in $M/10$ solutions of the three salts and the amount of magnesium applied to the leaves, as well as their subsequent magnesium content determined. It shows that the whole increase in leaf magnesium content brought about by the chloride or nitrate solutions occurred within 2 hr. but that, in the case of the sulphate, a significant increase within two hours ($P < 0.05$) was followed by a further significant increase overnight ($P < 0.05$). In each case the total increase in magnesium content up to 22 hr. represents about 50–60 per cent of the magnesium deposited on the leaf, the latter being substantially the same for each of the three salts. These observations conform with our general experience that although magnesium is usually taken up from chloride or nitrate applications on the day they are made with the sulphate this usually occurs during the following night although it can also be taken up on the day that it is applied, as in the present instance (Table 1), and in one experiment, magnesium was not taken up from this salt over a period of 48 hr.

Fig. 1 shows the magnesium content of detached apple leaves whole, in contrast were left immersed in $M/10$ solutions of one of the three salts for various times, and it will be seen that here the rate at which magnesium was taken up was independent of the anion. It is therefore reasonable to suppose that when leaves were momentarily dipped in a $M/10$ solution the initial rate at which magnesium was taken up was the same for all three salts, and since we have already shown that the same amount of magnesium was deposited on the leaves as a result of such treatments it would appear that the observed differences in rate of uptake which occurred when leaves were momentarily dipped must be due to differences in the physical nature of the deposits left behind on them.

A possibly relevant difference is that the chloride and nitrate are normally deliquescent, whilst the sulphate is not. A consideration of the relative humidities quoted in Table 1 shows that, in this

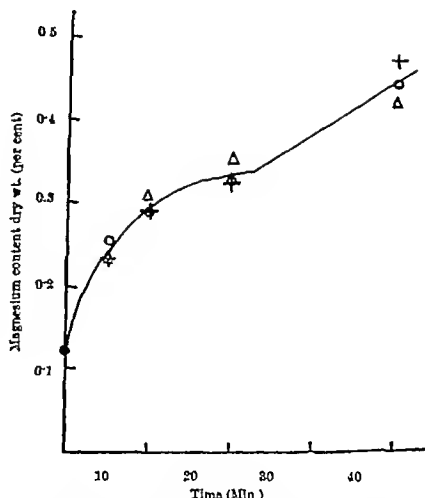


Fig. 1—The magnesium content of leaves immersed for various times in $M/10$ solutions of three salts. + nitrate, Δ chloride, \circ sulphate.

Table 1. DEPOSITION AND UPTAKE OF MAGNESIUM IN LEAVES AFTER DIPPING IN $M/10$ SOLUTIONS OF THREE SALTS

| Magnesium salt used | Magnesium content per leaf (per cent dry wt.) | | | |
|----------------------|---|-----------------------|---------------------|-----------------------------|
| | just prior to dipping | on the day of dipping | on the next morning | Initial superficial deposit |
| Sulphate | 0.03 | 0.15 | 0.20 | 0.27 |
| Nitrate | 0.08 | 0.24 | 0.23 | 0.24 |
| Chloride | 0.09 | 0.24 | 0.22 | 0.23 |
| None | 0.07 | 0.08 | 0.09 | — |
| Relative humidity(%) | 72 | 56 | 66 | — |

experiment, deposits of the chloride or nitrate which are deliquescent over this humidity range were likely to have remained in solution on the leaf surface over the period but that deposits of the sulphate which crystallize out at relative humidities below 82 per cent, would have dried out, and only been brought into solution again overnight. Assuming therefore that magnesium is only taken up by the leaf from solution entry from the sulphate would in this instance have been halted in the morning, and resumed when the relative humidity exceeded 82 per cent, during the night. The nature of the deposit as determined by the humidity of the atmosphere would therefore appear to be decisive in the uptake of magnesium by apple leaves.

It is suggested that these findings have an immediate importance in relation to the practice of applying foliar sprays of magnesium salts in attempts to remedy the widespread and economically serious deficiencies of magnesium occurring in apple orchards.

A detailed account of this work will be published elsewhere.

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Fisher, E. G., and Walker, D. R., *Proc. Amer. Soc. Hort. Sci.*, 64, 1 (1955)

born Nigerians examined by paper electrophoresis (barbitone buffer, pH 8.6, ionic strength 0.05). It was present at birth and its concentration fell with that of foetal haemoglobin during the first two months of life. It could no longer be detected by electrophoresis at three months (Fig. 1). This is an interesting finding which has never been reported in newly born Africans. Although its exact significance is still obscure, its occurrence in a pair of uniovular twins (in our series) suggests the possibility of a genetic control.

A full account of this work will be published elsewhere.

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¹ Fessas, P. and Papaspyrou, A., *Science* 126, 1110 (1957)

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PATHOLOGY

Chromosome Complement of Spontaneous Leukæmia in AKR Mice

A NUMBER of tumours of mice, rats, Chinese hamsters and man consist of a cell population with aneuploid chromosome numbers¹⁻⁴. These observations are frequently quoted in support of the theory that somatic chromosomal mutations are involved in the process of carcinogenesis. The greater part of the published results concerns tumours in the ascites form, or long-established transplanted tumours, and it is not clear whether these results also apply to primary tumours. The few results obtained so far on primary carcinoma of man show the occurrence of aneuploid cells^{5,6}, whereas the mammary tumour of C3H mice consists of a cell population with a diploid chromosome number⁷; the question can be raised as to whether the differences in chromosomal behaviour are due to different methods of tumour induction. In regard to this problem virus-induced tumours appeared of particular interest.

A lymphatic leukæmia spontaneously occurring in mice of the AKR strain was chosen for the present study. All the chromosome analyses were performed on leukæmic females having an enlarged thymus, swollen cervical, mesenteric and caudal lymph nodes and a greatly enlarged spleen. For the cytological examination colchicine was injected 2 hr before death, thymus, spleen and lymph nodes were removed and chopped in hypotonic sodium citrate solution, where they were kept for 10–20 min.⁸ The cells were stained with acetic-orcein for immediate observations and with Feulgen for permanent preparation.

The chromosome counts of cells from the spleen of a normal one-month-old male and of nine leukæmic females are shown in Table 1. Although the developmental stage of leukæmia could be considered similar in all nine mice examined, the chromosome complement differed greatly from animal to animal. Cells with a normal chromosome number and apparently normal chromosome morphology were encountered in the spleen of one mouse (AKR₃). On the other hand at least three different cell lines are present in the spleen of two animals (AKR₅ and AKR₁). The most frequently observed aneuploid value consists of

Table 1 CHROMOSOME COUNTS IN THE SPLEEN OF ONE NORMAL MOUSE AND NINE LEUKÆMIC MICE OF THE AKR STRAIN

| | Number of cells containing the indicated chromosome counts | | | | | | Total cells |
|-------------------|--|----|----|----|----|----|-------------|
| | 30 | 40 | 41 | 42 | 43 | 44 | |
| Control | 2 | 58 | | | | | 60 |
| AKR ₁ | | 48 | 2 | | | | 50 |
| AKR ₁₄ | 2 | 40 | 10 | | | | 52 |
| AKR ₂ | 2 | 40 | 16 | 1 | | | 59 |
| AKR ₃ | 1 | 10 | 20 | 1 | 3 | 1 | 45 |
| AKR ₄ | | 5 | 21 | 4 | | | 30 |
| AKR ₅ | | 8 | 48 | 2 | | | 58 |
| AKR ₆ | 1 | 6 | 40 | 3 | | | 50 |
| AKR ₇ | | 3 | 20 | 18 | 12 | | 53 |
| AKR ₈ | | 15 | 3 | 20 | 23 | 7 | 68 |

41 chromosomes, which was observed in six mice (AKR₁₄, 2, 7, 9, 10 and 12). (These results agree with observations made by Dr S. Ohno, City of Hope Medical Center, Duarte, California, according to a personal communication.) The additional chromosome was extremely small and easily recognized in two mice, but showed no particular characteristics in the remaining four specimens. The proportion of euploid and aneuploid cells varies greatly in the spleen of different leukæmic mice (Table 1). In general the occurrence and distribution of aneuploid cells in thymus and lymph nodes of the leukæmic AKR mice was similar to that of the spleen.

The various alterations of chromosome morphology cannot be presented in full in this report, but two examples are given in Fig. 1, which shows the chromosomes arranged in decreasing length. By comparing the ideogram of the aneuploid cells with the normal, differences in the morphology of the chromosomes become evident. The last three chromosomes in mouse AKR₁₂ and the last two in mouse AKR₈ are smaller than the smallest in the controls, which indicates that more drastic chromosomal rearrangements must have occurred during their formation.

If the results described above are compared with the chromosome patterns of radiation-induced leukæmia⁹ a similarity becomes evident. Aneuploid cells with chromosome numbers scattered in the relatively small hyperdiploid range of 41–43 chromosomes are most frequently encountered in both the spontaneous and radiation-induced leukæmia.

'Marker' chromosomes indicating chromosome breaks and reunions can, but do not necessarily, occur in the aneuploid cells. Finally the spleen and lymph nodes of several leukæmic mice might consist of cells having an apparently normal, diploid chromosome number, although the leukæmia is as advanced as in animals with aneuploid cells (Table 1, ref. 10).

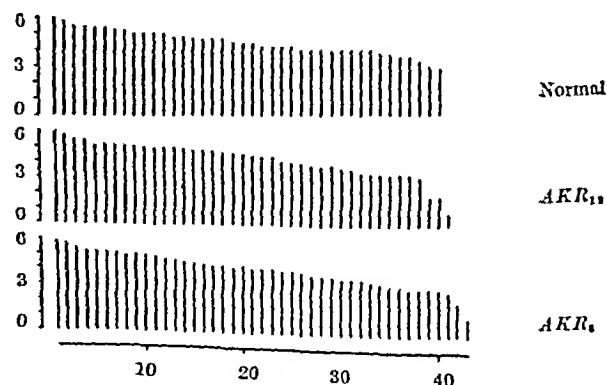


Fig. 1. Ideograms of one normal and two leukæmic mice. The chromosomes are arranged in decreasing length.

This similarity of the chromosomal deviations in radiation induced leukemias and in 'spontaneous' leukemia is of particular interest if the difference in their origin is considered. The chromosomal abnormalities in the first group of leukemias may result from a direct effect of the X rays on the chromosomes and mitosis whereas the cause of chromosomal alterations in the 'spontaneous' leukemia must be sought in an internal factor. Whether and how, a virus like agent which can induce leukemia¹, is able to produce chromosomal damage remains an open question at present. The problem is still more aggravated by our limited knowledge concerning the place of origin of the leukemic cells.

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HISTOLOGY

Periodic Acid-Schiff-Positive Material and Alkaline Phosphatase in the Uterine Wall of the Pig during the Sexual Cycle

Few histochemical investigations of the uterine wall in pigs appear to have been made judging by the literature. Systematic investigations on variations during the sexual cycle in normal sows or changes in different forms of sterility have therefore been started in this Department. In this preliminary report an account will be given of variations in periodic acid Schiff positive material and alkaline phosphatase during the sexual cycle in apparently normal sows.

The periodic acid Schiff method has been followed as described by Lillio¹ and alkaline phosphatase has been demonstrated by means of the azo-dye method of Menton-Junge-Green and performed in accordance with Grogg and Pearce².

The material for the histological sections was taken partly from biopsies obtained by laparotomy and partly from pieces cut out immediately after killing. In both cases material was taken from a point about 10 cm proximal to the uterine bifurcation and from a point about 10 cm distal to the cranial end of the horn. Immediately after removal fixation was performed in 10 per cent neutral formalin.

The investigations seem to show that periodic acid-Schiff positive material is present in three main areas—the surface epithelium, the glandular epithelium and the uterine musculature. There appears to exist a quite clear cyclic variation in these three main areas.



Fig. 1. Periodic acid-Schiff reaction in the endometrium. Paraffin sections of 2 μ m. thickness. Day 11 after heat. Positive reaction in glandular epithelium. No reaction in the surface epithelium. ($\times 90$).



Fig. 2. Periodic acid-Schiff reaction in the endometrium. Paraffin sections of 2 μ m. thickness. Day 14 after heat. Positive reaction both in surface and glandular epithelium. ($\times 90$).



Fig. 3. Alkaline phosphatase in the endometrium. Frozen sections of 25 μ m. thickness. Day 5 after heat. High activity in outer third of surface epithelium. ($\times 90$).

The entire uterine wall is practically free from periodic acid Schiff positive material during the eight days immediately following heat. From the ninth day until the reappearance of heat, the periodic acid Schiff reaction can be observed in the glandular epithelium and musculature. In the musculature the outermost longitudinal part is that richest in periodic acid Schiff positive material. In the surface epithelium, the first traces of this material were demonstrated on the twelfth day after heat with an increase the following days and a subsequent decline again nearly to the complete disappearance at heat.

born Nigerians examined by paper electrophoresis (barbitone buffer, pH 8.6, ionic strength 0.05). It was present at birth and its concentration fell with that of foetal haemoglobin during the first two months of life. It could no longer be detected by electrophoresis at three months (Fig. 1). This is an interesting finding which has never been reported in newly born Africans. Although its exact significance is still obscure, its occurrence in a pair of uniovular twins (in our series) suggests the possibility of a genetic control.

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PATHOLOGY

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41 chromosomes, which was observed in six mice (AKR_{1a}, ₂, ₃, ₅, ₆ and ₁₂). (These results agree with observations made by Dr S. Ohno, City of Hope Medical Center, Duarte, California, according to a personal communication.) The additional chromosome was extremely small and easily recognized in two mice, but showed no particular characteristics in the remaining four specimens. The proportion of euploid and aneuploid cells varies greatly in the spleen of different leukæmic mice (Table 1). In general the occurrence and distribution of aneuploid cells in thymus and lymph nodes of the leukæmic AKR mice was similar to that of the spleen.

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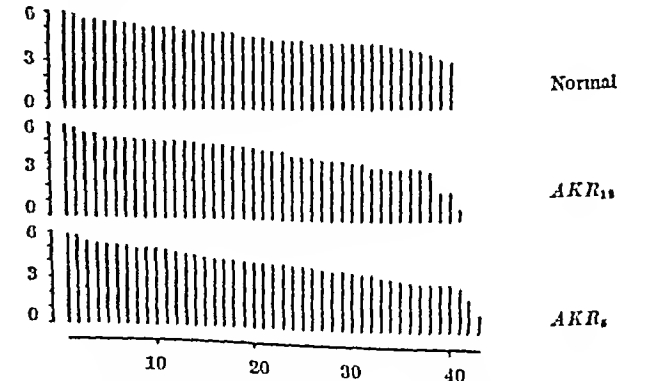


Fig. 1. Ideograms of one normal and two leukæmic mice. The chromosomes are arranged in decreasing length.

summer, stem rust developed on the aberrant plant, and in all probability this plant resulted from an outcross to common Kentucky bluegrass.

All the plants in the stem rust-free progeny remained free of stem rust throughout the growing season. However, a few pustules of one of the yellow leaf rusts were observed in this progeny in late fall. The plants within the stem rust-free progeny were similar in type and indistinguishable from spaced plants of the Merion variety.

Top growth on the majority of the infected progenies was killed back to ground level while the stem rust free progeny remained green and continued to grow. The damage attributable to stem rust is shown in Fig. 1. The variation in size among plants in the rust free progeny in Fig. 1 is due to the removal of tillers for cytological studies.

The stem rust-resistant progeny may have developed from an outcross to a rust resistant biotype but this possibility would appear to be rather remote. Plants with a high level of stem rust resistance are not common in most populations of Kentucky bluegrass and, in addition, outcrossing would not be expected to yield an apomictic progeny.

It seems logical to conclude that the stem rust free apomict resulted from a mutation. The mutation could have been spontaneous in origin, but there are strong arguments to support the conclusion that it was induced by the mutagenic treatment. No evidence of mutations for disease resistance has been found in untreated progenies included in this experiment or in those included in other extensive trials conducted at this station.

The basis for obtaining disease resistance through induced mutation may involve alteration in the availability of a food substance required by the pathogen.² The results obtained in this study should not be interpreted as suggesting that radiation is an efficient procedure for isolating stem rust-resistant lines of *Poa pratensis*. They do indicate, however, that when hybridization is difficult, radiation may be an effective tool for introducing variation within the progeny of selected individuals.

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BIOLOGY

Rete Mirabile in the Gas Bladder of *Coregonus lavaretus*

In fishes with gas secretion both a gas gland epithelium and a counter-current capillary system are usually found in the gas bladder. This is true of physoclists and a large number of physostomes. Data on the composition of the gas bladder gases in coregonids indicate the presence at least in some species of an oxygen transporting mechanism.¹ Experimentally gas secretion has been demonstrated in other salmonids as well.² Because no rete mirabile has been found in salmonids, it has been supposed that in these fishes a pure cellular gas secretion without participation of any counter-current multiplier



Fig. 1 Rete mirabile from the gas bladder of *Coregonus lavaretus* Indian ink injection



Fig. 2 Rete mirabile from the gas bladder of *Coregonus lavaretus* Fixed with Bouin's fluid stained with azan.

system takes place.³ The discovery of a rete mirabile in *Argentina*⁴ which is systematically related to the salmonids, might lead one to expect to find this structure also in the gas bladder of the latter. The fact that it has not been observed by previous investigators could be due to an unusual anatomy of the rete system.

In the course of a comparative study of the blood vessels in the gas bladder of physostomatous fishes, the question of the presence or not of a vascular rete in the gas bladder of *Coregonus* was re-investigated on some specimens of *C. lavaretus* from the Baltic. The blood vessels were studied in histological sections and by Indian ink injections. As a result of the investigation a rete mirabile could clearly be demonstrated. The arrangement of the blood vessels was as follows: an artery and a vein run along the pneumatic duct to the gas bladder. After reaching the anterior end of the bladder, both vessels split into two longitudinal vessels running backwards along the bladder. In their course they repeatedly branch in a similar way, with one artery and one vein practically always running together. By further ramification, an extensive plexus is formed consisting of more or less flat bundles of three or more parallel vessels. Close to the pneumatic duct the bundles often consist of ten or more vessels, further back they generally comprise only three vessels, the central one always an artery. In the larger bundles arteries and veins alternate fairly regularly. The lumina of adjacent vessels are separated only by the thin vascular walls. The number of the rete bundles diminishes rather abruptly about 30 mm from the anterior end of the bladder but flat bundles can be found even in the

posterior part of it. The average diameter of the vessels composing the rete bundles is $10\ \mu$. The bundles run 1–2 mm parallel with the wall of the bladder in the loose connective tissue (submucosa). Then they abruptly traverse the dense connective tissue (muscularis mucosae) and the lamina propria to the base of the epithelium. The total length of the vessels of the rete bundles calculated from measurements on transverse sections of a gas bladder of 80 mm length was about 50 m.

The vascular bundles described above are not a rete mirabile of a conventional type. Due to their abundance, however, they form together a counter-current circulatory system with a capacity comparable to that of the compact rete mirabile of physoclists.

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¹ Sandnes, G., *Nature* 183, 986 (1959).

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Isolation of Tobacco Leaf Cells Capable of Supporting Virus Multiplication

BECAUSE of its waxy cuticle, plant leaf tissue admits few substances applied to the leaf surface. Biochemical studies on the effects of exogenous additives on cell metabolism may require such substances to enter the cells with a minimum delay between application and absorption. Work in this laboratory on the multiplication of tobacco mosaic virus in tobacco leaf tissue has prompted the development of a technique for the preparation of quantities of isolated tobacco leaf cells. These cells support virus multiplication and overcome the barrier to penetration of low molecular weight substances, presented either by the intact leaf or the detached leaf or leaf piece.

This procedure is based on the enzymatic degradation of the intercellular pectic substances by pectinase—a technique applied previously to root meristems¹. Fully expanded leaves of *Nicotiana tabacum* var Turkish Samsun were rinsed and the midribs removed. The laminar tissue was cut into strips of about 3 mm, and shaken at room temperature for 3–4 hr. in a 0.1M Sørensen's phosphate buffer, pH 6.2, containing 0.35 moles of sucrose per litre and 0.2 per cent pectinase (Nutritional Biochemicals Corporation, Cleveland 28, Ohio). The separation of cells, dependent on vigorous shaking, occurs at the cut surfaces of the leaf pieces. Laboratory shakers with a reciprocating motion (200–250 excursions per minute) were suitable. bottles were half-filled with solution, leaf pieces were added in the proportion of 1 gm. of tissue to 20 ml. of solution, and the bottles placed on their sides for shaking. When shaking is terminated, the isolated cells in the mixture sink, while the remaining leaf pieces, vascular elements, and contents of broken cells tend either to float at the surface or to remain in suspension. After standing for a few minutes, the supernatant liquid above the cells is poured off and is then replaced by some of the sucrose containing buffer (without pectinase). This process is repeated at least twice; the suspension is then filtered through four layers of cheese cloth. If some of the isolated cells remain on the cloth pad, they may be washed through with the same fluid. Again allowing the cells to settle, the supernatant liquid is poured off and the

cells are centrifuged for 5 min. at 250g. The pellets are resuspended in either pH 6.2 or pH 7.0 sucrose-phosphate buffer. Centrifugation and resuspension is continued until the supernatant liquid clears—usually after two or three times—final resuspension is achieved by drawing the cells into a pipette to separate any clumps of cells resulting from the centrifugation.

Optimal conditions of pH, buffer and sucrose concentration for the preparation of cells were appraised from the appearance of the isolated cells in the microscope. Under the conditions described for tobacco, Brownian movement of the plastids may be observed, implying a fluid state of the cytoplasm, and the integrity of the chloroplasts appears to be maintained (Fig. 1). Pectinase activity is enhanced at pH's lower than the pH of 6.2 used above, but results in cells of a poorer appearance, particularly shrinkage of the protoplast from the cell wall and clumping of the chloroplasts. At pH 7 no pectinase activity is evident. Sucrose concentrations of between 0.3 and 0.4 M have yielded cells of equivalent appearance.

In routine experiments, 30 per cent of the chlorophyll of the leaf can be recovered in the intact cell preparations. With increased shaking time and careful attention to the recovery of the cells this can be increased to about 45 per cent. The cell types recovered probably do not appear in the same proportions as they would occur in the intact leaf but represent an enrichment of mesophyll cells. That is, the epidermal cells are reduced in number because the waxy cuticle holds them together, afterwards they are removed by filtration when the cells are separated from the reaction mixture. Vascular elements would be similarly eliminated by filtration because of their size. Most cells are isolated as individuals, but groups of 2–5 cells sometimes appear (Fig. 2).



Fig. 1. An isolated tobacco leaf cell, presumably from the spongy mesophyll. Suspended in pH 6.2 buffer, containing 0.35 moles of sucrose per litre. ($\times 405$)



Fig. 2. Group of tobacco leaf cells showing several types of cells. Medium as in Fig. 1 ($\times 120$). Photos: Andrew Tau.

From their microscopic appearance, a high proportion of the isolated cells are viable. Further evidence for viability is provided in the capacity of isolated cells prepared from infected tissue to support the multiplication of tobacco mosaic virus when incubated. To date, the synthesis of virus protein can be demonstrated only in an intact cell. Moreover, when isolated virus infected cells were incubated in the presence of a radioactive amino acid (glycine ^{14}C or DL leucine ^{14}C), the amino-acid was incorporated into the protein of the virus. In previous studies with tobacco mosaic virus, incorporation into virus protein was demonstrated only with intact leaf tissue and not in homogenized preparations of a cell free nature¹, although these cell free systems were active for the incorporation of radioactive amino-acids into proteins other than the virus. At a later date, I shall report in detail my studies of tobacco mosaic virus synthesis in isolated leaf cells.

To test the general applicability of the method, an *ad hoc* assortment of leaves of 12 species of plants was tried. Of these *Nicotiana glutinosa*, *Datura stramonium* and potato yielded cells which compared favourably both in yield and appearance with those of *N. tabacum*, *Oenopodium amaranticolor*, *Quercus borealis* and *Crotalaria spectabilis* gave relatively few cells of good appearance. Corn and *Ginkgo biloba* yielded no cells at all. There was good cell production from leaves of two species of *Prunus* (a peach and a cherry) quoniam and *Magnolia* sp., but the cells looked injured, being reminiscent of the appearance of the tobacco leaf cells prepared under conditions of either low pH or unfavourable sucrose concentration.

These studies were initiated at the Commonwealth Scientific and Industrial Research Organization, Division of Plant Industry Canberra. At the University of Missouri partial support was derived from a grant of the Herman Frasch Foundation.

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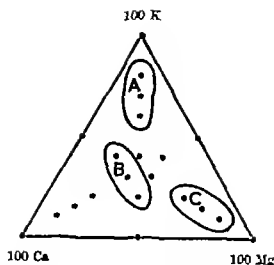
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³ Boardman, N. K. and Zaitlin, M., *Virology* 6, 758 (1953).

Effect on the Groundnut of Variations in Supply of Potassium, Calcium and Magnesium

GROUNDNUTS (var. Philippine Pink) were grown in pots using a typically infertile local soil with the primary object of studying Prof. M. V. Horne's 'Method of Systematic Variations' for the determination of major element requirements. With the exception of the controls, plants were supplied with 100 mgm equivalents of various proportions of potassium, calcium and magnesium, 100 mgm equivalents of a good fixed ratio of nitrate, sulphate and phosphate, and micronutrients at levels known to be suitable for many plants in sand culture¹.

There are three distinct optimum mixtures for the production of 'tops', shell and kernels (Fig. 1). There is a depressive effect of some mixtures on quantity and quality of seed production while the controls produced good-quality nuts. The effect of shortage of calcium on groundnuts is well known particularly in the United States, while the effect of a



| Mgm. Equivalents of added | | | Yields gm/pot, of | | |
|---------------------------|-----|-----|-------------------|-------|---------|
| K | Ca | Mg | Tops | Shell | Kernels |
| 100 | 0 | 0 | 84.0 | 5.03 | 2.10 |
| 80 | 10 | 10 | 71.0 | 9.00 | 1.20 |
| 70 | 15 | 15 | 60.4 | 12.0 | 1.09 |
| 60 | 20 | 20 | 57.5 | 13.1 | 0.93 |
| 40 | 30 | 30 | 41.5 | 10.4 | 10.7 |
| 20 | 40 | 40 | 32.5 | 11.1 | 17.4 |
| 0 | 50 | 60 | 22.4 | 7.72 | 13.1 |
| 0 | 100 | 0 | 20.7 | 3.51 | 10.8 |
| 10 | 80 | 10 | 21.5 | 6.72 | 11.7 |
| 15 | 70 | 15 | 23.3 | 5.15 | 12.2 |
| 20 | 60 | 20 | 23.0 | 4.55 | 12.8 |
| 30 | 40 | 30 | 21.7 | 6.52 | 16.0 |
| 40 | 20 | 40 | 40.7 | 14.1 | 2.5 |
| 60 | 0 | 50 | 45.0 | 0.31 | 0.23 |
| 0 | 0 | 100 | 31.0 | 10.8 | 6.70 |
| 10 | 10 | 80 | 47.0 | 14.4 | 3.35 |
| 15 | 15 | 70 | 60.2 | 13.0 | 1.72 |
| 20 | 20 | 60 | 46.4 | 15.2 | 3.24 |
| 30 | 30 | 40 | 44.2 | 14.1 | 4.22 |
| 40 | 40 | 20 | 23.9 | 7.25 | 20.5 |
| 60 | 50 | 0 | 53.7 | 15.0 | 8.09 |
| 0 | 0 | 0 | 9.90 | 1.60 | 3.53 |

* Tops are the dried vegetative parts of the plant with the exception of the roots. All yields are means of three replicates.

relative excess of potassium is known here in Gambia. 200 lb/acre of potassium chloride can result in an increase in groundnut hay yield of up to 30 per cent with a simultaneous depression in nut yield of 14 per cent. The apparent importance of magnesium in groundnut pericarp formation was unexpected, as was the completely different behaviour from tomatoes grown in similar conditions; the best ratio of potassium calcium magnesium (as equivalents) for tomato fruit production was approximately 40:12.5:47.5 while the optimum for vegetative growth was 35:40:25.

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R. COMBER

- ¹ Horne, M. V., *Soils and Fert.*, 18, 1, 101 (1955).
² Hewitt, E. J., *Sand and Water Culture Methods used in the study of Plant Nutrition*, 189 (Commonwealth Agricultural Bureaux, 1952).

Prefreezing as a Method enabling Animals to survive Freezing at an Extremely Low Temperature

In a previous paper it was demonstrated that, after sufficient extracellular freezing, some intact insects could survive freezing in liquid oxygen without any antifreeze agent¹. This might be a method for keeping an entire organism alive at extremely low temperatures, provided that it is sufficiently frost resistant. Some work along these lines has been carried out in our laboratory. In plant tissues, Sakai has already successfully applied the method to

various hard woods². In animal material it was examined with regard to various intact animals and to excised tissues or cells.

Our prefreezing method was found to be quite effective both for a fairly large butterfly chrysalis, about 1 gm body-weight, and for a tiny nematode. Overwintering pupae of the swallow tail, *Papilio machaon hippocrates* Felder et Felder, were kept at -30°C for one hour and then immersed directly in liquid oxygen for two days. After rewarming in air at room temperature most of them were found to be alive. Of ten pupae examined five were able to resume their development at 20°C . In these insects, however, the formation of imaginal tissue was restricted to the anterior half of the pupal bodies, the abdomen behind the third or fourth segment remained in the pupal state and survived for some ten days at least with an active heart beat even after the anterior halves had died. The control insects, which were treated in entirely the same way except for the immersion in liquid oxygen, appeared on the wing within about forty days at 20°C . The even less frost-resistant tissues of the oyster, if treated previously in glycerolated sea water, survived freezing at a super-low temperature after prefreezing by our method³.

The highest temperature at which the prefreezing treatment is sufficiently effective to enable an animal to withstand extremely low temperatures seems to be about -30°C . In the case of prepupa of a slug caterpillar, *Cnidocampa flavescentis* (Walker), nearly all the insects prefrozen at this temperature survived freezing in liquid oxygen⁴. Most of the caterpillars prefrozen at -25°C , on the other hand, died within several days of rewarming from a very low temperature, although some of them had been alive with active heart beat just after thawing. Further, the ciliary beating in oyster gill pieces always regained its full activity after a direct immersion in liquid oxygen provided they were previously frozen at a temperature lower than -30°C .

In a plant-parasitic nematode, *Aphelenchoides ritzemabosi* Schwartz, under freely swimming conditions in tap water, the most effective prefreezing temperature seems to be lower than -25°C . Nevertheless, as a result of a prefreezing oven at a temperature between -10°C and -25°C about one-fifth of the frozen animals maintained their motility after rewarming from an extremely low temperature (Fig. 1). Besides, it was interesting to note that a few specimens of this animal always survived freezing in liquid oxygen provided the medium they were in had previously frozen, even at a temperature near 0°C .

Although tiny nematodes can be vitrified rather easily, these results cannot be explained by the vitrification of their bodies, because some of them are always found to be alive even after slow rewarming from an extremely low temperature.

It seems likely that in most cases mentioned above scarcely any intracellular freezing occurs during the preliminary freezing, since the rate of cooling in the animal tissues must be lowered considerably by the liberation of latent heat of crystallization in large quantities of medium or body fluid. In hardy cells, at least, rapid cooling is one of the essential factors in decreasing the capacity of the cell surface to prevent frost⁵. Now it has been shown for various insects that the amount of water crystallizing at -30°C is more than nine-tenths of total water content, that is

nearly all the freezable water in these insects⁶⁻⁸. In addition, it was demonstrated in a previous paper that in insects rapidly transferred into liquid oxygen from a temperature higher than -20°C , some of the tissue cells seemed to freeze intracellularly¹. This is also the case with nematode or molluscan tissues. Considerable destruction of body structure was frequently found in killed nematodes after they had been thawed.

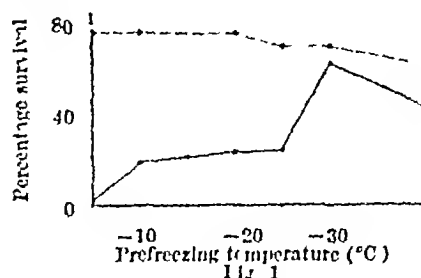


Fig. 1. Percentage survival in nematodes immersed in liquid oxygen after preliminary freezing at graded temperatures: ●—● Experiment, ○—○, control, with prefreezing only.

The results described above fully agree with the hypothesis suggested in a previous paper¹, namely, if animals are previously frozen extracellularly at -30°C , scarcely any water crystallizes in their tissue cells even in liquid oxygen. In hardy organisms the death by extracellular freezing takes a long time compared to that caused by intracellular freezing. Further, the speed of the process in the former type of frost injury may be slowed down considerably at extremely low temperatures. In fact almost all the caterpillars prefrozen at -30°C revived even after they were kept in liquid oxygen for more than two months (Asahina, unpublished). Therefore, an animal might certainly survive freezing at such a temperature provided it can withstand the prefreezing at -30°C .

Some of the experimental results from our Institute recently obtained for various organisms also seem to support this view. In tissue cells of very hardy plants, Sakai⁹ showed that the proportion of survival was never affected by the rate of rewarming from an extremely low temperature, if the cells were previously frozen at -30°C . Even in yeast cells, suspended in distilled water, prefreezing at temperatures lower than -30°C was remarkably effective in keeping them alive in liquid nitrogen (Noi, unpublished).

A relatively large proportion of nematodes prefrozen at temperatures higher than -30°C , and then transferred into liquid oxygen may probably be explained by a body structure particularly suitable for dehydrating their cells very rapidly when extracellular freezing is applied.

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¹ Asahina, E., and Aoki, K., *Nature*, **182**, 327 (1958).

² Sakai, A., *Low Temp Sci.*, **14**, 17 (1956).

³ Asahina, E., *ibid.*, **14**, 65 (1958).

⁴ Asahina, E., and Aoki, K., *ibid.*, **14**, 55 (1958).

⁵ Asahina, E., *Contr. Inst. Low Temp Sci.*, **10**, 83 (1956).

⁶ Scholander, P. F., *Illeg.*, **W. Hock R. J.**, and Irving, R., *J. Cell*

Comp. Physiol., **42**, Suppl. 1, 1 (1953).

⁷ Salt, R. W., *Canad. J. Zool.*, **33**, 301 (1955).

⁸ Shinzaki, J., *Zool. Mag. (Tokyo)*, **67**, 38 (1958).

⁹ Sakai, A., *Low Temp Sci.*, **14**, 41 (1958).

NATIONAL PARKS AND NUCLEAR POWER STATIONS IN BRITAIN

IN addressing the Conference of National Park Authorities at Bakewell recently, then Minister of Housing and Local Government, Mr H Brooke said that the national parks in Britain are not intended to be either museums without life in them or mere holiday resorts and he emphasized once more the need to carry with us in serving whatever purpose the national parks should meet, those who work and have their homes within those areas. The vital necessity of public understanding and support has been clearly demonstrated during the first ten years of the operation of the National Parks and Access to the Countryside Act but it has also been made abundantly plain that one of the major difficulties is that of finance. The failure of successive Governments to provide the means has been the main cause of lack of progress, both through the impossible burden it has put on local authorities and by hindering or even preventing the work of educating public opinion.

It would appear from his address to the Conference that the Minister was aware of much of this and it could be inferred from the tenor of his address that he had in mind the possibility of an amending or amplifying measure in the near future. It is true he specified a clear conception of what the national parks are intended to be as a pre condition of any fresh legislation and it is obvious that the time is ripe for a good deal of clear and constructive thinking over this whole question of amenity, of the relation between national and local interest and the balance between various national interests which may or may not be irreconcilable.

From this point of view alone, the report of the Forest of Dean Committee* merits attention. This Committee was appointed in June 1956, under the chairmanship of Sir Thomas Crook to review the situation in the Forest of Dean and, having regard to all existing rights and interests, to recommend such measures as are considered desirable and necessary to secure that the administration of the Forest, more particularly as regards the grazing of animals, may be adjusted to modern requirements. The Forest of Dean is one of the ancient royal forests second in area of woodland only to the New Forest, but although the forest does not lie in a national park area, it includes the first woodlands of the Forestry Commissioners to be designated a national forest park in England. Its administration involves problems of reconciling such interests as afforestation, common grazing, and mineral and other development, which give the report of this Committee a profound interest to all concerned in the problems connected with the preservation of amenity and development generally.

It is the recommendations of the report in regard to amenities, development and planning that are of

chief interest here, although those relating to grazing, which occupy the greater part of the report are of course equally important if damage either to sylviculture or features of special interest and beauty, which constitute the charm of the Forest and give it high amenity value, is to be minimized. The report firmly opposes any proposal to carry out open-cast coal working in view of the grave effect such operations would have on the amenities of the Forest and it will be noted that the National Coal Board on August 19 announced its intention of discontinuing such workings. Likewise the Committee recommends that the deputy surveyor the officer responsible for the control of the Forest should invariably be consulted when an application is made for a grant of land for mining or quarrying or for the extension of the period of existing grants. It is also recommended that the siting of overhead power lines should be planned to cause the least possible disturbance to the rural scene and should be subject to the prior consent of the Verderers.

Many of the recommendations relate to matters of detail such as the planting of the old colliery spoil heaps, the leaving of any disused railway track in a condition fit for other uses, the character of fencing and the immediate correction of such abuses of the open forest as the boiler works at Clearwell Meens (Slung). Tribute is paid to the valuable development work which has been done by the Development Association of the Forest of Dean which should be encouraged to continue but industrial development should be limited to that providing occupation for people who live in the immediate vicinity of the Forest and its surrounding villages and so far as possible should be concerned with the raw material of the Forest. It is recognized that there is scope for further development of the tourist industry by providing more hotels, but the Committee recommends that the whole of the Forest should be declared an area of 'special control' under the Town and Country Planning Act, 1947 and particular attention paid to outdoor advertising. Provision of additional caravan sites and camping grounds and further facilities for car parking and picnicing are also recommended, and the creation of additional points of view, with any necessary clearance of glades. The Forest is fortunate in having soils universally recognized as favourable for the growth of the more exacting broad leaved trees such as oak and beech, and it is recommended that the Forest should continue to be predominantly broad leaved, and that the practice of planting tree name boards where appropriate should be extended.

The most cursory reading of the debate on national parks in the House of Lords on July 1 reveals the relevance of such details to the functioning or even the existence of national parks themselves, and there was a subsequent debate on nuclear power stations in the House of Commons on July 30 which was

* Forestry Commission. Report of the Forest of Dean Committee 1958. Pp v+59+14 plates (Dmdn 636.) (London: H.M. Stationery Office 1959.) 8s net.

concerned specifically with the siting of overhead power lines. This latter debate arose out of the decision to place a nuclear power station at Dungeness and to convey power, by overhead line or pylons, thence to Canterbury. Other aspects of that decision are considered below, but the proposal to erect such overhead transmission lines from the power station to a sub-station at Lydd and to construct certain sections of an overhead transmission line from Lydd to a sub-station at Canterbury was also covered by the public inquiry on December 16-18, 1958. The Minister of Power, after consultation with the Minister of Housing and Local Government, announced on July 11 his intention to consent to the construction of the power station and of the overhead transmission lines.

The reports of the inspectors in charge of both these inquiries have been published, and that relating to the power station, a proposal which was uncompromisingly opposed by the Nature Conservancy, and its approval described by the Council for Nature as a scientific tragedy, merits close study by the scientist. The debate on July 30, however, is of interest for the reply it drew from Sir Ian Horobin, then Parliamentary Secretary to the Ministry of Power, first defending the Government's siting policy and then explaining further the position regarding overhead transmission. The Council for Nature had suggested that the Government should now review its policy of siting power stations on coast lands, as it would be impossible to continue indefinitely the siting of such stations away from built-up areas if any stretches of coast were to be preserved unspoiled.

Sir Ian advanced no fresh arguments in defence of the present policy, though it is implicit in his statement that the policy should be reconsidered as soon as practical experience has demonstrated the extreme remoteness of any possibility of accident. On the question of overhead transmission, he gave figures for underground transmission as of the order of £200,000 a mile, with a further 50 per cent to cover trenching and filling-in, and another £100,000 in certain circumstances to overcome instability due to the condenser properties of the cable. He did not, however, disclose the basis of this estimate of, say, £300,000 a mile, which Mr W F Deedes had challenged, and, although he assured the House that the question of design is receiving very careful attention, in view of the strong objections to overhead transmission on amenity grounds and the misrepresentations of which the electricity boards have been guilty from time to time, it would seem somewhat unreasonable not to prepare independent figures from a source the impartiality and technical standing of which are alike above suspicion. It was stated by Mr Reginald Maudling in a written reply in the House of Commons on July 13 that a decision on other parts of the transmission lines had been deferred, pending the examination of a possible alternative route which the Minister of Power had requested.

The debate in the House of Lords preceded the announcement of the Minister's decision, but took

place a few hours after work had been started on the Trawsfynydd nuclear power station—the outstanding example so far of the approval of the erection of a major industrial undertaking in the heart of a national park. The debate was primarily on the ninth annual report of the National Parks Commission, and it was notable for an outstanding speech by Lord Birkett. Lord Silkin, in opening the debate, had paid tribute to the value of the voluntary work now being done in the national parks, for example, by wardens, and in clearing away disfigurements, but after commenting that the Trawsfynydd decision was actually contrary to the opinion of the Ministry's own inspector, had stressed the need for adequate financial support from national rather than local sources. Lord Silkin was strongly supported in all this by Lord Birkett, who commented that the Minister of Housing and Local Government should pay much more attention to the recommendations of the Commission, and that even as little as one-eighth of a penny a week per head of the population would suffice to preserve and guard natural beauty in our parks compared with the 11s a week at present required for national defence.

The core of Lord Birkett's speech, however, did not lie in this plea for adequate financial support and publicity or even for the placing of the financial responsibility for a national interest where it properly belongs—on national and central rather than on local funds. It was rather in his reasoned argument that the National Parks Commissioners should have adequate power. This is partly a matter of appropriate administrative arrangements—national and not local—though Lord Birkett insisted on the need for local support and understanding, but it is much more a matter of recognizing that there are and must be occasions when amenity is the over-riding national interest, and on this point Lord Birkett supported the proposal to establish a special committee of the Privy Council as an appeal tribunal. Over the years, he urged, a body of decisions would in this way be collected which would constitute a continuing guide, and with this, and certain modifications to the National Parks Act in respect of such matters as compensation, Lord Birkett seemed to think the situation might be met satisfactorily.

While welcoming these speeches, the Earl of Dundee, in his reply on behalf of the Government, did not offer an assurance of legislation or meet the argument for the over-riding interest of amenity in certain circumstances. Lord Silkin, indeed, dissociated himself afterwards from Lord Birkett's proposal for an appeal tribunal, but that merely strengthens the argument for adequate authority for the National Parks Commissioners themselves. Even more than the Trawsfynydd decision, that approving the erection of a nuclear power station at Dungeness demonstrates the inadequacy of the assurance of the Earl of Dundee that the Government is conscious of its duty to preserve and enhance the beauty of national parks, and that such problems will be carefully studied.

The Dungeness proposal was strongly opposed on various grounds by the Kent County Council, the Botanical Society, the Royal Society for the Protection of Birds, the Council for the Preservation of Rural England, the National Farmers' Union, the Dungeness Fishermen's Association and others but it is the opposition of the Nature Conservancy and the Council for Nature that is of main scientific interest, and even from the national point of view is most significant. The Nature Conservancy did not oppose the proposal simply on the ground that the site chosen lay within a projected nature reserve. Its opposition was based much more on the unique and irreplaceable permanent importance to science of the land in question, for which there is no adequate substitute in Europe. As Mr E M Nicholson, director of the Nature Conservancy, explained in his evidence at the inquiry, the area, which is probably the most important stretch of new land added to England since 1600 and is the most suitable for tracing natural processes of coast-building as well as the largest cusped foreland in the British Isles and probably in Europe had long been treated throughout the world as a type example of a major coastal depositional feature. It combines a history of major shore changes with records of other related changes such as river outlets, ports and settlements and provides materials for research on the relations between the emergence of dry land and the variation of the shore line. Physiographers have made comprehensive studies of this area over a prolonged period generally involving investigations of the shingle composition of the various ridges which appear on the foreland. There is still however a wide divergence of views on how and why this massive deposition of shingle at Dungeness occurs. The presence of a power station on the site would probably prevent the continuance of the scientific work while the destruction of the shingle ridges would destroy the evidence from which scientists could reach their conclusions.

These studies, moreover are of practical importance to coastal engineers and their interruption would represent a great loss to the science of coastal studies. A subsequent statement issued by the Council for Nature describing the decision as a scientific tragedy went so far as to assert that one result might well be the eventual disappearance into the sea of yet more villages on the east coast of Britain through lack of adequate knowledge of the means to check erosion. Mr Nicholson emphasized that the site for the power station covered practically the whole of the remaining undisturbed area of shingle and coincided with the area where the recent ridges could be dated precisely from the nineteenth and twentieth century surveys. Any large-scale interference with this shingle would thus make it impossible for any further studies on the ground to link the present to the past in uninterrupted sequence and thus destroy for all time the area of scientific value to physiographers, sterilize the follow up of past studies and prevent future work from which important results were anticipated and for which much

fundamental material existed on the Dungeness site.

Besides these reasons, which were fully supported by the Council for Nature, other objections to the proposal are minor. Their force was fully admitted by the inspectors in charge of the inquiry, who recognized that the shingle ridges within the power station site would be destroyed but though they thought that the work of the bird observatory at Dungeness might also be affected, they did not think that the area would be entirely impaired as a nature reserve, or that the work of botanists and entomologists would be upset. Nevertheless with some reluctance the inspectors in their report recommended consent to the construction of the power station, and, as already noted the Minister of Power has now given his decision accordingly.

In announcing his decision, the Minister stated that he had had in mind the growth of the demand for electricity and the great importance of implementing the nuclear power programme. He also pointed out that, even if there were no nuclear power programme, it would not be practicable to site new power stations on the coalfields, because of the very large quantities of cooling water required. Nevertheless he did not meet the essential point that from a physiographical point of view the Dungeness site is unique and its loss irreparable. Alternative sites for power stations do exist and will ultimately have to be found. This is indeed the key issue and might well justify the decision being described as something more than a national tragedy. Until it is recognized that there are places where the national interest is primarily amenity or scientific, and where power development or even defence must be secondary, neither nature conservancy, national parks nor the planning of land development can have any real meaning. It is of the utmost importance that the fullest possible use should be made of such reports as those of the Forest of Dean Committee, the National Parks Commission and of the Dungeness inquiry itself. They demonstrate what is really involved and the price that has to be paid if in any part of this small island natural beauty, flora and fauna, or the scientific task of understanding and utilizing the natural resources of Britain are to be safeguarded against sectional and transient interests.

THE EARTH AS VIEWED IN 1959

The Earth

Its Origin, History and Physical Constitution. By Sir Harold Jeffreys. Fourth edition. Pp. xiv + 420 + 10 plates. (Cambridge. At the University Press, 1959.) 75s. net.

G EOPHYSICAL research has proceeded so rapidly since publication of the third edition of Jeffreys's "The Earth" in 1952 that he decided to revise it. Our information and hypotheses about the universe are changing rapidly, as any reader of *Nature* knows. These hypotheses provide new ideas about the origin of the Earth and our notions of its close

tronic computers accelerates interpretation of new results in many fields of geophysics and permits rapid checking of hypotheses. Total funds available for geophysical research, even after the International Geophysical Year, are many times more than they used to be. New conclusions, many of them about properties of the oceanic crust of the Earth, mount rapidly and many of them are making apparently well-confirmed hypotheses obsolete. We have to consider the possibility that phase changes in silicates are responsible for discontinuities in the Earth which before have been attributed to sudden changes in material. Our hypotheses concerning the source of the Earth's magnetic field are in a state of flux. It has been found that the temperature inside the Earth may be greatly affected by radiation, especially across portions of the Earth's mantle. There are other examples for the fact that, at present, many of our hypotheses concerning the Earth are changing much faster than during any earlier period. Moreover, hypotheses about new fields in geophysics, for example on the outer atmosphere, are added. As a consequence, it is now impossible for one person to be expert over the whole of geophysics, as Jeffreys points out in the preface, and he does not discuss the problems mentioned above.

This rapid progress in geophysics requires that any geophysicist who wants to be up to date must consult new books and publications. Since Jeffreys's "The Earth" is the most used and best accessible book about geophysical problems, it is very gratifying that the fourth edition has been published. Every scientist working with problems which are discussed in the book will have to familiarize himself with the new edition. Among the problems, for which Jeffreys has revised earlier discussions, are some related to non-elastic processes. Unfortunately, many of these, while playing a very important part in geophysics, are still poorly understood even by specialists. Lack of such information affects investigations of the processes connected with body tides, variation of latitude, Love's numbers for the Earth and related problems, etc. Among other sections which have been revised by Jeffreys are those related to the temperature in the Earth and the structure of the upper portion of its mantle. New results concerning both have been published since the new edition was written. The suspected wandering of the Earth's magnetic poles is mentioned in the fourth edition, but in connexion with this and the related problem of continental drift, Jeffreys has still too many doubts about the underlying processes to give details. However, his books are always inspiring, regardless of whether the reader agrees with his conclusions or not. To summarize, study of the fourth edition of "The Earth" is strongly recommended to all scientists investigating problems related to physics of the Earth.

B. GUTENBERG

GEMMOLOGY

Gemstones

By G. F. Herbert Smith. Thirteenth edition, revised by F. C. Phillips. Pp. 560+27 plates. (London: Methuen and Co., Ltd., 1958.) 50s. net.

HERBERT SMITH'S "Gemstones" has been a standard book of reference on precious stones and a text-book for students of gemmology ever since its first edition appeared in 1912. In its ninth

edition, published in 1940, it was considerably enlarged and still further additions were made to the tenth edition in 1949.

In the new edition Dr. Colos Phillips has shortened and simplified the chapters on crystal form and structure and the chapter on optical properties. Chapters on organic products—ivory, tortoise shell, coral, jet and the resins—have been reduced and a short chapter on the formation of gemstones has been added, and also a very welcome chapter on the polarizing microscope.

An important change in the arrangement is made in that the distinction of precious and semi-precious stones is dropped. Instead of the old arrangement the principal gemstones are described in fifteen chapters and the others are collected in alphabetical order in one long chapter. This chapter contains descriptions of 25 mineral species that provide gemstones of varying merit and scarcity, including two new species discovered as gemstones, painite and taaffeite, $\text{MgBeAl}_2\text{O}_6$. *Sinhaitite*, MgAl_2BO_4 , is described under olivine, with which it was confused until about 1957.

The book has been brought up to date wherever necessary and it has been possible to include a brief account of the successful crystallization of diamond in the laboratories of the General Electric Co., Schenectady, New York. Another piece of diamond news, concerning the famous Hope Diamond, was announced perhaps too late for printing in this book. This wonderful blue diamond of 44.4 carats, formerly the property of Mr. Harry Winston of New York, has now been presented by him to the Smithsonian Institution and is displayed in a special case in the newly designed mineral gallery of the National Museum in Washington.

In conclusion it should be added that print, paper and illustrations in this new edition are much improved and both author and publishers are to be congratulated.

W. CAMPBELL SMITH

TRENDS IN STATISTICS TEACHING

A First Course in Statistics

By Robert Loveday. Pp. xii+121. (Cambridge: At the University Press, 1958.) 8s. 6d.

Statistics

An Introduction. By Prof. D. A. S. Fraser. (Wiley Publications in Mathematical Statistics.) Pp. ix+398. (New York: John Wiley and Sons Inc.; London: Chapman and Hall Ltd., 1958.) 75s. net.

THE flow of statistical text books, which some years ago threatened to swell into a flood, has recently dwindled to a trickle, the appearance of two new books almost simultaneously is therefore a matter of some interest. But simultaneity is about the only thing these books have in common. The fact that they are aimed at different classes of students, in Mr. Loveday's case General Certificate of Education ordinary-level candidates, and in Prof. Fraser's case mathematical students in universities, accounts for only part of the difference. The main difference arises from a fundamentally different conception of what statistics is about.

Mr. Loveday is concerned throughout with distributions of empirical data and how to describe them. The concept of probability scarcely enters into the discussion, in the index, for example, the term is not even mentioned. No doubt Mr. Loveday has

succeeded in presenting a clear and simple introduction to descriptive statistics. Certainly he has collected together a set of exercises which will be useful in elementary teaching. But it may be questioned whether, in the light of the developments of the subject that have taken place during the past thirty or forty years, this exclusive concentration on descriptive statistics is the best way of introducing the subject even at the most elementary level. One would have thought that some of the time spent discussing measures of location and dispersion and similar matters could have been spared for an introduction to the more exciting topics of probability, sampling and inference.

For the choice of subject-matter the author is perhaps not so much to blame as the General Certificate of Education examining authorities. Mr Love day must, however, bear the responsibility for cluttering up the student's mind with unnecessary and esoteric terms such as 'ogive' in place of 'cumulative frequency distribution', 'Galton graph' for 'scatter diagram', 'histogram' for 'graph of a time series', 'direct correlation' for 'positive correlation' and so on. Those fortunate enough to become professional statisticians will never use these terms later in life. Why should they have to learn them as beginners?

It is hard to justify Mr Loveday's treatment of regression as he confines his discussion of the fitting of regression lines to methods which are almost never employed in practice. Why not give the student the formula for the least squares coefficient? The formula for the correlation coefficient is given in the succeeding chapter and this is certainly harder to understand, as well as to calculate, than the regression coefficient.

Two minor points. First, the definition of a random sample on page 93 as "one for which every member of the group has an equal chance of selection" is quite inadequate. For example a population of a hundred individuals could be divided into ten sub groups of ten in some systematic way and a sub group picked at random; then every individual would have exactly one chance in ten of being picked but we would not have a sample of the kind the author is concerned with. Secondly, the formula given for the normal distribution on page 107 should have the n deleted.

Prof Fraser's approach is completely different. He begins with probability and probability distributions and never mentions empirical frequency distributions. The question of what are the best measures of location and dispersion does not detain him at all; he plunges straight for the mean and variance and proceeds on at high speed. Such an approach is quite intelligible in the light of modern statistical methods where the emphasis has shifted away from pure description to the fitting and testing of mathematical models. Of course in the book under review the treatment can be, and is conducted at a fairly advanced level in view of the mathematical level of the reader for whom it is intended. Nevertheless one would like to see a similar spirit abroad at all levels, however elementary.

While reading the book one has the impression that among the author's guiding lights has been the wish to introduce students as early as possible to the ways of thinking about statistical problems that are customary among professional research workers. It was particularly good to find a thorough treatment of orthogonal transformations, projections on to sub spaces and pivotal reductions of the normal equations.

Once these basic ideas have been grasped the theory of multiple regression, the analysis of variance and covariance, and much else in statistical theory become straightforward.

In spite of the book's merits it must be confessed that parts of it are likely to be found hard going by some students, particularly Chapter 7 on sampling from finite populations and its applications to the analysis of variance. There are easier ways of deriving the formula for the variance of the mean of a sample from a finite population than that given on pages 136-7. Moreover, the misuse of the term 'stratification' should not pass unmentioned. Prof Fraser's 'nested sampling' corresponds in sample survey terminology to multistage sampling, not to stratified sampling. One feels that many of his results could be obtained more simply by current multistage theory than by the methods given in this chapter.

J. DORBIN

THE CULTURE OF CELLS

Cell and Tissue Culture

By Dr John Paul. Pp viii + 201 + 9 plates (Edinburgh and London: E and S Livingstone Ltd 1959) 30s net.

IN 1959 it can be said that the technique of tissue culture is well established and widely applied even on an industrial scale. This claim could not have been made in 1949. Yet more than fifty years ago the principles of cell cultivation outside the body were described and successfully demonstrated by Ross Harrison, and his work was energetically followed up by pioneer schools in the United States, Britain and elsewhere in Europe.

As is strikingly apparent in Dr Paul's book a new phase of confidence and application began about ten years ago and cell and tissue culture to-day provides the following opportunities. Mammalian and plant cells, adapted to culture conditions, can multiply indefinitely in chemically defined media. When required, great amounts of cells may be harvested after relatively short periods of growth. All aspects of cell multiplication and development can be accurately determined and recorded. Permanent cell strains including a number of human origin, are available and cultures can be sent safely to any part of the world.

Clones are now readily established from single isolated cells, the chromosomes can be made clearly visible and their metabolic effects determined. Viruses may be detected and their pathogenicity investigated. The metabolism of cancer cells and their response to treatment can be compared with the behaviour of normal cells, if these are freshly explanted from the body tissue.

Dr Paul's up to date text will be invaluable to every newcomer to the technique and it will also be welcomed by experienced workers. It describes lucidly all the technical aspects of the work from the organization of a suitable laboratory (including such time-saving detail as a list of manufacturers) to the special procedures required for cell research. The book is more than a laboratory manual for it contains well-considered accounts of developments in cell research and a valuable store of references. The only suggestion to be made is that future editions might include a section on the use of isotopic metabolites in tissue culture investigations.

The reviewer does not wish to leave the impression that the cultivation of cells is now an easy matter and that there are no pitfalls. The newcomer to the technique would be well advised to get some practical experience in an established laboratory. As Dr Paul explains, his book is based to a certain extent on the instruction material of the Tissue Culture Association Summer School, which has in recent years provided a basic training for a few hundred individuals in the United States. There is, as yet, no comparable scheme in Europe.

I LESLIE

MEASUREMENT OF VALUES

The Measurement of Values

By L. L. Thurstone. Pp. viii + 322. (Chicago University of Chicago Press, London: Cambridge University Press, 1959) 56s. 6d. net.

PROF THURSTONE, prior to his death in September 1955, was the world's greatest living psychometrist. Psychologists, ever since leaving the philosophical fold, regarded the topic of values as out of bounds. Most philosophers would probably be horrified at the idea of 'measuring' values. In recent years, however, many scientists have realized that the concept of values is essential to science and that the greatest problem of the modern world is how to bridge the gap between technical knowledge and skill on one hand and knowledge of humanistic values on the other. Some, however, regard the problem as insoluble or meaningless, forgetting that absolute laws are found neither in science nor in humanism. During the last thirty years of his life Thurstone developed scientific methods which bid fair to bring social, moral and aesthetic values within the realm of experimental psychology. He has ignored those interminable logical arguments concerning values.

Human values are essentially subjective. It was therefore necessary to establish a subjective metric, and a subjective unit of measurement which must satisfy the logical requirements of measurement as distinct from rank order. This objective was reached by Thurstone by means of his law of comparative judgement which dates from 1927. Weber's law is concerned solely with physical measurements. On the other hand, Fechner's law states the logarithmic relation between the subjective continuum and the physical stimulus continuum. But Thurstone's law of comparative judgement is completely independent of any physical stimulus magnitudes. It involves a new concept in psychophysics, namely, the discriminial error.

The book has a preface by his widow, Mrs. Tholma Gwinn Thurstone, herself a psychologist. There is a selection of twenty-seven papers which have appeared in various journals.

Part I of the book is an essay on "Psychology as a Quantitative Rational Science" where psychological concepts and strict mathematical formulation are emphasized. Part II deals with "Subjective Measurement". Part III with "Attitude Measurement". Thurstone and his students were pioneers in researches on attitudes which are well known to psychologists everywhere. They include such topics as prohibition, militarism-pacifism, and motion pictures.

In the study of social attitudes the cognitive and the affective appraisals may be entirely independent. For example, a group of people might dislike democracy but an examination might show that they

did not know what they were talking about. It is here pertinent to mention the views of the late Prof. Flugel in his classic work on "Man, Morals and Society" (Chapters 1 and 16, 1948) where the tendency to change from orectic (moral) judgement to cognitive (psychological) judgement is one of the marks of moral progress. It is true that the late Prof. Reichenbach, the logical empiricist, in his "Modern Philosophy of Science" (1959) holds that only a non-cognitive theory of ethics supplies an adequate explanation of ethical utterances. Prof. Flugel, however, did not hold that orexis is supplanted by cognition. Orexis still in the last resort supplies the goal at which we aim, cognition only guides us concerning the steps we must take to achieve that goal.

It only remains to add that Prof. Thurstone's book will long remain essential for all students of values.

LL WYNN JONES

CACTI

Die Cactaceae

Handbuch der Kakteenkunde. Von Curt Backeberg. Band 1. Einleitung und Beschreibung der Pereskioideae und Opuntioideae. Pp. xvi + 638 + 35 tafeln. 74 DM. Band 2. Cerooideae (Hylocereoae—Coreoae (Austroceroinae)). Pp. xvii-xxiv + 639-1360 + 72 tafeln. 87 DM. (Jena: Gustav Fischer Verlag, 1958 and 1959.)

THE first two volumes of this new 'handbook' to the Cactaceae provide a taxonomic treatment of the entire subfamilies Pereskioideae and Opuntioideae and reach the end of the 'subtribe' Austroceroinae of the 'semitribe' Austrocereoae of the tribe Cereoae, within the third and last subfamily Cerooideae. In the opening key to the higher categories of the family the author recognizes a total of 220 genera, as contrasted with the 124 genera of Britton and Rose's comprehensive "Cactaceae" (1919-23) and the 41 genera of Alwin Berger's handbook to cultivated species, "Kakteen" (1929), in which *Rhipsalis*, *Cereus* and *Echinocactus* were treated in a broad sense with a large number of subgenera.

Botanical exploration in South America, especially in Peru, eastern Bolivia and north-eastern Brazil, has yielded many new species to add to Britton and Rose's work, and it is good to have a new treatment with keys, descriptions and copious illustrations, some of them coloured. Herr Backeberg has 57 species of *Tephrocactus*, 213 of *Opuntia*, 60 of *Rhipsalis*. The elaborate system of categories in his classification of genera will not please everyone: we are given, in descending order, *Unterfamilie*, *Tribus*, *Semitribus*, *Subtribus*, *Sippe*, *Untersippe*, *Gattung*, *Untergattung*, *Sektion* and *Untersektion*.

The first volume begins with introductory chapters on the history of the Cactaceae in art and literature, on their uses by native tribes or in medical science, on classification, and on the maintenance of living collections. In discussing cultivation, methods of grafting, etc., the author does not descend to the level of the small amateur grower, flat-dweller or floral decorator, but keeps strictly to the botanical and horticultural point of view. This vast work, misnamed 'Handbuch', may well be open, like all big revisions, to much taxonomic criticism and, if only for that reason, will be indispensable to all serious students of Cactaceae.

N. Y. SANDWITH

The Threshold of Space

The Proceedings of the Conference on Chemical Aeronomy, sponsored by the Geophysics Research Directorate Air Force Cambridge Research Center, Air Research and Development Command Cambridge, Mass., 25-28 June 1956. Edited by M. Zelikoff. Pp. xi+342 (London and New York: Pergamon Press, 1957) 105s.

A MORE specific short title for this volume of papers on chemical aeronomy would be helpful. The particular threshold of space is that of atmospheric photochemistry and spectroscopy. While most of the papers are concerned with theoretical and laboratory researches, important experiments using high altitude rockets, and some descriptions of phenomena produced by hypersonic flight, are also included.

The book as a whole has both the shortcomings and the merits perhaps inevitable in a collection of individual papers. There is a lack of coherence and the assumption of an extensive background knowledge by the reader. However, the papers themselves, mostly by workers leading the field, are generally of a high standard. Those dealing with theoretical and laboratory studies of photochemistry and spectroscopy related to the atmosphere of the earth and of Venus, lead to accounts of rocket probing in the upper atmosphere. Some of these papers relate to work such as the investigation of far ultra-violet radiation in the night sky, and the seeding of the upper atmosphere by sodium and nitric oxide which may well have heralded the opening of new branches of old disciplines.

There is no doubt that both the problems and the experimental tools of hypersonic flight research will stimulate and facilitate further understanding of the physics and chemistry of the atmosphere. The introduction of these aspects to the Conference proceedings is welcome. Each paper is followed by a short verbatim discussion and a useful bibliography.

The Insect Pests of Cotton in Tropical Africa

By E. O. Pearson, assisted by R. C. Maxwell Darling. Pp. x+355+8 plates (London: Empire Cotton Growing Corporation and the Commonwealth Institute of Entomology, 1958) 40s.

THIS book sets out to provide a vade mecum for the study of the cotton pests of Africa and is written both for 'those concerned with the welfare of the cotton crop who are not entomologists' and for the field entomologist. The main text occupies a little more than 300 pages of which the first fifty contain a succinct account of the cotton plant, *Gossypium*, its African environment, history, distribution and pests. This section ends with an invaluable field key by means of which observed damage to the crop can be ascribed to its most likely cause, whether it be a fungus, an invertebrate or even 'big game'. The rest of the book is devoted to comprehensive and critical accounts of specific pests which are grouped primarily by order, then, where convenient, by the parts of the host plant which they most usually attack. This discussion is exhaustive yet always terse and gains much from the frequent and extended references to features of the environment relevant to the entomological data under discussion. The authors do not hesitate to look outside Africa when they feel it will throw additional light on their subject and occasionally topics are treated almost in world-wide review. The result is a satisfactory

summary of current knowledge as well as a record of the authors' life-long personal experience.

The book is well illustrated and indexed and is gratifyingly free from errors. It may perhaps be worth noting that *Empoasca lybica* (de Berguin) is not confined to Africa as stated but has been found also in Palestine, Arabia and in the Aden Protectorate, in the last of which it was reported on cotton. A further natural enemy of *Empoasca fascialis* Jacobi may also be added to those listed in the book, since there is in the British Museum (Natural History) collection a specimen of this leafhopper, from Sorere, Uganda, which has been parasitized by a species of *Dryinid*. W. E. CHINA

Parasitic Animals

By Dr Geoffrey Lapage. Pp. xxiii+355. Second edition (Cambridge: W. Hoffer and Sons, Ltd, 1958) 25s. net.

THE publication of the second edition of *Parasitic Animals* will be welcomed by many people, particularly those concerned with the teaching of parasitology. Dr Lapage's treatment of his subject makes the book very readable and provides good background material for students. It is, however, to be regretted that the author has not taken this opportunity to correct some of the errors of fact and to clarify some of the possibly misleading statements which appeared in the earlier edition. I refer in particular, to the perpetuation of such statements as that on p. 107 that the male gametes of *Plasmodium* are 'each about 15-20 mm. long' and that on p. 109 that the gametocytes of the same parasite 'pass back from the mosquito to man'. They also enter man through the sucking tube and enter it passively being unable to effect entry by their own efforts. On p. 01 a slight alteration has been made to the original text but the inference to be drawn from the passage is still the same: that adult *Taenia solium* can normally develop in the intestine of the pig. Reference might be made to several other points but no doubt the observant reader will find these for himself. The only major difference between the two editions is the inclusion in the second of a list of literature for further reading. This is a useful addition but it is disappointing to find that Baer's

Ecology of Animal Parasites, surely the most important book on the subject, has been omitted.

C. A. WRIGHT

Fundamentals of Papermaking Fibres

Transactions of the Symposium held at Cambridge, September 1957. Edited by Francis Bolam. Pp. x+487 (Kenley, Surrey: Technical Section British Paper and Board Makers' Association Inc., 1958) 75s.

THE salient features of this Symposium were summarized in *Nature*, 180, 1175 (1957). The 18 papers presented have now been published in book form, complete with illustrations, references and reports of the discussions. The foreword quotes the view of Dr Otto Maas expressed in his concluding remarks at the Symposium, namely, that it had been a landmark in the science of paper making and had set a new standard for conferences in this field. It is obvious that this book is indispensable to those directly interested in the subject. Workers in allied fields however will also find in it much that is of great use and interest. The inclusion of a subject index would have increased the value of the book for reference purposes.

JELVIS GRANT

by a particle and by self replication. There can be little doubt that permease is particulate and macromolecular in nature. The maintenance of the steady-state system in a growing culture requires a continuous supply of inducer (or substrate) in order that more permease may be produced. Somehow, between them, and of course in the environment of the living cell of which they are a part, the system of inducer and permease holds information needed to make more permease, that is, to convert or mould some other cell product to its own image. The production of this other cell product is under the control of the rest of the cell, including the genetic information of the nucleus. Thus underlying the steady-state system in this particular case is the genetic competence of the lineage of cells to respond in the particular way to the presence of the inducer.

The thiomethyl galactoside permease system has another interesting property. When the kinetics of induction are studied¹⁹ under conditions of continuous culture, the degree of adaptedness in the culture rises linearly with time (measured as generations) if a low concentration of thiomethyl galactoside, just able to cause induction, is used. In such a culture, a proportion of the cells is fully induced or adapted, the remainder being quite unadapted. There are no intermediates, or rather the state of intermediacy is too transient to detect. Once some permease has been formed in a cell, a full complement of it is rapidly acquired, presumably according to a logistic curve. Thus the stable states are discontinuous.

Such a steady-state system has some of the attributes of genetic material, but may be thought to differ from genes and plasmagenes in certain essentials. Especially it is inherited only so long as it is expressed. Secondly, if lost it can be regenerated by a simple manipulation of the environment, provided the genetic basis is still present in the nucleus.

The contrary view is that heredity is dependent upon certain homeostatic material and that various different expressions of it, no matter how persistent, do not differ in a truly hereditary manner. Nanney²⁰ distinguishes these two aspects as 'genetic' and paragenetic or 'epigenetic'. As it was believed that paragenetic is etymologically unsound, 'epigenetic' was suggested, although this word is used for embryological theory and may be unacceptable for that reason. Indeed, Lederberg² avoids the difficulty by going to the extreme and speaking of 'nucleic' and 'epinucleic'. Nucleic information is defined as that depending upon the sequence of nucleotides in a nucleic acid, while epinucleic information is expressed as an aspect of nucleic acid configuration other than nucleotide sequence or in associated materials, such as polypeptides or polyamines. It may also reside in molecules or reaction cycles not directly connected with nucleic acid.

Whether this particular differentiation between the two levels of genetic information will stand the test of time, it is clear that the distinction is not only provocative but also the crystallization of ideas towards which many have struggled. No other biological system, short of the whole organism, approaches the properties of nucleic acid in conveying information, or equally justifies the supposition that it carries the bulk of germinal genetic information. A minor part of the genetic information, the plasmagene, is presumably extranuclear nucleic acid. Likewise, the functionally active ribonucleic acid in the cytoplasm may carry nucleic information. Equally, if nucleic acid conserves genetic information,

it is difficult to see how cellular differentiation could be determined by systematic gene mutation, that is to say, by systematic alteration of nucleotide sequences.

The epinucleic spheres of action may be extra nuclear, like the steady-state systems, or nuclear, and even involve the chromosomes. There is now strong circumstantial evidence of differentiation occurring in nuclei, so that the nuclei of different tissues come to have different heritable potentialities²¹. This may be reflected in differences visible in polytene chromosomes, as in *Chironomus*²², as well as the substitution of histone for protamine in different nuclei, but the differences could also reside in nucleoli. The local variations in behaviour of the chromosomes may sometimes be seen as intense deoxyribonucleic acid metabolism at certain regions²³. This kind of intranuclear differentiation appears to be the basic step in the expression of mating types in *Paramecium*. Such changes could be stochastic, but it seems likely they are directed in some way not, as yet, understood. The interesting occurrence of paramutation²⁴ at the *R* locus in maize and the controlling elements described by McClintock²⁵ seem to offer models of particular systems, as also does lysogeny.

In considering cytoplasmic inheritance *sensu stricto*, we are therefore faced with the problem of distinguishing hypothetical extranuclear nucleic material from extranuclear and intranuclear epinucleic phenomena. It must be conceded that completely sufficient criteria for achieving this have not yet been recognized. It cannot yet be said whether there are macromolecules which persist permanently in the cytoplasm in the same sense as genes persist in the nucleus. Chloroplasts and mitochondria are candidates only in the same sense that the nucleus as a whole is nucleic information. The critical point would be reached if the physical bases of non-chromosomal, hereditary systems, possibly nucleic or epinucleic, could be identified. In any event, whether or not we speak of epinucleic phenomena as constituting heredity, clearly they can determine the inheritance of a particular character through a considerable lineage of cells.

A complete understanding of the function of the cytoplasm in heredity is likely to involve an understanding of the nature of gene action and replication. Gene replication is generally thought to be by some kind of template mechanism, a pre-existing structure organizing smaller units to form a replica of itself. The various modifications of this basic idea need not be considered here, all would lead, theoretically, to the duplication of the gene material, most probably deoxyribonucleic acid. The heterocatalytic property of the gene, in directing functions elsewhere in the cell, may well be through the medium of replicas of itself, or of translations in a chemically different form, perhaps ribonucleic acid or protein or both. The precise activity of these will depend upon how they are integrated with the rest of the cell. If, as seems probable, they are originally filamentous, like the gene material of the chromosomes, their activity will depend upon how and where they are folded into the structure of the cell. In this respect they are likely to be influenced by the existing architecture of similar and associated units, as well as by the presence or absence of regulating substances, such as inducers or repressors. Thus, the organization for expression appears likely to involve another sort of template or mould mechanism, an architectural plan

for using the unit bricks produced by the genes¹². In more specific terms, Mitchell (unpublished work) has suggested that the cytoplasmic information is carried by the proteins and that these co-operate with ribonucleic acids, carrying the information from the nucleus, in forming ribonucleoprotein templates which direct the formation of enzymes. Neither system alone possesses all the information needed for the building and functioning of a cell. Both involve heredity, though probably the cytoplasmic system has a lesser degree of permanency.

The expression of the nuclear products has, therefore, been shown quite often to require extragenic information. Knowledge of the exact nature and mode of action of the latter is highly important for understanding the functioning of the living cell. While it is possible that extragenic information may be carried in a variety of ways, it may be a more economical hypothesis to suppose that it lies in one type of material capable of interacting directly with products from the nucleus. In this respect, protein architecture in all its variety seems a more plausible candidate than does a system of alternative steady states, such that the functional one in the cell suppresses the action of all genes having alternative functions. The latter encounters severe difficulties in view of the great variety of specific inhibitions, acting in a huge range of combinations, that would be required. This is the major obstacle to interpreting for example the serotypes of *Paramecium aurelia* as mutually suppressive systems of steady states.

D G CATCHELSE

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THERMONUCLEAR RESEARCH IN GREAT BRITAIN

THE present state of the research programme, both theoretical and experimental, on the subject of thermonuclear fusion was the main topic at a recent two day meeting of the Physical Society held at the Imperial College of Science and Technology, London, during September 17-18. The conference was attended by representatives from most of the major centres in Britain, and formed an interesting continuation of the meeting of wider scope at Uppsala in August. It is an indication of the present high level of activity in this work that, with the exception of review papers, little duplication of material occurred.

The main session was devoted to contributions outlining the research programmes at the various laboratories, universities and research institutions.

Activity in Great Britain has largely centred around the toroidal pinch devices *Zeta* and *Sceptre*, where the discharge is confined by the magnetic pressure produced by the toroidal current in the discharge itself. Papers by M. G. Rushbridge (Atomic Energy Research Establishment Harwell) and A. A. Ware (Associated Electrical Industries, Ltd Aldermaston) showed that steady progress is being made in understanding the complexities of this type of discharge. In *Zeta*, experiments on the magnetic field distributions in the torus have led to a suitable choice of dimensionless parameters which can be used to characterize the discharge and compare it with

various models. In *Sceptre*, much effort has been put into the measurement of ion and electron temperatures by spectroscopic means, and the electron temperature at $2-3 \times 10^4$ °K has now been checked in several ways. Similar magnetic field distributions to *Zeta* are obtained in which the magnetic field lines within the plasma are helices of constant 'wave length' around the torus and the mutual plasma relationship of which is the same at all points. This has led to a tentative explanation of the results in terms of the kind of helical instability found in some American experiments on large size linear discharges. The energy balance in these discharges is also being examined as part of a search for an explanation of the low electron temperature, but the energy losses have not yet been completely accounted for.

The work of the group at the Atomic Weapons Research Establishment Aldermaston, described by K. W. Allen, is in an interesting state of development. The original very fast linear pinch work which was pioneered at the Establishment is now being supplemented by an apparatus similar to the American *Scylla* at Los Alamos which also requires a condenser bank of very low inductance. In these experiments a circumferential electric current is induced in a cylindrical plasma and causes rapid compression. G. B. F. Niblett showed some very clear streak photographs of an end view of this compression in which it is seen to be quite a complex process with

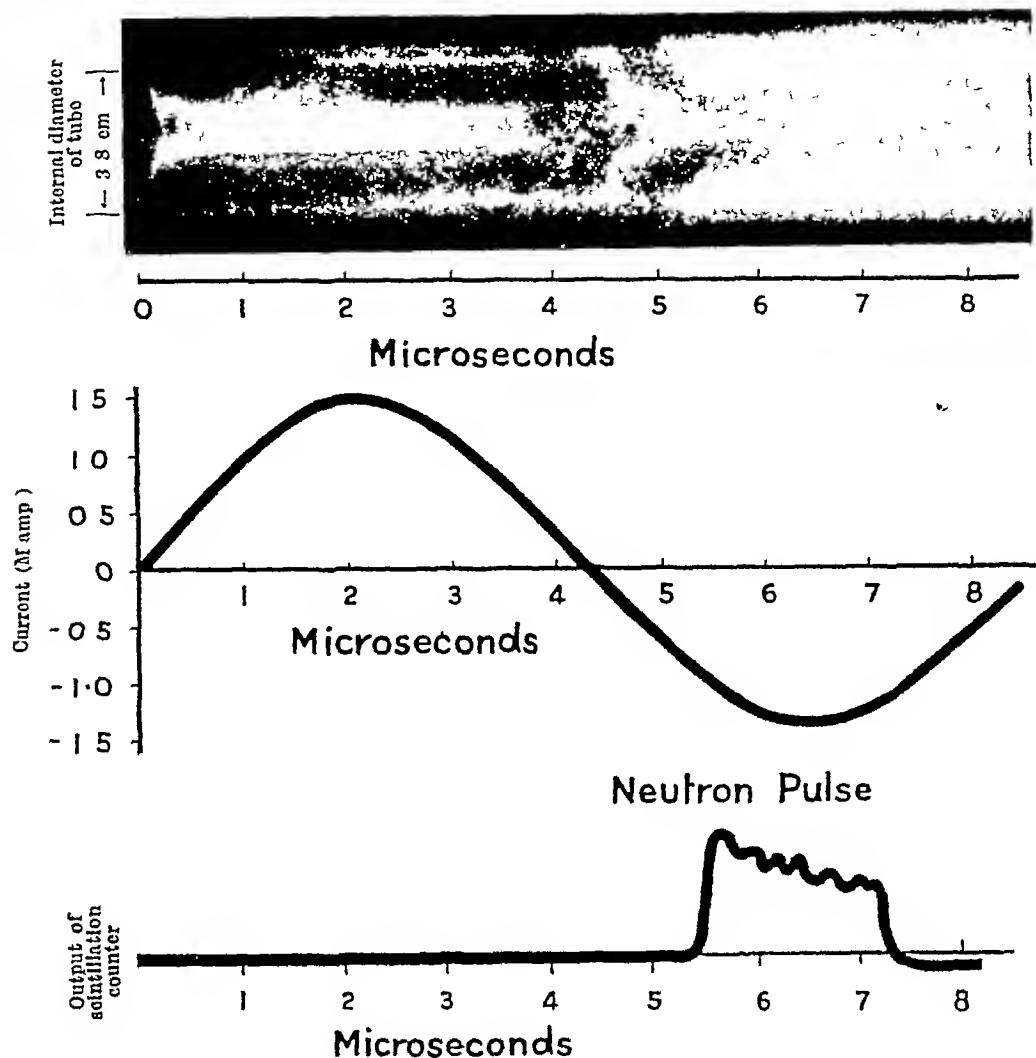


Fig 1 Streak photograph of a discharge in deuterium with current wave form and neutron output (Atomic Weapons Research Establishment, Aldermaston)

marked differences between the phenomena in the first and second half-cycles (Fig 1). The differences are ascribed to the presence of magnetic fields retained within the plasma. Neutrons are omitted, as in *Scylla*, in the second half-cycle of the discharge and the origin of these is being studied.

A further interesting possibility was mentioned which, though experimentally difficult, is now being actively considered. This is to fire a beam of fast-moving neutral atoms into the kind of magnetic bottle developed for *DCX* in America and *OGRA* in the USSR. The injection of neutral atoms instead of molecular ions should lead to better confinement, since the former can penetrate without deflection into the centre of the apparatus before being ionized and trapped. The technical difficulties in producing such a beam must be overcome, but this can be done as an independent problem.

The work at the Imperial College of Science and Technology reported by R. Latham is based on the simplest form of linear discharge. In this the disadvantage of electrodes is compensated for by the low inductance of the tube, which is essential for rapid compression, and by the simplicity of the geometrical arrangement which allows the discharge to be viewed both from the side and the end. The first constriction, which appears as a very narrow column of high-temperature plasma (Fig 2), the subsequent growth of instabilities (Fig 3) and the appearance

machine

The three subsequent sessions are concerned with diagnostic methods, theoretical problems and the role and use of shock waves in thermonuclear work.

In the first of these, the emphasis was on time-resolved photography and spectroscopy, which are necessary for a study of pulsed discharges of short duration. Single-shot photography with Kerr cells and image converters has been the subject of much research, and exposure times of 0.1–0.2 μsec are now in common use. Time-resolved spectra taken at the Atomic Weapons Research Establishment by A. H. Gabriel have shown the sequence of growth and decay of lines in a linear discharge which is completed in 3–4 μsec . Such spectra are beginning to give evidence on how near those discharges are to thermodynamic equilibrium. The consequences of lack of thermodynamic equilibrium, its effect on temperature measurements and recent developments in measurement technique in the range 10,000–50,000°K were discussed in a review paper by H. Edels (University of Liverpool).

Theoretical work on hot plasmas covers a refreshingly wide range of topics and illustrates the close connexion between plasma physics and astrophysics. It may well turn out that thermonuclear experimenting will produce ideas on phenomena in the solar atmosphere, for example, solar prominences and

of impurities from the walls at a later stage have all been studied by means of careful photographic techniques. The use of metal liners to reduce the effect of impurities has been tried with some success.

Two papers from industrial laboratories completed the programme. P. C. McNeill, of the British Thomson-Houston Co., Ltd., Rugby, described an attempt to influence the properties of an electrical arc by placing a pair of magnetic mirrors along its length. L. A. King described work at the Electrical Research Association Laboratories, Leatherhead, where a persistent and successful attack has been made over a period of years on the thermal properties of gases as applied to the formation of cores in high-current electric arcs. The facilities at Leatherhead are now being applied to a study of the high-current vacuum arcs in use in the *DCX*.

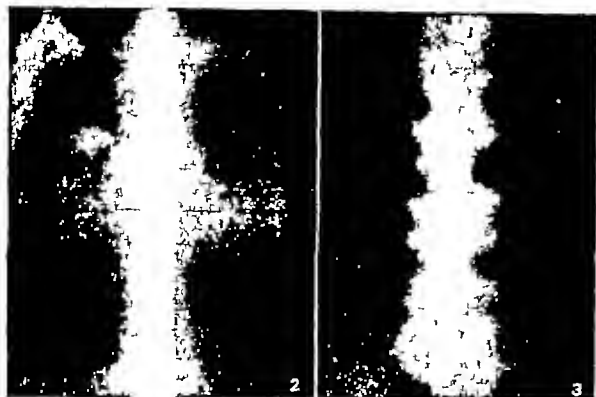


Fig. 2 Side view of linear discharge taken at the time of maximum constriction. (Imperial College of Science and Technology)

Fig. 3 Side view of linear discharge showing the unstable plasma boundary (Imperial College of Science and Technology)

flares, and in a wider context on the generation of cosmic rays. This is not surprising when it is remembered that a star is a naturally occurring thermonuclear reactor, and stellar atmospheres have much in common with laboratory discharges. Indeed astrophysicists have been studying thermonuclear and magneto hydrodynamic problems for many years, long before these subjects became important in the laboratory.

Problems common to astrophysics and discharge physics were discussed by Prof V C A Ferraro (Queen Mary College London) in a contribution on current bearing streams from the Sun, by Prof T G Cowling (University of Leeds) on mechanical effects of the interaction between a plasma and a magnetic field, and by Prof H Bondi (King's College, London) on 'Magnetostatics', with the emphasis on astrophysics.

Among the other theoretical papers one by W B Thompson (Atomic Energy Research Establishment Harwell) contained in outline a derivation of the transport coefficients of ionized plasmas which avoided the arbitrary introduction of the Debye length. This was replaced by a statistical treatment of the potential fluctuations related to the theory of electrical noise. It is encouraging that the expressions previously used are in agreement with those derived by the new method. A paper by M G Haines (Imperial College) considered the skin effect and showed how the familiar skin current of alternating current theory occurs only on the rising part of the wave form of the current in a transient discharge. As the current decays, the theory predicts an inverse of the skin effect with the current becoming a maximum at the centre of the discharge, and even negative at the outer surface. This could in principle lead to the surface layers being violently ejected from the discharge. R J Taylor (Atomic Energy Research Establishment Harwell) has extended his stability calculations on a cylindrical discharge to include the effect of the transport coefficients. He has con-

sidered a cylinder of incompressible plasma with given combinations of the coefficients of electrical conductivity and viscosity. Diagrams showing the growth rate of the $m = 0$ (sausage like) and $m = 1$ (helical) perturbations as a function of their wave length indicated the presence of unstable regions in both cases.

The last session was on shock waves in gases. These have relevance to very hot plasmas because of their use in heating the gas on one hand, and because of their appearance as a result of rapid magnetic compression on the other.

In two papers, K Dolder (Atomic Energy Research Establishment) and H J Pain (Imperial College) reported on the use of shock heated argon to find values of the non-dimensional parameter, analogous to the Lundquist number, which governs the mag-

nitude of the interaction between a plasma and a magnetic field. When plasma flows through the magnetic field of a short axial coil and interaction does occur, a characteristic pattern in the downstream gas is observed similar to that obtained with an annular constriction in the shock tube.

Measurements of electrical conductivity in shock heated argon have been made by A von Engel (Oxford) using the potential developed between two probes as the plasma moved between them in a transverse magnetic field. In this case the requirement of electrical neutrality lowered the conductivity to that associated with the ions. P Smy (Imperial College) reported on electrical conductivity measurements in which an azimuthal current was induced in the moving plasma as it passed through axial magnetic field coils. The induced current was detected magnetically by a search coil. In this instance the current flows in a closed loop in the plasma and the electronic conductivity is appropriate. In both cases the results were in good agreement with the values expected theoretically.

A critical account of the use of shock wave heating as a first stage in obtaining a thermonuclear plasma was presented by J K Wright (Atomic Weapons Research Establishment Foulness). He considered electromagnetically driven shocks and discussed

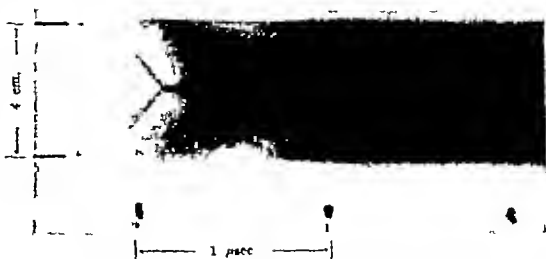


Fig. 4 Streak photograph showing two colliding shock waves. The shock waves move vertically and time increases from left to right. (Atomic Weapons Research Establishment, Foulness)

theoretically the limits imposed by residual inductance and the requirement that the thickness of the shock-front be kept small compared with the size of the apparatus. After being heated by the shock wave, the plasma was assumed to be subjected to a further stage of adiabatic compression. Experiments on electromagnetically driven shocks are continuing, and an interesting streak photograph was shown of two colliding shock waves produced by this means (Fig. 4). Papers were presented by D. L. Schultz and K. C. Lapworth (National Physical Laboratory, Teddington) dealing with microwave reflectivity of shock-heated plasma and with temperature determination by the method of line reversal. The reflexion of shock waves from a region of high magnetic field was examined theoretically by E. J. Morgan (Engineering Laboratory, University of Cambridge) as a basis for future experiments.

It is evident from both the Uppsala Conference and this meeting that the approach to thermonuclear

research has changed since the Geneva Conference a year ago. The emphasis has moved from a few projects requiring large-scale equipment to many simpler experiments designed to clarify the basic principles of plasma physics. It is obvious now that in such matters as stability, plasma oscillations, energy-loss and transport processes, there is much more to be learnt. The lack of immediate success of the larger machines, therefore, though disappointing is by no means without its compensations. It will result in plasma physics being put on a firm basis in which the fully ionized gas will take its place with the other states of matter as leading to an accepted branch of physics. This is a task for the future, and one which can be shared by many smaller groups with modest resources. The outcome will undoubtedly lead to important developments of wide application both in pure science and in technology, with the generation of thermonuclear power as the final target.

R. LATHAM

PUGWASH INTERNATIONAL CONFERENCE OF SCIENTISTS

STATEMENT ON BIOLOGICAL AND CHEMICAL WARFARE

THE fifth in the series of Pugwash Conferences of scientists, aimed at assessing the dangers to humanity arising from developments of modern science and technology, met in Pugwash, Nova Scotia during August 24-29, as guests of Mr. Cyrus Eaton. The purpose of the Conference was to assess the potentialities of chemical and biological agents as weapons, and to explore possible means for preventing their production or use in war.

The subject of chemical and biological warfare has been shrouded in official secrecy. For years, large projects have existed in several countries with the stated purpose of developing means of defence against such weapons. We have no direct information about the results of these projects, but inevitably they increase the efficiency and destructiveness of various types of biological and chemical weapons, and result in the development of new techniques. Judging from the number of technical workers involved in such projects and the money expended, much knowledge related to the production and delivery of micro-organisms for war purposes has probably been gained. Moreover, unsupported statements appear which suggest that such weapons have enormous lethal or incapacitating effects against man, can destroy plants and animals, and have advantages under certain conditions of war. Recently, a concerted effort appears to have been made to suggest that these weapons are more 'humane' than other means of warfare.

We have discussed the general nature of such weapons as well as the properties of the individual agents and their methods of delivery, and have compared them with other weapons. Our discussions suggest that the difficulties of establishing a stable and lasting peace are aggravated by the fact that all nations, whether or not they possess nuclear weapons, might produce biological and chemical weapons, international tension would consequently be increased.

Potentialities of Biological and Chemical Weapons

Biological weapons—microbes, viruses and their toxic products—can be delivered and dispersed in such a way that fatal or incapacitating diseases might be produced over large areas. They can be produced cheaply on a significant scale, even in a country the technological development of which is not highly advanced. Such weapons could be used either alone or together with others. The attack could be local or massive or could consist of individual acts of sabotage. The agent could be selected to cause a great many primary casualties, or to initiate epidemics.

Infective agents or toxins used as biological weapons would presumably have the following characteristics: (a) lethal or incapacitating when applied in small amounts, (b) remain potent when stored or dispersed, (c) the diseases they produce should not be preventable by simple sanitary precautions, or by customary practices of immunization, (d) neither the agents themselves nor the diseases they produce should be easily identifiable, (e) the diseases they produce should not be curable by customary drugs or antibiotics. Many well-known biological agents possess several of, or all, these attributes. The simultaneous use of two or more pathogenic organisms might assist the spread of infection and confuse diagnosis.

Highly virulent strains of some pathogenic agents can easily be selected, as can strains of virulent bacteria resistant to the usual antibiotics, drugs and to some disinfectants. Recent advances in microbial genetics make it possible to produce variants, some of which may be even more suitable for biological warfare than naturally occurring strains.

Quantitative information on the infectivity and toxicity for man of biological agents that might be used as weapons is too meagre for their effects to be compared at all accurately with those of nuclear weapons. However, a surprise attack on a city might

in time cause numbers of casualties approaching those caused by a small atomic bomb. An attack with an infective agent, originally meant to be localized, might lead to an epidemic because of abnormal routes of delivery, the large number of primary casualties, or the disorganization of public health.

The meteorological and other conditions required for biological or chemical attacks on man are so exacting that the military effects will be far from certain. The necessary conditions for a successful attack might prevail only on some days and at limited times of the day, and would be subject to the errors of meteorological forecasting. The discharged material, instead of moving into and staying in the intended area, might recoil on the aggressor. Biological weapons would presumably be stabilized to withstand exposure to the atmosphere and so might remain active for long periods and ultimately fall anywhere.

Attacks on economically useful animals are subject to many of the same limitations as attacks on man. The most likely use of biological warfare on animals would be to disrupt the economy, which could be done by introducing various infections that spread very rapidly and some of which are transmissible to man.

There are also agents that could be used to destroy crops, but their effects are unlikely to be important compared with attacks on human beings and animals. Chemicals such as plant hormones would produce the quickest and perhaps the most serious results, but to be effective would have to be applied over great areas. Some infectious diseases of plants could also be damaging, their introduction, however, could adversely affect the economy of a region for a long time, but most of them spread too slowly to influence the outcome of a war.

Chemical weapons (poison gas or other poisonous substances) were used in the First World War and several subsequent occasions. In recent years, now poisonous substances have been produced which are many times as active as the earlier agents. Means for their bulk production have also been improved as have procedures for their dissemination over areas very much larger than those covered during chemical attacks in the First World War. The production of chemical warfare agents could easily be disguised as peacetime chemical industry, or such industry could be quickly converted to produce them.

The so-called nerve gases which are chemically similar to certain insecticides, are extremely potent and cheap, and cannot easily be countered with effective defensive measures. Masks and appropriate clothing can partially protect against them, but it is difficult to apply such protection to large populations, and it is unlikely that nerve gas casualties could be treated with antidotes soon enough after an attack to prevent serious consequences. New types of hallucinating agents or of poisons that give rise to transient mental disorganization, without recognizable permanent injury, have been advocated as means of 'humanizing' war. Although they do not kill directly, their use could have serious consequences because individuals or groups of people exposed to them behave unpredictably and often irresponsibly. The extremely high level of toxicity of new types of poisonous materials as well as the means available for their delivery, permit their effects to be compared with those of certain types of atomic weapons.

Summarizing the previous paragraphs biological and chemical agents clearly represent considerable additions to modern arsenals. Yet, we realize that nuclear weapons particularly modern hydrogen bombs, have a destructive power several orders of magnitude greater than chemical or biological weapons. As means of immediate and certain destruction, these weapons cannot compare with hydrogen bombs. The dependence of biological weapons on uncontrollable factors, such as meteorological conditions, and the difficulty of confining the effects to the attacked territory, make them especially unpredictable in scope and effect.

World wide apprehension about biological and chemical weapons can be allayed only by measures tending to assure that they will not be produced or used. But, however difficult the international control of atomic weapons may be, the international control of biological and chemical weapons by any system of inspection seems incomparably more difficult.

The first reason is that the specific weapons or combinations of weapons, likely to be used in a particular instance cannot be foreseen.

The second is that chemical or biological weapons can be selected and prepared in ordinary chemical or microbiological laboratories. The fact that no elaborate or large-scale facilities are needed makes it difficult to identify possible places of preparation for biological or chemical warfare. Even elaborate installations would resemble those normally used in the production of vaccines or antibiotics. It follows that small and large nations, whether industrially undeveloped or highly industrialized might secretly prepare to use such weapons and with each added nation possessing such capabilities, the danger of war would mount.

A third reason is that means of dispersal of chemical and biological agents of warfare are diverse, including aeroplanes, submarines and missiles as well as saboteurs. Their delivery therefore cannot be prevented because it would require a ban on all forms of transport, civil as well as military.

If control by inspection is so extremely difficult, what alternative ways are there to decrease the danger that chemical and biological weapons will be used? It seems clear that international renunciation of the use of such weapons, as in the 1925 Geneva Protocol cannot allay apprehension unless all nations small as well as large, ratify such an agreement without reservation. This is the first necessary step.

Secrecy is clearly essential to preparations for biological and chemical warfare. On one hand it enables any nation planning aggression to depend upon the element of surprise and upon the opponent's lack of effective counter measures taken in advance. On the other hand, the unknown is, of itself, a potent cause of human anxiety, and is even more so when associated with weapons of any kind. Any actual danger there may be will certainly be exaggerated wherever information about any aspect of the situation is denied. Secrecy on the part of possible enemies is even more productive of anxiety suspicion and hostility, and may precipitate hostile reactions. Free and frank revelation of all scientific and technical developments is essential to a degree of mutual trust necessary to resolve the acute tensions that now plague the world.

The most hopeful approach to international regulation therefore seems to comprise (a) a general agreement to prohibit the use of such weapons, and

(b) the renunciation of official secrecy and security controls over microbiological, toxicological, pharmaceutical and chemical-biological research

In considering how to implement the second of the foregoing proposals, we note the already excellent effects of the Report of the U N Scientific Committee on the Biological Effects of Radiation. A comparable scientific committee, or a permanent U N Scientific Commission on biological and chemical modes of warfare, could help to dispel apprehension. A subsidiary function of either group might be to investigate impartially the claims by plaintiff nations that others had openly or surreptitiously used methods of biological or chemical warfare against them.

The very existence of such a Commission might in time arouse the conscience of the individual scientists of all nations, the only ultimate effective safeguard against violations.

In agreement with the Third Pugwash Conference in Vienna, we repeat that, in the end, only the absolute prevention of war will preserve human life and civilization in the face of chemical and biological as well as nuclear weapons. No ban of a single type of weapon, no agreement that leaves the general threat of war in existence, can protect mankind sufficiently. We therefore must look forward to a day when the preservation of peace will transcend the ambitions of individual nations.

Trust between nations cannot be established by proclamation, but only by experience, particularly by experience in co-operative work toward common aims. There is already an extensive interchange of scientific information and people in the sciences basic to the problems discussed in this statement. We must build on this. The Commission proposed to collect and evaluate information bearing on chemical

and microbiological warfare should serve not only to allay the fears of mankind that new and ever more horrible weapons of such types will be invented but also to dispel the miasma of secrecy that fosters international suspicion and tension, and in its place to extend the benevolent application of microbiological and chemical knowledge for the benefit of all men.

Dr BROCK CHISHOLM (Canada)

Prof CLAUDE E. DOLMAN (Canada)

Prof DONALD KERR (Canada)

Sir ROBERT WATSON-WATT (Canada)

Dr PREBEN VON MAGNUS (Denmark)

Dr ANDRE LWOFF (France)

Dr PIERRE THIBAUT (France)

Dr M. L. AHUJA (India)

Academician MIKHAIL M. DUBININ

(Soviet Union)

Prof ALEXANDRE A. IMSHINETS

(Soviet Union)

Mr VLADIMIR P. PAYLICHENKO (Soviet Union)

Prof A. A. SMORODINTSEV (Soviet Union)

Prof SVEN GARD (Sweden)

Mr F. C. BAWDEN (United Kingdom)

Dr PATRICIA J. LINDOP (United Kingdom)

Prof GORDON MANLY (United Kingdom)

Prof JOSEPH ROTBLAT (United Kingdom)

Prof M. G. P. STOKER (United Kingdom)

Prof H. BENTLEY GLASS (United States)

Dr CHARLES C. HIGGINS (United States)

Dr MARTIN M. KAPLAN (United States)

Prof CHAUNCEY D. LEAKE (United States)

Prof HUGO MURACH (United States)

Prof EUGENE RABINOWITCH (United States)

Prof ALEXANDER RICH (United States)

Prof THEODOR ROSEBURY (United States)

OBITUARY

Dr B. van der Pol

AFTER a brief illness, Dr Balthasar van der Pol, a director of research in radio science, university professor and international civil servant, died at his home in The Netherlands on October 6, at the age of seventy.

Dr van der Pol was born on January 27, 1889, at Utrecht, The Netherlands, where he was educated and obtained his degree in physics at the University of Utrecht in 1916. In that year he went to study under Prof J. A. Fleming at University College, London. He proceeded to Cambridge in the following year, where he worked in the Cavendish Laboratory as a foreign research student under Sir J. J. Thomson. He was very interested in the Heaviside layer theory of the reflexion of radio waves, and carried out experiments designed to show that ionized air in an electric discharge could act as a radio wave reflector. He was successful in this work, and on returning to Holland in 1919 he was awarded his doctor of science degree for a thesis on "High Frequency Measurements of Glow Discharges", and became assistant to Prof H. A. Lorentz at Teyler's Institute, Haarlem.

In 1922, Dr van der Pol was appointed physicist in the research laboratory of the N.V. Philips works at Eindhoven, where he later became director of research in radio science. He was appointed knight of the Order of Oranje Nassau in 1927, for establishing

the first radio telephone communication between the Netherlands and the Dutch East Indies. Concurrently with his service in the Philips organization, he was professor of theoretical electricity in the Technical University, Delft (1938-49), and he was president of the temporary University founded at Eindhoven to replace other Netherlands universities in occupied territories, for which service he was appointed knight of the Order of the Netherlands Lion in 1946.

Van der Pol was interested in a wide range of mathematical and physical subjects, and was the author of a number of papers published in scientific journals, these included two lectures delivered before the Wireless, and later Radio, Section of the Institution of Electrical Engineers in London on "Discontinuous Phenomena in Radio Communication" (*J. Inst. Elect. Eng.*, 81, 381, 1937), and "The Fundamental Principles of Frequency Modulation" (*J. Inst. Elect. Eng.*, Part III, 93, 153, 1946). He also published a book jointly with Dr H. Brenner on "Operational Calculus based on the Two-sided Laplace Integral" (Camb. Univ. Press, 1950). He was a member of both the American and London Mathematical Societies, of the Netherlands Royal Society, a founder member of the Netherlands Radio Society, fellow, and vice-president for 1934, of the Institute of Radio Engineers (N.Y.), and an honorary life member of the Institute of Radio Engineers.

(Australia) He was awarded the Medal of Honour of the Institute of Radio Engineers (N.Y.) in 1935 for contributions to circuit theory, and in 1953 the Danish Academy of Technical Sciences presented him with the Valdomar Poulsen Gold Medal for outstanding contributions in the field of radio research and for international scientific co-operation in matters related to radio communication.

Dr van der Pol became greatly interested in the scientific and technical aspects of international radio affairs and from 1927, he was a well known participant in a large number of conferences in all parts of the world. He was vice president of the International Scientific Radio Union during 1934-50 and was elected an honorary president in 1952.

He was appointed the first director of the International Radio Consultative Committee in 1949, and held this position until his retirement in 1956. As the permanent executive officer of the Committee, he was the technical adviser to the International Telecommunications Union on the planning and

development of radio communications during the post-war years. Until a few weeks ago he was attending the present conference of this Union in Geneva, representing other international scientific bodies on the allocation of frequencies for radio astronomy and space research. In later years his interest in mathematics developed towards the Heaviside calculus, to the extension of which he made notable additions, he was also interested in the theory of numbers. Since his retirement in 1956 he had been an active lecturer in these subjects particularly in the United States.

Dr van der Pol was very well liked and respected by the vast number of friends with whom he came in contact throughout the world. His qualities as a scientist and his administrative abilities as an international civil servant always received the highest recognition. He never spared himself in his devotion to the pursuit of knowledge and human understanding on a wide international basis. He was happily married and leaves a widow, a son and two daughters.

R. L. SMITH ROSE

NEWS and VIEWS

Nobel Prize for Medicine for 1959 Prof S Ochoa

THE Nobel Prize for Medicine for 1959 has been divided between Prof S Ochoa and Prof A Kornberg. Dr S Ochoa has long been regarded as one of the principal exponents of the highly successful enzymological approach to the study of intermediary metabolism. His recent contributions to the mechanism of the biosynthesis of nucleic acids have been preceded by a succession of outstanding biochemical discoveries principally concerned with the metabolism of carboxylic acids and with associated phosphorylation reactions. One of the most notable of these discoveries was made in 1939 while he was a research worker at Oxford. He found that large quantities of inorganic phosphate are esterified when pyruvic acid is oxidized by dispersions of brain tissue. This 'oxidative' phosphorylation is recognized as part of the fundamental mechanism whereby energy is made available from biological oxidations. With his students and colleagues at New York University he has since discovered a number of important enzymes which are involved in the tricarboxylic acid cycle and the oxidation of fatty acids.

Dr Ochoa's work on nucleic acids originated from experiments on phosphorylation reactions in enzyme preparations from *Acetobacter*. In 1955, together with Dr M Grunberg-Manago, he reported the discovery of an enzyme which is able to catalyse the removal of the terminal phosphate group from ribonucleoside diphosphates accompanied by the polymerization of the resulting nucleoside monophosphate residues. In this way, a mixture of the four appropriate nucleoside diphosphates can be converted into a polynucleotide which closely resembles naturally occurring ribonucleic acid although it is not yet understood how the arrangement of the nucleotides in the polymer is controlled. The discovery is notable because of the structural complexity of ribonucleic acid and because of the essential functions of this material in the synthesis of proteins.

Prof A Kornberg

BEFORE making their discoveries in the biosynthesis of nucleic acids, Dr Kornberg and his colleagues were responsible for many important advances in several areas of intermediary metabolism including the biosynthesis of nucleotides and nucleotide coenzymes. In 1956, Drs Kornberg, Lehman, Bossman and Simms described experiments indicating that deoxyribonucleic acid could be synthesized by an enzyme system prepared from *Escherichia coli*. Further study with a purified preparation of the enzyme has shown that the nucleic acid is made from the triphosphates of the four kinds of deoxyribonucleosides and requires the presence of some preformed deoxyribonucleic acid. The detailed results substantiate the elegant hypothesis proposed by Drs Watson and Crick in 1953. Thus it seems that the double strand of the primer deoxyribonucleic acid becomes separated into its complementary single chains which then act as templates for the assembly of new polynucleotides and finally become two molecules having the detailed structure of the original double stranded one. Within the past year, Dr Kornberg and his very active group of research workers have reported an outstanding series of experiments on the synthesis of deoxyribonucleic acid in *E. coli* infected with certain bacterial viruses. Their experiments show that the viruses induce the infected bacteria to develop a number of enzymes which, between them, cause rapid multiplication of the deoxyribonucleic acid of the virus while preventing the formation of bacterial deoxyribonucleic acid. The great interest of these exciting developments is that deoxyribonucleic acid is a characteristic component of chromosomes and is considered to act as the principal carrier of genetic information, the sequences of the four kinds of nucleotides in the long polynucleotide chains are thought to determine the structure of the proteins and hence to control the hereditary properties of living cells.

Applied Physics at Durham. Dr. D. A. Wright

It was decided recently to set up a Department of Applied Physics in the Faculty of Applied Science within the Durham Division of the University of Durham. This is the first 'applied' department in the Durham Division and is intended to give Durham students closer contacts with industry and to contribute to the training of applied scientists. The first professor of applied physics, Dr. D. A. Wright, will take up his appointment on April 1, 1960. Dr. Wright graduated with a first-class honours degree in physics at the University of Birmingham in 1932 and later carried out research at Birmingham for which he was awarded the M.Sc. In 1955 he was awarded the degree of D.Sc. of the same University. Since 1934 Dr. Wright has been a member of the scientific staff of the research laboratories of the General Electric Company, Wembley, and is now head of the Combined Electron Physics and Solid State Physics Laboratory. His research groups have published work of high quality in the fields of thermionics and semi-conductors. Dr. Wright's recent work has been concerned with thermo-electricity, a subject which may well have considerable industrial and commercial applications. Dr. Wright has taken an active interest in the Physical Society and the Institute of Physics. He is treasurer of the Physical Society and represents it on the Parliamentary and Scientific Committee.

New Geophysical Observatory in Belgium

THE magnetic observatories founded in the nineteenth century near large cities are steadily having to be transferred to areas remote from electric transport. This happened many years ago for Kew and Greenwich. Now the Royal Belgian Meteorological Institute has had to transfer its magnetic observatory from Uccle, near Brussels, to Dourbes in south-east Belgium. The new observatory had to be sited at least 15 km from present or potential electric transport, a requirement more difficult of fulfilment in Belgium than in the British Isles. The opportunity has been taken to build a truly magnificent comprehensive geophysical observatory, equipped for recording the terrestrial magnetic elements, earth currents, atmospheric electricity, radio atmospherics, radioactivity in the air, seismic waves, and ionospheric variations. The observatory is lavishly described with detailed descriptions of buildings and instruments, photographs (many in colours) and architectural plans in a recent publication of the Institute (*Institut Royal Meteorologique de Belgique Publications Serie A, No 7 Réalisation du Centro de Physique du Globe à Dourbes* Par Prof. E. Labayo Pp 104 Bruxelles Institut Royale Meteorologique de Belge, 1958). This publication will be studied with great interest, and some envy, by those responsible for geophysical observatories in other countries. The detailed building plans which it contains will be invaluable in designing other new observatories or in re-designing existing ones.

Atmospheric Sciences Advisory Panel

THE U.S. National Science Foundation has announced the names of six scientists who will form the Foundation's Advisory Panel on Atmospheric Sciences. The purpose of the Panel is to provide advice to the Atmospheric Sciences Programme on the development of a programme of basic research and supporting facilities, including such fields of science

as physics, engineering, oceanography, meteorology and mathematics. The Panel will consist of Dr. Thomas F. Malone, director of research, Travelers Insurance Co., Hartford, Connecticut; Dr. Walter H. Munk, professor of geophysics, University of California at La Jolla, La Jolla, California; Dr. Walter Orr Roberts, director of the High Altitude Observatory, University of Colorado, Boulder, Colorado; Dr. Verner E. Suomi, professor of meteorology, University of Wisconsin, Madison, Wisconsin; Dr. Arthur H. Wayne, director of the Ionosphere Research Laboratory, Pennsylvania State University, University Park, Philadelphia; and Dr. E. J. Workman, president, New Mexico Institute of Mining and Technology, Socorro, New Mexico.

U.S. Expenditure on Research and Development for 1957

A PRELIMINARY report on a survey conducted by the Bureau of the Census for the National Science Foundation indicates that funds for research and development in private industry in the United States in 1957 totalled 7,200 million dollars, compared with 6,000 million dollars in 1956 (*Reviews of Data on Research Development No 14 August 1959 Funds for Research and Development Performance in American Industry, 1957* Pp 6 Washington, D.C. Government Printing Office). The aircraft and electrical equipment industries accounted for more than half (2,544 million dollars and 1,170 million dollars, respectively), representing increases of 21 per cent and 24 per cent on 1956 figures. Motor vehicles and other transport, and the machinery industries, were next with 708 million dollars and 688 million dollars, followed by industrial chemicals (384 million dollars), petroleum refining and extraction (230 million dollars) and communications (206 million dollars), the percentage increases over 1956 being 6, 22, 14, 23 and 16. Scientific and mechanical measuring instruments increased by 30 per cent, to 126 million dollars. Of the total of 7,200 million dollars, 3,700 million dollars came from Federal funds, which represented 85 per cent of the total in the aircraft industry and 61 per cent in the electrical industry. Expenditure on basic research totalled 241 million dollars, and of this 52 million dollars were expended by the aircraft industry, 38 million dollars by the electrical equipment industry, 30 million dollars by the petroleum refining and extraction industry, and 20 million dollars by the chemical industry. The physical and mathematical sciences claimed 54 per cent of the expenditure on basic research, engineering sciences 36 per cent and the biological sciences about 10 per cent.

The Acute Radiation Syndrome

ACCIDENTS which result in exposure of man to doses of ionizing radiation in the lethal range are sufficiently rare to be extremely important. A report by the United States Atomic Energy Commission (*Report ORINS-25 The Acute Radiation Syndrome—a Medical Report on the Y-12 Accident, June 16, 1958* Compiled by Marshall Brucer Pp viii+188 Washington, D.C. Office of Technical Services Department of Commerce, 1959 1 dollar), which follows closely to a similar one from France (Jannet, H., et al., "Étude de six cas d'irradiation totale aigue accidentelle", *Rev. Franc. d'et. Clin. et Biol.*, 4, 210, 1959), therefore merits study by physicians, radiobiologists, health physicists, administrators and the

daily Press. It is an account of the men who were subjected to mixed neutrons and γ rays from an unanticipated critical assembly of enriched uranium five to doses of some 200-400 rads three to some 30-60 rads. The clinical features and progress are compared with haematological findings and the dosimetric estimations and calculations of the health physicists. Twelve sections are contributed either by the various physicians and scientists responsible for the routine handling of the cases or by special research workers. A final section is a complete appreciation by Dr Marshall Brucer, chairman of the Medical Division, Oak Ridge Institute of Nuclear Studies. Dr Brucer makes the point that initially the physician is on his own. The health physicist can at first classify those at risk only into three groups according to dose: low (less than 250 rads), high (greater than 1,000 rads) and intermediate. The first need no specific medical treatment, the second humanitarian care, but the third present problems requiring judgment. The symptoms (especially vomiting and fatigue) can help the physician initially to identify the three classes. The lymphocyte-count in peripheral blood is the next guide. Later, particular amino-acidurias will be important, and later still the platelet-count of the blood. Meanwhile the health physicist can have reconstructed the incident assayed the body fluids for induced radioactivity, and made a more refined assessment of the doses received. 'A conservative rule to follow during the first few weeks is that there should be a plain and unmistakable indication for anything that is injected into the body. Probably the most important feature in treating psychological upsets is to see to it that the hospital is not turned into a zoo.'

Health and Industry

The annual report of the Chief Inspector of Factories on Industrial Health for 1958 is notable for two special chapters, one of which deals with occupational cancer, while the other describes a study of medical supervision in 210 factories (Ministry of Labour and National Service. Pp iv+61. Cmd 811. London: H.M. Stationery Office, 1959. 3s. 6d. net). The report also particularly invites members of the medical profession generally who could add to available knowledge of health hazards to report to the Medical Branch of the Inspectorate cases of interest coming to their notice in which occupational factors might be involved. Such information could assist the discovery of new industrial hazards and lead to a fuller assessment of the extent and distribution of recognized industrial diseases. The Industrial Health Advisory Committee besides considering the report of a survey by the factory inspectorate on cardrooms in the cotton industry designed to ascertain progress made in meeting exhaust ventilation requirements appointed a sub-committee to collect and assess information as to the need for more chemical, physical and biological testing in factories with a view of reducing the risks of injury to health. Although the Work in Compressed Air Special Regulations, 1958 have not been in force sufficiently long to assess their effect on the incidence of compressed air illness, progress is apparently being made and often a high standard of welfare achieved beyond the minimum standards laid down. Attention is directed to the need for a careful watch for any health hazard from dust from the new 'chromizing' process of forming a surface

layer of chromium over steel articles, and of aiming at complete suppression of dust or fume in the fabrication of alloys by addition of 2 per cent of beryllium to copper. The chapter on occupational cancer gives a concise summary of existing knowledge that medical supervision in factories in diseases that medical examination of work people is usually regarded as the most important function of a works doctor: advice about factory conditions appear to come next and then emergency and accident treatment and treatment for minor sickness.

Study of Corrosion

The fifth report of the Corrosion Committee of the Iron and Steel Institute appeared more than twenty years ago. Although no further report was published the work has been carried on continuously and the present sixth report which is now available deals with this (Iron and Steel Institute. Sixth Report of the Corrosion Committee. Compiled by Dr J. C. Hudson. Pp x+217. Special Report No 66. London: Iron and Steel Institute 1959. 63s.). The Committee of the Iron and Steel Institute ceased to function as such in 1946 when its work was taken over by the British Iron and Steel Research Association and the work now published was therefore carried out under the auspices of both organizations. This report consists of an extensive introduction in which the work of the Committee since 1938 is discussed as a whole. This is followed by two sections dealing at length with unreported work on atmospheric corrosion in air, soil and water. The final results are given of an extensive series of field tests on a wide variety of structural irons and steels carried out all over the world, and in some cases with an exposure time of up to fifteen years. Section 3 of the report deals with the protection of steel against highly corrosive humid atmospheres at temperatures up to 300°C while Section 4 is devoted to marine corrosion and includes the results of several service trials of painting procedures and anti-corrosive compositions for ships' hulls. There can be no doubt that the work published is of first-rate importance to all concerned with the preservation of structures land and marine against rust, and it is doubtful whether the Iron and Steel Institute has ever published a report of more far-reaching significance.

Building Research in Britain

The annual report of the Building Research Board of the Department of Scientific and Industrial Research will be of interest to all who plan, design or construct buildings (The Report of the Building Research Board with the Report of the Director of Building Research. Pp iv+72+12 plates. London: H.M. Stationery Office, 1959. 5s. 6d. net). The summary of research work in hand or recently completed, includes topics as diverse as the development of large perforated bricks, design of radiation shields, earth pressures on tunnels, supplementary artificial lighting, reinforced light-weight concrete, and rubber concreting skips. The need for durability in buildings causes some investigations to extend over many years and summaries of results obtained so far are a useful feature of the report. The building industry is often accused of being the least efficient branch of engineering, and the slowest to apply the results of research, although the Building Research Station devotes much effort to making its discoveries known. In order to improve the methods employed a survey

has been started of what information reaches contracting firms, and what is done with it at various levels. This investigation might well be extended to include architects, engineers and other research organizations. The inquiries and special investigations undertaken during the year reflect trends in the industry. Curtain walling systems were prominent, and interest is increasing in heating, heat and sound insulation, acoustics and lighting. The appendixes include lists of building research publications and of films on loan.

Radio Research

In the years immediately prior to the International Geophysical Year, routine vertical incidence radio soundings of the ionosphere were carried out at about seventy stations, and during the International Geophysical Year both the number of sounding stations and the scope of the observing programmes were greatly increased. The experimental data, which such soundings provide, take the form of curves of equivalent height of reflexion (h') against frequency (f), so called 'ionograms'. It has always been recognized that the equivalent height of reflexion of the radio waves is often quite different from the actual height of reflexion and, indeed, in the early years of radio sounding it was shown that, in general, the experimental $h'(f)$ curve could not yield unambiguously the true height/electron density profile. Furthermore, the calculation of true height is itself a matter of some complexity, especially when proper allowance is made for the influence of the magnetic field of the Earth. Hence it is, until recent years, that ionospheric workers have based their studies on parameters such as the critical frequency, the equivalent height and the 'M' factor—quantities which could be immediately read from the ionograms. However, the advent of the electronic digital computer has made possible the large scale conversion of $h'(f)$ curves into $N(h)$ profiles, and as part of the world-wide International Geophysical Year programme a number of organizations formulated programmes for the determination of $N(h)$ profiles for representative stations and for selected observational periods. The Radio Research Special Report No. 28 prepared by Dr J. O. Thomas and Mr M. D. Vickers describes in detail the electronic computer programme and method adopted as part of the British International Geophysical Year ionospheric programme (Department of Scientific and Industrial Research. The Conversion of Ionospheric Virtual Height-Frequency Curves to Electron Density-Height Profiles. Pp v+48. London: H.M. Stationery Office, 1959. 3s. 6d. net). A useful manual method for making these calculations is described in an appendix to the report and an excellent classified list of papers on this subject is also included.

Natural History in the Midlands

In connexion with the centenary celebrations of the Birmingham Natural History and Philosophical Society in 1958, Mr K. L. Kenrick has written an interesting and very readable account of the records of the Society and the story they tell (Pp. 52. Birmingham Natural History and Philosophical Society, 1959). The longest of these deals with the sixteen volumes of the *Midland Naturalist*, 1878-93, including brief biographical notes on leading members of the Society, as does the section dealing with the activities of the Society between the two World Wars. After the destruction of the Society's rooms at Avobury House

on October 25, 1940, activities were suspended until the end of hostilities, but the Society in 1954-55 was once more installed in the Birmingham and Midland Institute, its original home, where the Society's library, its Wynn entomological collection, the J. W. Moore collection of British butterflies and moths, a purchased entomological collection and the Archer-Overton collection of land, freshwater and marine shells are housed.

Equus przewalskii

THREE short articles by A. G. Bannikov, E. Dagva and D. Tzevegmid (*Priroda*, 5, 50; 1959) deal with the Mongolian wild horse (*Equus przewalskii*) in its native habitat and in captivity. Its present habitat area is roughly delimited by 41° N to 46° N and 90° E to 95° E, a small area situated on the border between Mongolia and Sinkiang. Recently a herd of wild horses has been observed along the Taklan Shara-Nuru range, but in the opinion of observers, both the area and the number of individuals are rapidly being reduced. Drastic legislation is suggested to combat the illicit hunting of these rare animals. The effects of acclimatization of the Mongolian wild horse and the hybrids are discussed in another article by I. S. Sles (*Priroda*, 5, 53, 1959).

Spilogale Revised

VOL. 117, article 5, of the Bulletin of the American Museum of Natural History (pp. 229-392. New York, 1959. 2 dollars) is a taxonomic revision of the spotted skunks of the genus *Spilogale* by R. G. Van Gelder, assistant curator in the Department of Mammals. The spotted skunks are distributed over the greater part of the United States and Central America; they are black animals with a complex pattern of white markings which, although almost infinite in their variations, appear to be modifications of a single basic pattern of stripes. The older taxonomists regarded most of the variations as distinct species so that by 1906 Howell listed fourteen species and six subspecies. As a result of the present author's study of a long series of specimens (nearly two thousand), and particularly of local populations, this list is now mercifully reduced to two species, one *S. putorius* polytypic with fifteen subspecies, the other, *S. pygmaea*, monotypic. The characters and measurements of the different subspecies are discussed in detail and illustrated with excellent figures of colour pattern and skull form. The paper concludes with a discussion of the evolutionary trends of the genus in size, colour pattern and skull characters, and a consideration of the clines that occur in the populations of many areas. There is a full bibliography.

Female-sterile Flowers in *Fuchsia*

THE production of female-sterile flowers by hermaphrodite plants of *Fuchsia procumbens* has been described and discussed by M. Holdsworth (*Trans. Roy. Soc. New Zealand*, 86, 105 (1959)). *Fuchsia procumbens* flowers annually in late summer. The brief flowering season begins and ends with the production of a proportion of imperfect flowers—some fall without opening, others open normally but have defective styles and stigmas. Continuous long-day treatment extends the flowering season and increases the number of flowers produced throughout, but this is supposed not to be directly a day-length

effect on flower initiation but on vegetative growth. Neither bud abscission nor female sterility could be shown to be simple day length effects, but both appear to be induced primarily by low temperatures, in conjunction, perhaps, with long days in the case of abscission, and short days in the case of style abortion.

Reorganization of Root Apices after Irradiation

UNDER this title F. A. L. Clowes has described experiments in which roots were irradiated with X rays and then fed with adenine $8^{14}C$ at various intervals afterwards to observe the effect of the radiation on the sites of deoxyribonucleic acid synthesis and hence on the behaviour of the meristem (*Annals of Botany*, N.S., 23, 205 (1959)). Dividing meristem cells may be so badly damaged that they stop synthesizing deoxyribonucleic acid and dividing; and when this occurs root growth may continue by the formation of a new meristem. The latter often originates in the quiescent centre, the cells of which do not normally synthesize deoxyribonucleic acid or divide. These apparently constitute a reservoir of cells which are less vulnerable because of their quiescence, but are able to restart deoxyribonucleic acid synthesis and division when the normally meristematic cells cease to do so. Because of this re-organization of the apex, Clowes considers that it is not legitimate to argue about the behaviour of normal root meristems from chimeras induced by irradiation.

Paleotemperatures and the Origin of the Deep Sea Fauna

A CRITICAL review of the methods of determination of the temperatures of ancient seas by the measurement of the oxygen isotope ratio in fossil calcareous organisms is given by Y. A. Burstein (*Prirada* 5, 21, 1959). It is based partly on the work published in the Soviet Union and it lends to certain new ideas regarding the origin of the deep sea fauna. Thus the author of this review is casting doubt upon the conclusions of O. Emilian and O. Edwards (*Nature*, 171, 887, 1953), regarding the sharp changes of sea temperatures during the late Tertiary era and also about those of A. Fr. Braun (*Nature*, 177, 1105, 1956) regarding the extinction of the deep sea fauna. According to the author all the deep oceanic regions must be considered to be regions of a relatively constant temperature affording a place of refuge to many animal species which have eventually died out in the waters of a lesser depth.

Liquation Differentiation in Magma

A NEW contribution to one of the most controversial problems in petrology—liquation differentiation—was made by V. I. Lobodinsky (*Prirada* 12, 99, 1958), whose original paper, which he wrote in collaboration with Mo. Ko. Min, was published separately (*Bull. Acad. Sci. U.S.S.R., Sér. Géol.* 12, 64, 1958). In these two papers the authors describe certain peculiar liparite lavas from the Kalgan region of Northern China. The lavas in question contain spherulites and spherulitic aggregates, made of a fibrous mineral. The chemical analysis of the spherulites differs from that of the ground mass in which they are immersed by a greater amount of silica, soda and potash, and a lower amount of magnesia, lime and water. The author suggests that this rock is a solidified emulsion formed by the separation of the original magma into two immiscible liquid fractions.

A number of petrologists deny the possibility of liquation in natural magmas, although there are a number of experimental results published proving that in certain cases such a phenomenon does occur. Such are, for example, the papers by D. P. Grigorov (*1955*), D. P. Grigorov and F. V. Iskyul (*1937*), J. W. Grogg (*1927, 1928*), O. F. Tuttle and I. I. Friedman (*1948*) and E. Roedder (*1951*). On the other hand there are also numerous works dealing with spherulitic rocks and spherulites as developed in commercial glasses. Beginning with the classical studies by A. Lagerlöf (*1887*), many petrologists were attracted by this subject. A number of them like F. Y. Loewinson-Lessing (*1884, 1905, 1935*) and T. L. Tanton (*1925*), tried to prove that certain spherulitic rocks were indeed products of magmatic liquation. On the other hand, there were many petrologists such as, for example, D. S. Bolyankin (*1933, 1940*) who has studied both spherulitic rocks and spherulitic commercial glasses, who do not believe in magmatic liquation, and would attribute the spherulitic structure to devitrification in the solid state.

Medicina Experimentalis

ALTHOUGH some think there are already too many scientific journals—and people!—in the world, the birth of a new one is always an interesting event. *Medicina Experimentalis* is the name which has been given to the latest arrival, to be published by S. Karger, and to be devoted to experimental medicine in its widest sense (*Medicina Experimentalis*, 1, No. 1, 1959. International Journal of Experimental Medicine. Pp. ii+68. Six numbers per volume (two volumes annually). Subscription price per volume 50 Swiss francs. Basel and New York: S. Karger, 1959). The foreword deplors the tendency of research workers "to shut themselves up hermetically in their ever narrowing specialist circles and states that the aim of the sponsors is to provide a completely international journal which will cover the wide—and over widening—fields of experimental physiology, pathology and therapeutics and help to bridge the gap between their multiplying specialities. Papers will be published in English, French and German and are to be limited to an overall length represented by 10,000 words. Authors will rarely be allowed to exceed this and will be charged for the excess. In return for this restriction on the verbosity of their clients the editors promise to publish the papers submitted within three months. In these days of specialization and editorial congestion, these aims are laudable but may be rather difficult to achieve and the small international conferences which have become so popular may be a better way of dealing with the frustrations of slow publication in parts of the world where they can be conducted successfully in a single language. The first number contains eight papers in German and one each in French and English. As the foreword says the new journal will be what readers and authors make it. We wish it well.

Improved Gunmetals

THE Mond Nickel Co., Ltd., has announced the production of a new alloy for gunmetal. 85/0 5/3/3 5/2 copper:tin zinc lead nickel. It is claimed that it has better mechanical properties at both atmospheric and elevated temperatures than 85/0 5/5/5 gunmetal and still retains the same adaptability to the production of pressure-tight castings. When properly made, castings in this alloy have a 0.1 per cent proof stress of around 8 tons/sq. in with

a maximum stress of 16-17 tons/sq in in sections up to 3 in thick. The use of the new alloy will enable castings to be more effectively designed, as regards the use of thinner sections, and this could result in a saving of weight and, therefore, cost.

New Multi-range Voltmeter

'TAYLORMETER Model 100A' is claimed by its manufacturers, Taylor Electrical Instruments, Ltd., to be the first multi-range meter in Great Britain with a sensitivity of 100,000 ohms/V d.c. The instrument is suitable for voltage measurements in high-resistance circuits, laboratory and research work, and in television and other electronic fields. It can be used in place of a valve voltmeter but without the inconvenience of zero drift, valve replacement and alternating-current supply connections inherent in valve voltmeters. The d.c. current and voltage ranges are 0.2 μ amp to 10 amp and 10 mV to 2,500 V (25,000 V by means of an external adaptor). The sensitivity on a.c. is 5,000 ohms/V and the inaccuracies on the d.c., a.c. and ohm ranges are 2, 3 and 5 per cent respectively. Another new instrument in the Taylor multi-range universal meter series is 'Model 127A', which is a pocket-size meter with a sensitivity of 20,000 ohms/V d.c. and 1,000 ohms/V a.c. It is compact and inexpensive, and utilizes the new rugged Taylor moving-coil centropole meter and is specially ranged to give maximum reading accuracy for radio and television servicing and maintenance of electrical equipment. A large scale, which is easy to read, with a $3\frac{1}{2}$ in arc, is fitted.

Medical Electronics

A DETAILED and well-indexed bibliography on medical electronics, consisting of 2,200 references, has been prepared by the Medical Electronics Center of the Rockefeller Institute and published by the Professional Group on Medical Electronics, Institute of Radio Engineers, 1 East 79 Street, New York 21, New York (Bibliography on Medical Electronics. Pp 91. 2.50 dollars). The term 'medical electronics' has been taken to comprise applications of any of the branches of electronics, such as acoustics, communications, television techniques, spectrophotometry, or dielectric heating, to any problems of biological or medical research, therapy, public health and related fields. The bibliography is intended to serve as source material, and though a selection has been made from all the available material, references useful both to investigators trained primarily in physics or electronics and to those engaged in biology and medicine have been included. The entries are arranged in three sections, the main section consisting of references which are numbered consecutively, listed in numerical order, and grouped together in related topics, a subject index with some cross-referencing, and an author index from which anonymous and editorial matter is excluded although it is included in the previous sections.

A Fossil Meteorite (?)

WHAT may prove to be a fossil meteorite was discovered at a depth of 32 metres when excavating a mine shaft in the district of Magadan, north-eastern Siberia. As described by A. I. Shulzhenko (*Priroda*, 5, 115, 1959) it is an iron meteorite weighing about 15 kgm, and of a specific gravity of 7.82, and which on analyses proved to be composed mainly of iron, with 5-6½ per cent nickel and 0.4-0.5 per cent carbon.

University News

Birmingham

THE following appointments to lectureships have been made: Dr M. E. Davies (in botany), Dr C. R. Sladden (in biology in the Department of Zoology), D. J. Blundell (in geology), K. B. Haley (in engineering production), Dr N. A. J. Rogers (in chemistry), P. W. Dykes (in medical biochemistry and experimental pathology in the Department of Experimental Pathology).

Glasgow

THE report of the University of Glasgow Appointments Committee for the year ended December 31, 1958 (Pp 15 Glasgow The University 1959), records a steep rise in the number of men registered, which at 1,051 is almost double the total for 1951. This is attributed to increasing use of the Committee's services by students, a continuing upward trend in the number of older graduates seeking the advice of the appointments officers, and the increasing number who remain at the University after registering in the final year. Of the total, 735 are in science and engineering, and of these, 302 registered during 1958. Of 574 male students obtaining first or second degrees in 1958, 155 were in science, 122 in engineering and 74 in other technology. Of the total, 333 remained in Scotland. In science, particularly chemistry, there was a proportional increase in the number entering postgraduate research. In spite of the effect of the new defence policy there was no shortage of opportunity except for the less able candidates. Of all honours degree candidates, 122, or 21.3 per cent, entered the teaching profession compared with 19.6 per cent in 1957, and in science the proportion rose from 21.3 to 23.8 per cent. There was a further increase in the number of women registered and a slight decrease in the notifications of vacant posts, but the picture is not significantly different from that of 1957, and insufficient opportunity in Scotland for women graduates persists.

Announcements

To commemorate the late Sir Francis Simon, who was Dr Lee's professor of experimental philosophy and head of the Clarendon Laboratory, Oxford, the Low Temperature Group of the Physical Society has instituted a Simon Memorial Prize. This is an award to the value of £250 which is to be made at about three-yearly intervals for distinguished work in experimental or theoretical physics. Dr Heinz London, of the Atomic Energy Research Establishment, Harwell, is the first recipient of this award.

THE third reactor school course on the Control and Instrumentation of Reactors will take place during February 1-12, 1960, and will be open to British and overseas students. It will be held at Dursley Hill, Bournemouth, Hampshire. Further information can be obtained from the Principal, Reactor School, Atomic Energy Research Establishment, Harwell, Didcot, Berkshire. All application forms must be returned by December 11.

ERRATUM In the letter entitled "Colour Centres produced by Radiation in Silica Gel", by Harold W. Kohn, published in *Nature* of August 22, "50° C" in line 12, paragraph 2, column 1, p. 631, should read "500° C".

DEVELOPMENT TRENDS IN AUSTRALIAN SCIENTIFIC RESEARCH

THE tenth annual report of the Commonwealth of Australia Scientific and Industrial Research Organization covers the year ended June 30, 1958 (pp 174 Canberra Government Printer, 1958 14s) in which the Organization expended £6,861,278 on normal research activities, £429,328 on capital works and £123,055 on grants to outside bodies. Of its total income of £7,414,261, £5,702,804 was from Treasury funds and £1,207,928 from the Wool Research Trust Fund. Grants to research associations totalled £41 260 and for Overseas Research Student ships £80,793. Expenditure on investigations into plant problems amounted to £754,835 into animal health and production problems, £737,848, into food preservation and transport, £245 126, into forest products, £310,322, into entomology, £215,638 into fisheries, £171,458, and into industrial chemistry, £824,160. £577,186 was spent on the National Standards Laboratory, £140 098 on building research, £383,072 on radiophysics research, £384 823 on wool textiles research, £175,792 on fuel research, £110,338 on the wild life survey, and £154,929 on land research and regional survey. A list of staff as well as published papers is included in the report.

A representative committee appointed to consider the future development of the National Standards Laboratory found that while the Laboratory was functioning at a high level of efficiency, the staff and accommodation were too limited and future plans should include a well planned programme of research. The testing and calibration service for industry also required expansion, and in sequence with a further recommendation, Mr N. A. Eserman has been appointed as first director of the Laboratory. Further new arrangements with the universities were concluded during the year, including the development of a Biological Inorganic Chemistry Unit in co-operation with the Australian National University, establishment of a joint electron microscopy laboratory at the University of Sydney, and of a reader ship in dairy husbandry also at Sydney. The design study of the proposed giant radiotelescope has been completed and the instrument is to be constructed on a site near Parkes New South Wales. Some extension of the technical liaison services of the International Wool Secretariat and its affiliated organizations was agreed and the Secretariat and the Australian Wool Bureau are co-operating in making known to clothing manufacturers throughout the world the Organization's Siroset process for the permanent pleating and creasing of garments. The heavy pellet developed in the Division of Biochemistry and Animal Nutrition for administering cobalt supplements to sheep has been widely adopted by graziers in Australia. The work of the Organization's Plant and Soils Laboratory, Brisbane, has already established that the carrying capacity of the area of Queensland south of the Tropic of Capricorn and receiving good rainfall can be greatly increased by replacing natural pastures by sown pastures, and the work is of special interest to the beef cattle industry.

The Division of Soils has developed a new section to meet the increasing demands for study in soil

microscopy and its Soil Mechanics Section continued to widen its interests, especially in foundation problems in building, in pavement engineering and in the stabilization of soils. Morphological and chemical data are being compiled for three representative profiles of each of the great soil groups which have been recognized in Australia. It is proposed to base the main research of the Division of Plant Industry on semi arid native grasslands at Deniliquin, New South Wales, and to use this as a centre for studies of the establishment and maintenance of sown pasture species under dry land conditions. Studies were continued on the effect of clover on the fertility of the soil and the residual effects of phosphorus sulphur boron and molybdenum on the extraction from *Thiobacillus X* (Thioparus) of an enzyme and some cytochrome components which catalyse the oxidation of thiosulphate to tetrathionate, and on the effect of individual growth substances on cell division and size of fruits. Experiments continued on the transfer of resistance to blue mould (*Peronospora tabacina*) from Australian species of *Nicotiana* to commercial varieties of *N. tabacum*. An extremely dry year was utilized to study the capacity of sown pastures to carry sheep and to persist under high rates of stocking and under different systems of utilization. Studies of the effects of nitrogen supply and extension of the growing season on four strains of *P. tuberosa* were completed and an improved electron dialysis technique involving a minimum of damage to the plant tissue has been developed for determining the cation-exchange capacity of plant roots. Studies continued on the beneficial effects of wilting on the ensilage of ryegrass and on the drying characteristics of pasture plants as affected by air velocity, humidity and temperature.

The two irrigation research stations on which the ways in which irrigated land can be made to keep its fertility are being studied, and the techniques which can be used to reclaim waterlogged or salted soil, continued their research programmes without major change, and the Department of Agriculture, New South Wales is co-operating in the Murrumbidgee areas in studies of control of iron chlorosis and of effects of waterlogging and salting on the nutrition of apricots and peaches. The Division of Animal Health and Production has commenced work on the protozoal blood parasites which cause 'tok fever' in cattle. Good progress is being made towards an understanding of the physiological characteristics which determine heat tolerance in cattle with a view of selecting them within the European breeds or importing them, by crossing with such breeds as the Zebu or Afrikaner. Diseases of sheep now receiving special attention are foot rot and foot abscess, mycotic dermatitis and worm parasites. Sheep husbandry and wool production are two of the Division's major research undertakings with the view of understanding the genetic basis of high wool production, and the nutritional and other physiological mechanisms which enable the inherited capacity for high wool production to be manifested reducing the heavy losses due to poor fertility and

neo-natal mortality in lambs, and discovering the best and most economic means of offsetting the effects of drought by appropriate maintenance rations and husbandry. The present status of animal husbandry and production investigations by Commonwealth and State organizations is under review to reveal the nature of the major problems on which attention could most usefully be focused. At the Division of Biochemistry and General Nutrition's field stations experiments are being conducted on salt tolerance and supplementary feeding and on cobalt and copper deficiencies, including trials of the cobalt pellets developed to protect sheep from cobalt deficiency and phalaris staggers.

No major changes are reported in the research programme of the Division of Entomology, and great stress continues to be placed on the ecological approach. An officer has been appointed to study the ecology of the cattle tick in North Queensland, and work on cattle dips and pasture spelling is being intensified. In systematics some progress has been made on a revision of the Calliphoridae or blowflies, and revisions of the Pyrgotidae and Acroceridae have been completed. Preparation for the Commonwealth-State trial in New South Wales of a proposed method of suppressing outbreaks of the Australian plague locust advanced considerably, and in work on insect pests of stored grain the density of insect population is being studied under conditions of controlled oxygen leakage. Relations between chemical structure and insecticidal activity have been examined in the volatile ketones and N-substituted amides of long-chain fatty acids.

The Wildlife Survey Section intensified its study of rabbit populations and has initiated investigations of the dingoo (*Canis familiaris dingo*) and the fox (*Vulpes vulpes*). Besides land surveys of the underdeveloped regions by the Division of Land Research and Regional Survey to determine their needs and population, the Division of Biochemistry and General Nutrition is investigating problems of plant and animal nutrition on the Coonalpyn Downs, South Australia, the Division of Animal Health and Production is breeding cattle at Belmont, Rockhampton, Queensland, and the Plant and Soil Laboratory is studying the wallum country in eastern Queensland. The Division of Fisheries and Oceanography has built an experimental aquarium at Cronulla to study the behaviour patterns of commercial fish and has devised and tested a method for counting and differentiating phytoplankton at sea. There was no change in emphasis of the work of the Division. The Division of Food Preservation and Transport initiated, jointly with the New South Wales Department of Agriculture, a three-year investigation of levels of fruit spray residues and their removal. The cheese curd fusing machine developed by the Dairy Research Section was put through successful trials and could be the first effective attempt to mechanize cheese manufacture completely. Work on the biophysical properties of the giant cells of *Chara australis* was resumed, and a study of the properties of sucrose synthesized by enzymes was completed. The co-operative research programmes undertaken by the Division of Building Research steadily increased during the year, including an investigation into the use of ordinary household hot-water heaters, fired by brown coal briquettes for space heating as well as water-heating to lower- and medium-priced houses.

The Wool Textile Research Laboratory has developed an improved sampling device for wool and devoted greater effort to shrink-proofing, including the use of oxidizing agents. Studies continued on the exchange of water between a mass of wool and the air passing through it, and work in the Division of Industrial Chemistry on the structural analysis of amino-acids has been extended to the peptides. A major activity of the latter Division has been in the techniques of extractive metallurgy and a full-scale unit is to be installed for final tests on the recovery of uranium from Dyson's ore by the Weiss-Swinton jigged bed process for continuous ion exchange. Also in co-operation with industry the Division has completed an investigation of the fluid bed roasting of copper concentrates and the subsequent locating and electromining of copper. A process has been developed for obtaining thorium of high purity, and further kinetic studies were made on the decomposition of sulphide minerals in the presence of water and oxygen. The investigation of the constituents of tar from Lurgi gasification plant continued, as well as the study of the production and properties of various kinds of defects in crystals and their bearing on chemical and physical properties of solids, while increasing effort was devoted to the design and development of optical and spectroscopic equipment. An investigation on the preparation of substituted sebacic acids of possible value as plasticizers and low-temperature lubricants showed that the isomeric dihydroxyteric acid easily prepared from oleic acid, as well as erythro-dihydroxyteric acid can be converted to α -hydroxy- α -octylsebacic acid by alkali fusion and in considerably higher yields. The Coal-Research Section is continuing work on the properties, composition and structure of light oils, tars and pitches produced by the carbonization of Australian coals.

The Division of Tribophysics continued its fundamental studies in metal physics, surface physics and the chemistry of solids, and in some co-operative work on the refining of lead the surface properties of liquid lead have been measured in various media by a radiographic technique. No new major projects were initiated in the Division of Physics, where the accuracy of the Laboratory's realization of the International Temperature Scale at high temperatures has been considerably increased, and proposals have been formulated for its extension to well below the present lower limit of -183°C , based on an investigation of the dependence on temperature of the electrical resistance of platinum. Electronic apparatus designed or constructed includes a photoelectric servo system for the control of a physical balance for measuring strong magnetic fields, a nuclear resonance thermometer using the quadrupole resonance of chlorine, and the control to 1 in 10 of currents up to 10 amp in an electromagnet with a galvanometer amplifier and power transistors. No major changes are reported in the work of the Division of Electrotechnology, but its high-voltage measuring facilities are to be expanded. Special furnaces have been constructed and preliminary experiments made to determine the conditions of crystal growth most likely to yield satisfactory single organic crystals, while further studies have been made on the dielectric properties of polycrystalline materials and liquids. Determinations of the frequency factors and energies of activation of methyl ethers and ketones confirmed that in long-chain compounds the logarithm of the frequency varies linearly with the energy of activation.

The continuance of the investigations of the Division of Radiophysics into the practicability of increasing rainfall by seeding clouds with silver iodide by a further large-scale field trial is in progress in the Northern Tablelands region of New South Wales. Development continued of a method for obtaining bearings from existing Distance Measuring Equipment Beams and also research into the purification of semiconductor materials and growth of mono crystals, the transport of charges in semiconductors and the development of junction photo devices. An all sky camera was installed in October 1957 and photographs of the whole night sky have been taken regularly at five-minute intervals since that time, recording any aurora that may occur, and in conjunction with cameras at other stations, enabling positions and height of aurora to be

deduced. In solar physics the association between a class of radio bursts conventionally known as type II and optical features in the chromosphere has been investigated, while the main observational programme of the 15-metre wave-length "Cross" aerial was directed towards completing a survey of a belt of the sky, 10° wide, around the galactic equator. The crossed grating interferometer is producing each day a detailed radio picture of the Sun, and observations of solar radio disturbances continued throughout the year with the Dapto radio spectrograph which records the Sun's spectrum in the range of wavelengths between about 1.5 and 7.5 m. The Mathematical Instruments Section completed the construction of the transistorized digital differential analyser and the techniques are being applied to the development of a small general purpose computer.

DELAYED HYPERSENSITIVITY IN IMMUNOLOGY

THE mechanism of the delayed form of hypersensitivity, originally and still exemplified by Koch's tuberculin reaction, has proved much more difficult of analysis than that of the immediate reaction about the main immunological features of which much is now known. In the symposium on "Delayed Hypersensitivity" held by the British Society for Immunology in London on May 8, the allergic phenomena associated with reactions of this type provided the central theme for discussion.

Little progress towards the understanding of the mechanism of the tuberculin reaction can be expected, as pointed out by S. V. Boyden in opening the Symposium, until the nature of the specific change in the tissues responsible for the hypersensitivity is recognized and can be detected and measured *in vitro*. The injection of tuberculo-proteins, when in soluble form, leads to the production of specific antibodies in the blood but not to the appearance of delayed hypersensitivity. Even when these proteins are adsorbed on carbon granules or red cell stromata to provide them with a particulate vehicle, their injection almost invariably results in the development of Arthus type hypersensitivity. It seems that it is only when these antigens enter the tissues as an integral part of the bacillus, and consequently pass through some intracellular experience in phagocytes, that the animal will respond to a subsequent skin test with a typical delayed tuberculin reaction.

In part, the characteristic delay in the development of the tuberculin reaction might be attributable as J. Peppys has observed, to the period of several hours needed for the full fixation of the provocative agent to the tissue cells. The simultaneous injection of any agent, such as histamine or hyaluronidase which can accelerate the loss of the tuberculin from the site of inoculation, or of adrenalin which can ensure its retention in the area, consequently much affects the intensity of the ensuing reaction. It follows, therefore, that any constituent present in the tuberculin preparation used that might evoke even a relatively inconspicuous immediate reaction could, by so doing, lead to the dispersal of the factor which was the cause of the delayed reaction and so mask any later manifestations of delayed hypersensitivity. On the other hand, the introduction of the tuberculin in a lipid vehicle prolongs the local retention of the

tuberculin, thereby enhancing its potency and revealing in man the presence of degrees of hypersensitivity too low to be demonstrable by intracutaneous tests with large doses of tuberculin.

The discovery by Landsteiner and Chase that in guinea pigs specific delayed hypersensitivity can be transferred by an inoculum of leucocytes when one of serum is ineffective has been further analysed for human beings by H. S. Lawrence. He sought, by making extracts from such cells after their lysis, to identify the transfer factor concerned. This he found to be a stable agent capable of resisting exposure to deoxyribonuclease, ribonuclease and trypsin. With Pappenheimer he found that it may be liberated from the sensitizing leucocytes by incubation alone or by contact with tuberculo-proteins, the latter procedure caused the cells themselves to lose their distinctive property of sensitizing a recipient. Delayed hypersensitivity to coccidioidin is similarly transferable with extracts of sensitizing leucocytes and the specific systemic reactivity so conferred may persist for more than a year.

In seeking some biological meaning for delayed hypersensitivity reactions Lawrence proposed an extension of Burnet and Fenner's 'self marker' concept to postulate that interaction between host cells and phagocytosed microbes may produce slightly altered versions of the individual's cellular components by forming intimate (self plus x) complexes. The latter, recognized as foreign by the host, may provoke a cellular immune response (transfer factor) directed against the complex. The cellular immune response takes effect against the host's own tissues in the form of a local homograft reaction wherever and whenever his cells are in appropriate combination with the antigen (x) which has induced the alteration. The effector mechanism (transfer factor) is uncovered following transfer to recipients and in the presence of the test antigen (x) it is postulated that it evokes a train of events similar to that called forth by the intact microbe in the cells of the donor.

N. A. Mitchison further followed up the possible resemblances between delayed hypersensitivity and the homograft reaction by pointing out that in both the immunological responses appeared to be attributable to the participation of cell bound antibody. A graft of tissue from one animal to another of the

same species provokes the production of both humoral and cell-bound antibody, but the former generally does not destroy the graft. Transplantation immunity thus possesses an important feature in common with delayed hypersensitivity. Further similarities arise from the routes of immunization used—the intravenous injection of cells provokes only a poor response in the rabbit—as well as from the tempo of the full transplantation immunity reaction which develops before the production of humoral antibody reaches its maximum. More significantly, the cellular infiltration of homografts resembles the granuloma induced by tubercle bacillary wax. The nature of the cell first stimulated by the antigen may determine the type of the response, so that a single antigen may, in different circumstances, elicit either a humoral or a cell-bound antibody. Alternatively, tissue cells may be supposed to possess isoantigens of different kinds each responsible for one kind of antibody.

The possibility that a single molecular species of antigen can provoke simultaneously both delayed and immediate sensitivity to different determinant groups on it was discussed by P. G. H. Gell and B. Benacerraf. In a study of various types of immunological reaction to proteins conjugated with such active haptens as picryl chloride, they have demonstrated a dissociation between immediate and delayed skin reactivity to the same antigen. The absence of recognizable antibodies to the protein carriers used in these conjugates, at a time when their intradermal injection proved capable of exciting a delayed skin reaction, confirms the view that reactions of this type do not depend on conventional antibodies in the circulation. At this time, antibodies were present specific to the haptenic group. Under other conditions, delayed sensitivity to the haptenic group was also demonstrable. They questioned the

view that the state of delayed hypersensitivity can be regarded as an early, perhaps immature, stage of immunity. Rather, they felt that it should be considered as a distinctive response to certain qualitatively different, possibly less dominant, groups on the antigenic molecule.

With the recognition of the close participation of leucocytes in the transference of specific delayed hypersensitivity, J. L. Gowans's account of the life history of lymphocytes acquires particular relevance. Experiments on rats have shown that the output of these cells from the thoracic duct is sufficient to replace all the lymphocytes in the blood many times daily, the production of new small lymphocytes is much lower and their survival time much longer than was formerly supposed. These cells, moreover, appear to circulate freely through the tissue spaces and in this extravascular transit they may be the effector cells in immunological reactions of the delayed type.

The features of the immediate and delayed 'tuberculin-type' reactions to trichophyton in guinea pigs that can be evoked either after an infection or an inoculation with the killed mycelium were described by C. N. Cruickshank, M. D. Trotter and M. R. Wood. They found that these responses were associated with a transferable passive cutaneous anaphylaxis, but that they could occur in the absence of any detectable precipitating antibodies. Chemical fractionation of the mycelium showed that the antigenic material was mainly a polysaccharide containing equal proportions of glucose and mannose. Finally, R. M. Gordon and M. Lavoipierre, in discussing immediate and delayed reactions to insect bites, pointed out that in certain instances the late reactions ordinarily attributed to the saliva of the vector may be confused with that caused by some parasite introduced into the tissues at the time.

THE ELECTRIC ARC IN WELDING

FOLLOWING the practice of the previous two years, a third "Joining of Metals" Conference was held at the University of Birmingham on June 25 under the chairmanship of Prof. E. C. Rollason, head of the Department of Industrial Metallurgy. The subject on this occasion was "The Electric Arc in Welding", five papers were presented, and the conference was attended by about one hundred representatives of industry, the research associations and the universities. Prof. Rollason explained that the purpose of these conferences was to further the development and teaching of the basic processes underlying the practice of metal joining, and pointed out that, in arc welding in particular, much less effort had been directed towards fundamentals than to the empirical development of modern arc welding processes. He then suggested that there were three ways in which the arc interacted with the metal which were of significance in welding. First, there was heat transfer from the arc which was responsible for the formation of the weld pool, secondly, the chemico-metallurgical reactions taking place between the high-temperature gases in the arc atmosphere and the weld metal, and thirdly, the transfer of metal droplets across the arc which can take place against

gravity and for which no satisfactory mechanism had yet been advanced.

Mr. D. R. Milner, of the Department of Industrial Metallurgy, then surveyed the present state of knowledge of those aspects of arc physics which were pertinent to these problems. Throughout the main body of the arc electrical energy is utilized to heat the gas to such a temperature that it becomes thermally ionized and is thus able to provide the electrons and ions necessary to carry the required current. At the anode the electron stream, and at the cathode the positive ion stream provide the source of energy for melting the metal. For low current arcs the anode processes are reasonably well established, but less is known of conditions at the cathode. However, for high-current welding systems little information is available in either case. Heat and mass transfer from the arc column to the electrodes, which determines the reactions occurring between the arc atmosphere and the weld metal and controls the rate at which they take place, is dependent upon the energy dissipated, the gas properties and the mode of heat transfer. Of particular interest in this respect are plasma-jets, which Macker has demonstrated exist wherever there is a constriction in the arc, such as a

cathode spot, giving rise to gas velocities of the order of 10^4 to 10^5 cm per sec

Dr G R Salter, of the Department of Industrial Metallurgy, contributed a paper which described the results of an investigation of the absorption of oxygen by titanium melted by an electric arc in an atmosphere of argon containing controlled quantities of oxygen. The effect of time, oxygen partial pressure, arc length, current, electrode composition and gas flow conditions had been determined. The interpretation of the results led to the conclusion that in this system the rate controlling process was the diffusion of oxygen across a stagnant boundary layer of gas of the order of 10^{-3} cm thickness adjacent to the molten metal, which took place over a high temperature active area where the oxygen was dissociated. The magnitude of the active area was determined by the current and arc length, and the thickness of the boundary layer by the velocity of the cathode plasma jet which impinged on the anode.

Mr J B Wilkinson, also of the Department of Industrial Metallurgy, gave an account of work on heat transfer in which onergy balances had been determined for arcs operating between a tungsten cathode and a water-cooled copper anode in atmospheres of argon, nitrogen, helium and hydrogen. The existence of plasma jets in these arcs had been demonstrated, their velocities estimated and attempts made to separate the heat transfer from the plasma jet from that due to electron heating of the anode. The interpretation of the measurements of the heat transferred from the plasma jet was along similar lines to that proposed by Salter for mass transfer, that is to say, with convection transferring the heat to a boundary layer adjacent to the metal surface. Some success had been achieved by the application of a conventional non-dimensional treatment of convective heat transfer with the plasma jet replaced by an equivalent source of hot gas emerging from a tube.

In addition to their role in heat and mass transfer, plasma jets are also responsible for the transfer of metal droplets from the molten wire electrode to the weld plate. This was shown by Mr J C Needham, who described work carried out at the Electrical Research Association in which a study had been made of the detachment and flight of aluminium droplets

by high speed colour photography (8,000 frames per sec). The existence and effect of the plasma-jet could be inferred from a stream of metal vapour emanating from the droplets flowing in the direction of the jet and from the fact that the velocity of the drops continued to increase, with accelerations of 10g to 100g, after they had been detached from the electrode wire attaining terminal velocities in excess of 500 cm/sec. Experimental determinations of the droplet velocity as a function of current, derived from the photographs taken by Needham, and from trajectory determinations by Mr C J Cooksey of the University of Birmingham compared well with theoretical calculations based on a model in which the drop became detached when the force exerted on it by the plasma jet exceeded the restraining force of surface tension, and was then freely accelerated across the arc by the impinging gas stream.

An interesting characteristic of the electric arc is that if it is intensively cooled, for example by operating it through a narrow cooled orifice, then the core temperature is increased. This is because the conducting area contracts, so that which remains must have a higher degree of ionization and hence a higher temperature in order to maintain the required current. Spectroscopists and arc physicists have utilized this property of the arc to heat gas to temperatures up to 50 000° C for the measurement of collision cross sections and the transition probabilities of ionized and excited atoms and for fundamental magnetohydrodynamic studies. Mr A R Moss, of the Ministry of Supply, elaborated on the behaviour of the constricted arc and showed how it could be harnessed to technological advantage. He described the various types of plasma jet projectors and constructed arc torches developed in the Armament Research and Development Establishment, with emphasis on the design and characteristics of devices operating with a power consumption up to 100 kW amp., although much more powerful equipments were mentioned. Their many potential technological applications include the melting, cutting and spraying of metallic and non-metallic materials in non-contaminating atmospheres, chemical synthesis and the production of high temperature gas streams at hypersonic velocities. D. R. MILNER

INTERNATIONAL CONGRESS ON ACOUSTICS

THE third International Congress on Acoustics was held in Stuttgart during September 1-8 under the presidency of Prof Erwin Meyer.

The first of the series was held in Delft in 1953 and the second in Cambridge, Massachusetts, in 1955. Already the number of participants has risen from the original 600 to more than 1,000, and in the recent congress necessitated the individual papers being read in eight concurrent sessions. The mornings were devoted to review lectures, which all could attend. These, and the papers presented, covered architectural acoustics, ultrasonic techniques and their applications to the study of molecular physics, acoustical properties of materials employed in industry, noise and its abatement (in particular aircraft noise) physiological and psychological acoustics.

If one tries to assess the progress made since the last congress and which is likely to continue in the future, one would perhaps select the last two of these as of most interest. The two reviews given on the subject of the noise of jets and the quantity of smaller papers which followed illustrated the strides which have been made since the last congress where the subject of aeronautics interested but a few speakers. The increasing noise level to which we are subjected has stimulated more research into the functioning of the ear and the human processes of sound perception, which also brought out a stimulating array of papers.

In building acoustics and molecular acoustics one has the feeling that the peak of development has passed. In the former subject it seems now to be a

question of fine adjustments to existing knowledge, while in the latter new developments may only be expected by going to extreme temperatures and pressures with adaptations of existing techniques. To illustrate the importance of noise in daily life and methods of measuring it, the regional authorities of Baden-Wurtemberg opened to the public an exhibit in a Stuttgart Museum entitled "Weniger Lärm".

It was announced that the next international congress would be held in Copenhagen in 1962, and if the number of participants should continue to increase at the present rate this will involve the local organization in much hard thinking about how they are to

lodge them and deal with the reading of the many papers expected.

This situation is not peculiar to acoustics, but there is a possibility of splitting the auditory into roughly equal numbers of those concerned with physical and physiological acoustics and those interested mainly in architectural, musical and industrial applications. Perhaps two congresses *en suite* with a week-end of social activities and excursions sandwiched between them might overcome some of the difficulties of organization.

The proceedings of the congress are to be published in book form by Elsevier Press. E. G. RICHARDSON

PHOTOGRAPHY IN THE INTERNATIONAL GEOPHYSICAL YEAR

A SYMPOSIUM on photography in the International Geophysical Year was held in Edinburgh on June 6, under the auspices of the Scientific and Technical Group of the Royal Photographic Society of Great Britain.

Following his address of welcome on behalf of the University of Edinburgh, Sir Edward Appleton stated that he believed the effect of the International Geophysical Year on association between geophysicists would be a permanent one, and recalled the descent of the recent great collaboration from earlier International Polar Years. He then described some of the ionospheric work carried out during the International Geophysical Year and directed attention to the valuable part played by photography in making possible permanent records. In conclusion, he spoke of the most striking discovery of the Van Allen radiation belt. Miss Harker, president of the Royal Photographic Society, replied and went on to discuss the wide compass of photography, illustrated by the nature of the subject of the symposium.

The study of aurorae by all-sky cameras was described by Dr G. M. Thomas, of the Balfour Stewart Auroral Laboratory. He pointed out that remoteness and erratic occurrence make auroral data scanty, and that any casual collection of data is bad statistically. However, full-time observation is a costly matter, but sky cameras could provide the necessary supplement to visual observation. A system was described consisting of a motion picture camera viewing a large convex mirror, the mirror being heated to keep off frost and snow, and a calendar and watch placed in the field of view. Timing of the camera's function was provided by a synchronous motor. A film illustrating the systematic motion of the aurorae was shown. It is of great importance to correlate the sudden alterations which occur with changes in the magnetic field at the ground.

The next contribution reviewed some of the contributions of photographic techniques to rocket and satellite work, and described particularly the ballistoc cameras developed at University College, London, for the 'grenade' experiment. This is a method of finding upper-air winds and temperatures by measuring the time of travel of sound from grenades fired from an ascending rocket. The special function of photography here is to locate the grenade bursts with great precision. When the experiment is carried out

in daylight, special techniques are necessary to obtain rapid triggering of the shutters by light from the grenades. Experiments under preparation for X-ray observation of the Sun and ultra-violet astronomy of the stars were also described. The latter work is being conducted in collaboration with Dr H. E. Butler, of the Royal Observatory, Edinburgh, who then described his use of a technique, due originally to Dr Baker, of the same Observatory, to bring up the detail of very faint interstellar absorption lines. Basically, the problem is to bring out the signal from the 'background noise' grain in the plates, and it is accomplished by careful photomicroscopy and summing of the results from many plates, together with subtraction from a standard spectrum to remove the emission structure. The results were extremely impressive, as indeed was the amount of work required to obtain them, a million separate readings from twenty-seven different exposures were obtained.

Dr C. J. Waddington, of the University of Bristol, described his subject as the study of the 'footprints' of cosmic ray particles. Due to the vastness of his subject, he limited his discussion to an extended series of high altitude balloon flights with nuclear emulsions made with the avowed intention of monitoring the long-term variation of the primary cosmic radiation. Seventy-three balloon flights were made by a group led by Prof E. P. Noy (Minnesota). A typical payload consisted of a dozen 4 in. x 4 in. 600 μ Ilford G 5 emulsion plates, together with a single counter and an ion chamber. Although protons are more abundant, α -particles were chosen for the study for a variety of reasons, among which were the complications of an albedo of protons from disintegrations and the greater ease of finding and counting α -particle tracks in nuclear emulsions. The results of these observations are still being analysed, but already it is clear that differences in the variation of α -particle and proton flux after a solar flare should ultimately throw light on the properties of the space between us and the Sun.

A paper by Dr W. I. Arvogitch, of the U.S.S.R. Academy of Sciences Institute of Geography, was read for him in his absence. His paper discussed photo-topographic methods used by his Institute for the study of glaciers. For more than a decade glaciation has been studied by aerial photography although stereo-photogrammetric surveys from the

ground are still considered to be the most reliable means of recording the state and behaviour of glaciers. Recently, however, aerial photography, with its advantage of the avoidance of 'dead areas' due to obstacles, has been applied to the study of glacier dynamics. Unfortunately, the paper gave no information on the experimental equipment, either aerial cameras or the new Soviet stereograph 'SD 1', which was claimed to be notable for its precision, having a relative mean square error of vertical control in the neighbourhood of $1/3\,000$. It was a

conclusion of the paper that aerial photography could greatly speed up a survey, especially with the use of helicopters, but that no single method in phototopography is appropriate in every situation.

The meeting ended with projection of the Russian research film, 'North Pole', showing Soviet scientific research in the Arctic and describing the results of oceanographic and meteorological work. Of special interest were sequences showing the oscillatory movements of water and ice flows about the Pole.

R. L. F. BOYD

GLASSHOUSE CROPS RESEARCH INSTITUTE

OPEN DAY

THE Glasshouse Crops Research Institute, Little Hampton, Sussex, held its annual open day on June 10 when nearly two hundred visitors attended. The laboratories were open for inspection during the morning, and after lunch, at which the director, Mr F. W. Toovey, reported on the Institute's progress during the past year, a series of demonstrations were arranged in the experimental glasshouses and mushroom sheds.

In tomato variety trials by the Plant Breeding Section (Mr L. A. Darby) special interest was shown in hybrids with the 'Baby Lee' variety, some of which are in the F_2 generation and beginning to breed reasonably true. This variety has a compact habit of growth (short internodes), and an attempt is being made to incorporate this habit into known good combining varieties with the aim of producing an F_2 hybrid of good early and total yield, bearing high-quality fruit, and which will not suffer from the excessive vigour of hybrids at present grown commercially. A cucumber breeding trial which was also demonstrated, tests the value of F_1 hybrids for commercial use with special reference to early and total yields, and to fruit quality.

The Plant Physiology Department (Dr E. R. Leonard) showed the concluding stages of a time-of-planting experiment carried out as part of its growth analysis studies on the tomato. Previous work has suggested the influence of day length on the growth of all the major organs of the plant, including the roots, and in order to investigate this more fully sowings at one of the dates included in the main time of planting experiment have also been carried out at three other centres in the British Isles, ranging from Guernsey in the Channel Islands to Auchincruive in Scotland, and in Malta and Finland. A prototype temperature-controlled glass cabinet, erected in a glasshouse, for studying the growth of tomato plants under controlled day length throughout a cropping season was also on display. Another exhibit was equipment for the production of artificial temperature gradients across a tomato fruit in connexion with the Department's investigation of fruit ripening disorders including those loosely referred to as 'blotchy ripening'.

The Chemistry Department's programme, under Dr G. W. Winstor, includes a comprehensive study of the nutrition of the tomato, and a wide range of glasshouse experiments was on view. These comprise a basic factorial trial, testing nitrogen, phosphorus, potassium, calcium and magnesium, two experiments

on liquid feeding, and an investigation of the effect of magnesium deficiency on yield and its control by applying magnesium sulphate to the soil or to the foliage. Determinations of nutrient uptake are a special feature of these experiments. Laboratory studies of tomato fruit composition were also demonstrated, these have particular reference to fruit-ripening disorders and may shed light on factors determining flavour. Changes in the enzyme activity associated with ripening are also being investigated. The Department also works on other glasshouse crops, and of topical interest were the studies being made of the effects of manganese toxicity on tomatoes, lettuce and carnations. A factorial nutritional trial on carnations, testing three levels of nitrogen and potassium in the presence or absence of added phosphorus, magnesium or calcium, was also on view. With the cultivated mushroom certain cultural problems are studied, particular attention being paid to various factors of the casing layer in relation to fruiting, evidence has accumulated that total moisture stress has an important influence on fruiting. An investigation of the effect of factors of the atmospheric environment on mushroom growth is also about to be taken up and a prototype controlled environment chamber for this was on view.

The Plant Pathology Division (under Dr L. Broadbent) demonstrated the work of its three Departments: Entomology (Dr N. W. Hussey), Mycology (Mr P. H. Williams) and Virology (Mr M. Hellings). At present the Entomology Department is devoting a great deal of attention to ecids affecting the cultivated mushroom, observations on their life history were illustrated and results were presented on the very rapid rate of increase of the larvae in compost. The results of experiments on the control of ecids by the application of γ BHC to compost or casing were also displayed. The Mycology Department showed aspects of its work on the *Didymella* stem rot of the tomato, on cucumber mildew, on carnation wilt and on mushroom fruiting disorders. In connexion with the investigation of carnation wilt diseases, a glasshouse experiment on the survival of the pathogens in soil and plant roots was in progress, this involves the growing of carnations, chrysanthemums and tomatoes in rotation in concrete lined beds to see whether the wilt organisms can be carried over on hosts other than the carnation even though producing no visible symptoms on those hosts. Mushroom fruiting disorders associated with greatly reduced cropping have caused much concern to the

industry during the past few years, but then investigation has proved very perplexing because of the variety of symptoms produced. At the Instituto the possible transmissibility of the disorders has been particularly studied, and in recent experiments, which were demonstrated, evidence of artificial transmission and natural spread following the inoculation of beds has been obtained. Of special interest in the Virology Department's programme, which is about to be greatly expanded, was the success achieved in rooting meristem cultures of carnations and transferring them to conventional growing media; this work has been undertaken as a prelude to the investigation of heat therapy for carnation virus diseases.

The Crop Protection Department (Mr W H Read) had a striking demonstration of the effect of captan in protecting tomato plants from *Didymella* stem rot. A glasshouse trial showing the value of the chemical soil sterilizing agents, metham and chloro pierin, in comparison with steaming, was also on view.

Among the current activities of the Statistics Section (Mr D Cooke) attention was directed to a survey that is to be carried out, in collaboration with Rothamsted Experimental Station and the Ministry of Agriculture, on the tomato varieties in commercial cultivation in relation to earliness and district. This should provide information of particular interest in connexion with the breeding programme and experimental work generally.

F W TOOVEY

STUDIES IN RECREATION

UNDER the title "After Work Leisure and Learning in Two Towns", the National Institute of Adult Education has published, for the Manchester and District Advisory Council for Further Education, studies in Bolton and Rochdale by Mr R Ruddock and Dr A Wilson (pp 63 London National Institute of Adult Education, 1959 3s 6d). Prof R D Waller contributes an introduction explaining the purpose and basis of the two surveys, which give special attention to the twenty to thirty age group, and suggesting a few generalizations. Dr Wilson's survey of Rochdale started a few months later than Mr Ruddock's survey of Bolton, and he stresses the quality and quantity of educational and cultural activity in this town of some 86,770 inhabitants. While this is probably not less than that of any other industrial town of comparable size in Great Britain probably as many as 40 per cent of young adults have no connexion with any organization outside their job and home. The Rochdale Literary and Scientific Society, founded in 1878, has always had the backing of influential scientists, doctors, teachers and others and often exercised considerable influence in educational and cultural matters; its membership has fluctuated between 233 and 350 during the first half of this century, but has since reached 650. Nevertheless, apart from societies promoting religious, musical, dramatic or highly specialized leisure pursuits, the voluntary societies have little success in attracting people in the 18-35 age group, and during the past five years the membership of voluntary societies has fallen by 12-13 per cent.

The survey suggests that some of the young adults would welcome the opportunity to live a fuller social life and that others might adopt a similar attitude if parents, school-teachers and employers broadened their horizons and developed their latent interests in society and the problems which face its responsible citizens. Dr Wilson suggests that the links between technical students and liberal or non-vocational studies could be developed, for example, by residential courses organized by the Extra-Mural Department of the University of Manchester. Nor is full use yet made of the facilities for further education under the part-time day release scheme with a school population of 12,287 in sixty schools, day release from 2,239 technical college students is only 943, 76 from 243 School of Art students, and 19 from 1,883 Further Education Centre students.

For Bolton, with approximately double the population (163,800), the statistical picture is similar. The population per acre, rates per head and birth-rate are very similar. There are 25,374 students in 102 schools and the total expenditure on education is roughly double (£2,278,812 compared with £1,115,567). Of the 6,700 technical college students, 2,800 are day release, but there is no day release among 748 School of Art students and 2,700 Further Education Centre students. Like Rochdale, Bolton is becoming less dependent on the textile industry, and employment in the textile industries has dropped to less than 25 per cent of the working population, compared with 47 per cent in Rochdale. Mr Ruddock estimates that the voluntary societies contribute only perhaps one-twentieth to the cultural activity of Bolton and that the whole cultural life of Bolton is sustained by some 6,000 of its citizens. Among the suggestions he makes, all concerned with the upper 30 per cent of the population, in the educational sense, is extended publicity to ensure that more young adults know of the Workers' Educational Association and other serious organizations in the cultural field. Many premises require improving and equipment. The Central Library is admirably situated for sponsoring experimental provision, and although there is much good teaching of the plastic arts in Bolton, local amateurs could benefit by experience of a more exciting and vital practice which might be offered from outside. Besides the provision of special courses for those conducting classes and meetings, Mr Ruddock suggests that the many graduate teachers, lawyers, doctors, ministers, scientists and administrators in Bolton might be encouraged to associate more freely and that executive members of local businesses would gain much from organized group contacts with specialists in science, administration, education and social science, many of whom could be reached through the University Extra Mural Department or Bolton Technical College.

Prof Waller points out that neither survey says much about the large undifferentiated mass—what its members' spare-time activities are, what could be done to interest them and involve them in socially healthy and worth-while pursuits. Both surveys support explicitly and implicitly Dr I Trenaman's conclusion, that all cultural and educational activities touch only about half of the population, and that

half includes all those who have received higher education. It is the late school leavers who are the most likely to carry on cultural interests into mature life and there seems good reason to believe that longer schooling, the sensible organization of continuation work and youth activities and the liberal treatment of vocational training would all considerably affect cultural and intellectual interests in later life. Prof Waller also notes Dr Wilson's observation that those of the 20-30 age group who are most deeply addicted to television seem to have taken no course since leaving school have no connexion with church or voluntary society and no interest in any other local society and organization. Possibly only

television could induce any desire to participate in communal activities among this group. While the position of established societies and organizations varies—the thriving state of the Bolton branch of the Workers Educational Association contrasts with a decline of 12-13 per cent of the membership of the Rochdale branch during the past five years—all seem likely to gain from an improved educational system and a better developed service of youth. All would be helped by better and co-operative publicity, perhaps with the assistance of local authorities, and all would be greatly strengthened by public provision of central premises, available to them all without crippling rental charges.

MARITAL FERTILITY IN ENGLAND AND WALES

THE census of 1951 was the first general census since 1911 to include questions relating to the fertility of married women of England and Wales. The answers to these questions have been analysed in the fertility report which has recently been published (Census 1951, England and Wales, Fertility Report, Pp xxi+251, London: H.M. Stationery Office, 1959, £4 10s net).

The analysis of fertility movements has become of increasing interest to demographers and other social scientists for a number of reasons. In the first place, fluctuations in marital fertility and long term changes in the fertility rate have most important effects on the size and structure of the population, particularly in low mortality areas like Great Britain. Secondly, differences in the fertility of various sub groups of the population are of considerable sociological interest by themselves, and changes in differential fertility may throw important light on other aspects of social change. It is thus likely that questions on marital fertility will figure in future British censuses as a matter of routine.

The growth of interest in fertility has also led to considerable developments in the method of analysis. In particular, the use of cohort analysis in which the fertility experience of a group of women who were either born or married in the same calendar year is traced throughout their reproductive lives. This method of analysis was used in the statistical reports of the Royal Commission on population, and is now also applied in the Fertility Report in discussing the problem of population replacement.

The fertility questions asked in the 1951 census were limited to married women under the age of fifty at the time of the census. These were asked to state the date of their marriage (and their first marriage, if married more than once), the number of live born children, and whether they had given birth to a live born child in the twelve months preceding the census. In addition the census schedule contained the woman's age and if her husband was enumerated on the same schedule, particulars relating to his occupation. In order to simplify the analysis, a sample of 20 per cent of the 7.4 million married women was selected for analysis. An 80 per cent sample of women aged 45-49 was taken to obtain more detailed data on completed fertility. A complete analysis was made of all women who had been married more than once, but such women constituted only 4.1 per cent of all married women.

The fertility report aims to answer three questions. First, what is the current level of marital fertility in England and Wales? Secondly, what differences in fertility between various groups may be detected from the data? Lastly, what are the implications of present trends on population replacement?

It will be convenient to deal with the last topic first. It is interesting to note official recognition of the fact that the question as put is incapable of being given a definite answer. On p. xci of the report a number of different hypothetical replacement rates calculated on different assumptions, are put forward varying between 0.965 and 1.084. The official comment is that current habits imply in the long run approximately full replacement of one generation by the next and possibly very little more" (p. xci). This is a far cry from the position in the 1930s when warnings about incipient rapid population decline were common. To be fair however, it should be pointed out that women born in the early years of the century did not have sufficient children to replace themselves (women born between 1903-8 had a generation replacement-rate of only 0.672, those born between 1913-18 0.765). It is clear, however, that in the immediate future, violent changes in total numbers are unlikely.

There are slight indications that the recovery in average family size after the end of the Second World War was slowing down in the middle 'fifties, but it will be necessary to wait for the 1961 census data before we can be certain of this.

It is not the function of an official census report to speculate upon the causes of the reversal in fertility trends, but the chapter on differential fertility gives information about differentials between occupational groups (both the traditional five fold classification and the twelve socio-economic groups), between different geographical areas, and also an analysis of fertility differences by differences in the ages of husband and wife. The indices studied are mean family size, proportion infertile and current fertility rate. These figures confirm the impression that clerical workers, shopkeepers and the lower professional, administrative and managerial groups are now the least fertile section of the population, their fertility being about 20 per cent below that of the population as a whole. On the other hand, semi-skilled and unskilled manual workers continue to show an excess of about the same amount.

The report, of course, contains much additional information, some of it incidental to the principal topic. For the calculation of replacement-rates, a female nuptiality table showing the proportion of the female population at different ages by marital status had to be computed, assuming current rates of death, marriage and dissolution of marriage, and interesting facts emerge about the marriage habits of different groups of the population.

One hopes that the fertility questions will be repeated in 1961, and that the questions will be asked of all married women this time. It is only through periodic inquiries such as this that the fertility of the population as a whole can be adequately studied, and the importance of the subject warrants inquiries of this kind to be made at intervals more frequent than once in forty years.

E GREBENIK

JOHN INNES HORTICULTURAL INSTITUTION

ANNUAL REPORT, 1958

THE accommodation and facilities at the John Innes Horticultural Institution, the annual report of which was recently published (Forty-ninth Annual Report, 1958 Pp 44 Bayfordbury, Hertford John Innes Horticultural Institution, 1959 3s), continue to expand. In the Department of Plant Breeding, much work has been carried out in an effort to improve the apple, with special attention to breeding for apple scab and apple mildew. Secondary emphasis has been placed on hybridization to fill varietal gaps. Pear-apple hybrids have been found to be only possible using the pear as female parent, and there appears to be no fundamental genetic barrier to crossing the two genera, however, hormone treatment is necessary for success. Very few of the hybrids have survived the seedling stage, due to rapid breakdown of root tissue. This weakness is only partly overcome by grafting and only about 2 per cent of those produced up to 1956 have survived. It has been claimed that parental performance can be improved by selection combined with inbreeding and that undesirable characters, such as disease susceptibility, can be removed without impairing the general breeding behaviour of the original genotypes. Whether or not worth-while results can be obtained in this manner is controversial, but a programme of inbreeding strawberries has been designed to answer some of these questions. The results so far suggest that selfing causes a considerable loss of vigour. In practice, changes affecting only one character are seldom brought about by selection after hybridization. Such changes are more likely to be achieved if genetic variability can be produced without crossing. Experiments on increasing genetic variability of inbred lines of tomato by irradiation using phosphorus-32 indicate that it may be possible to increase quantitative variation in tomato by this means.

Self-compatibility in the family Solanaceae and in the genus *Linaria* is being investigated in the Department of Genetics as well as the genetics of *Coprinus lagopus*. The Department of Potato Genetics has continued work on various aspects of species relationships. Until recently, breeding for resistance to late blight has been based on genes for resistance derived from *S. demissum*. At first, varieties possessing a single gene for resistance were satisfactory, but eventually succumbed to new races of *Phytophthora infestans*. Resistance based on field resistance presumably controlled by a number of genes is thought to be more promising. Selection of field-resistant varieties is slow and there is probably

scope for varieties incorporating two or three different genes for resistance. The genetic variability of the fungus is also being studied as well as resistance of potato varieties to virus X and virus Y. The Department of Plant Cell Biology has continued studies on leaf growth. Observations have continued on the relative contributions of cell division and cell expansion to the second pair of leaves and the tenth leaf of *Helianthus annuus*. The tenth leaf reached an area about three times greater than a leaf at the second node, on the other hand, the average volume of the cells of the tenth leaf was only about one-half that of the second leaf. The greater size of the tenth leaf is therefore due to longer duration of division rather than a greater final cell size. Division continued until the leaf was more than three-quarters fully grown. The results refute the older idea that during early development of the leaf, growth is due mainly to formation of new cells and that after division has ceased subsequent growth is due to cell enlargement. It is concluded that division and expansion do not determine leaf growth in two distinct developmental phases. Experiments have been initiated to investigate the metabolic activities of the shoot apex in both its vegetative and reproductive states. Observations are recorded on the terminal meristem of winter rye at a stage when the reproductive state of the apex is being initiated.

In the Department of Physiology and Plant Culture much attention has been given to design of growth rooms which will give the highest practical uniformity of light intensity, air temperature, air velocity and relative humidity in the space available for plants. Attention has also been directed to maximum flexibility. From the experience gained it has been possible to formulate the essential features necessary in such growth rooms. These facilities have been used to study the early growth and development of tomatoes. In all the conditions tested, plants grown in compost were found to have a higher growth-rate than can be obtained in vermiculite watered with nutrient solution. The factors involved are being studied. The light/temperature regimes in glasshouses are very important and it is hoped that a detailed study will prove of value in balancing the temperature of the glasshouse (which can be controlled especially at night) with the amount of light received, which cannot be controlled. If such a balance could be achieved, a great economy in glasshouse-tomato production would be attained.

A REVISED CLASSIFICATION OF THE LUDLOVIAN SUCCESSION AT LUDLOW

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RECENT detailed studies of the shelf facies of the Ludlovian at May Hill¹, Usk², Woolhop³, and Malvern⁴ have revealed a consistent pattern of faunal divisions. For some years workers in the Ludlow Research Group have been convinced that the same general pattern obtains in the type area at Ludlow. Unpublished work on areas to the west of Ludlow, at Leintwardine (J H McD Whitaker) and Elton (B J Williams), has strengthened this conviction. Unfortunately the published accounts of the type area¹⁻⁴ fail to recognize the two most distinctive faunal divisions (Lower Brinewood Beds and Upper Leintwardine Beds of the proposed classification) and leave the other divisions inadequately defined, often in terms of unreliable 'zone fossils', such as *Oamaroia echia nuda* and *Dayia navicula*. A revision of the geology of the Silurian in the Ludlow district was therefore, undertaken by us. The area investigated extends from Downton Gorge in the west to Ludlow itself and then southwards as far as a line joining Aston and Richard a Castle; it lies between the Leintwardine area to the west and the Elton area to the south west. This work has been completed and a detailed account is being prepared for publication. It will include details of localities, faunal lists and a geological map. Standard sections for the classification will be chosen, after discussion with Mr B J Williams and Mr J H McD Whitaker, from the whole area of the Ludlow anticline. The detailed description of these sections excavated if necessary, will include maps, sketches and photographs. It has been considered necessary to present this preliminary synopsis of the revised classification in order to facilitate stratigraphical correlation in impending publications on other Welsh Borderland areas of Ludlovian rocks. Moreover, several overseas geologists have made extensive collections based on the new scheme and need to refer to it in their publications.

The revised classification and its relationship to the existing scheme are shown in Table 1

Table 1

| PROPOSED CLASSIFICATION | PREVIOUS CLASSIFICATION |
|-------------------------|---|
| Upper Whitcliffe Beds | Upper Whitcliffe or <i>Chonetes</i> Flags |
| Lower Whitcliffe Beds | Lower Whitcliffe or <i>Rhynchonella</i> Flags |
| Upper Leintwardine Beds | Mocktree or <i>Dayia</i> Shales |
| Lower Leintwardine Beds | |
| Upper Brinewood Beds | Armestry or <i>Conchidium</i> Limestone |
| Lower Brinewood Beds | |
| Upper Elton Beds | Lower Ludlow Shales |
| Middle Elton Beds | |
| Lower Elton Beds | |

The introduction of new names has not been undertaken lightly and raises a number of problems. These nine divisions in the Ludlovian succession are defined essentially on their characteristic faunal assemblages and are therefore biostratigraphical units⁵. At Ludlow, because the faunas are to some extent facies faunas, these biostratigraphical units tend to coincide with lithostratigraphical units (divisions defined on the basis of lithological change). Consequently they are easily mappable divisions and it may be justifiable to consider them as formations, although many stratigraphers insist that formations should be distinguished on lithological criteria alone. For the kind of unit with which we are here concerned, the American Commission on Stratigraphic Nomenclature recommends the use of the term 'assemblage zone'. It further recommends that such assemblage zones be named after one of the fossils of the assemblage.

There are, however, serious objections to this latter practice. Taxonomic revision of a fossil name which has been used in this way causes confusion. Moreover, the selection of one fossil name from the assemblage is liable to throw undue emphasis on the one chosen, even when it is made clear that it serves merely as a label for a whole fauna. Misunderstanding arises especially where as is often the case the chosen fossil actually occurs also outside the stratigraphical unit defined. In fact, in the succession of faunal assemblages outlined here it would be difficult to find fossils which do not range beyond the limits of one such unit. In the absence, at present, of a more satisfactory method of naming such divisions we prefer to use the non-committal term 'Beds' and to distinguish these by appropriate local place names.

The *Elton Beds* are named after the village of Elton (SO 457 708), in the vicinity of which is the Elton Lane section described by Wood⁶ in establishing her Lower Ludlow graptolite zones. *Brinewood Chase* is the general name for the highest wooded ground (SO 458 733) between Ludlow and Downton Gorge, north of the Ludlow-Wigmore road. The name *Leintwardine* (after the village at SO 404 740) is preferred to *Mocktree*⁷ because of the possibility of these names being used for stages ending in *ian*. Finally, *Whitcliffe* (SO 508 742) refers to the right bank of the River Tern at Ludlow, the name of which was used by Elles and Slater⁸. Its retention seems unlikely to cause confusion but it is pointed out that these authors included the Ludlow Bone Bed within their 'Whitcliffe Flags' while we, following White⁹, regard this distinctive horizon as forming the base of the Downtonian.

In Wood's⁶ classification of the Lower Ludlow rocks on the basis of their graptolite faunas the *Monograptus tumescens* zone is succeeded by the zone

of *M. leintwardinensis*, which is said to include the Aymestry Limestone, "above which no graptolites are known" Elles and Slater⁷, and later Alexander⁸, extended the recorded range of *M. leintwardinensis* into the Mocktree Shales. We have recorded *M. tumescens* from the Lower Bringewood Beds of our classification and have found *M. leintwardinensis* in the Leintwardine Beds only. We know of no confirmable record of *M. leintwardinensis* from below the Leintwardine Beds.

The following notes are intended as a brief indication of the essential characteristics of the subdivisions proposed. Fossils are listed in each case which are common, fairly common, or characteristically present. A few localities are given at which the various beds may be examined.

(1) LOWER ELTON BEDS (Approximate thickness 100–150 ft.) Soft, poorly bedded, shaly and flaggy, pale olive calcareous siltstones, with layers of limestone nodules. The beds often have a speckled appearance due to the presence of numerous shell fragments. There is a shelly fauna of Wenlockian aspect, in which small brachiopods and trilobites predominate. Graptolites are exceedingly rare, these being the 'Barren Beds' of the Lower Ludlow Shales⁹.

Fossils *Atrypa reticularis* (Linnaeus), *Chonetoida grayi* (Davidson), *Dicoelosa [Bilobites] biloba* (Linnaeus) (characteristically present), *Leptaena rhomboidalis* (Wilckens), *Resserella [Parnorthus] cf. elegantula* (Dalman), *Skemadioides lewisi* (Davidson) (characteristically present), *Dalmanites vulgaris* (Salter), *Beyrichia maccoyana* Jones.

Localities (a) Overlying Wenlock Limestone in old quarry (SO 4725 7300) on south side of Ludlow–Wigmore road, about one mile north-east of Aston Church. The soft siltstones of the Lower Elton Beds contrast strongly with the nodular limestones of the top Wenlock Limestone. (b) Stream section (SO 4360 7265) in wood about half a mile north-west of Burrington Church.

(2) MIDDLE ELTON BEDS (Approximate thickness 150–350 ft.) Well-bedded, shaly and thinly flaggy, light olive-grey to yellowish-grey, more or less calcareous siltstones, with smooth, conchoidal fracture. Graptolites and orthoconic nautiloids predominate. These are the Lower Ludlow Shales of the *Monograptus nilssonii* and *M. scanicus* zones of Wood⁶.

Fossils *Chonetoida grayi* (Davidson), *Dalmanites vulgaris* (Salter), *Beyrichia maccoyana* Jones, *Monograptus bohemicus* (Barrande), *M. colonus* (Barrande) (common), *M. dubius* (Suess), *M. nilssonii* (Barrande) (characteristically present), *M. scanicus* (Tullberg) (characteristically present), *M. uncinatus* (Tullberg), *M. varians* (Wood), *Slava [Cardiola] interrupta* (Broderip), orthoconic nautiloids (common).

Localities (a) Stream bank (SO 4785 7328) about 580 yards south-west of Mary Knoll House. (b) Exposures in stream referred to under Lower Elton Beds above, for example, at SO 4338 7264.

(3) UPPER ELTON BEDS (Approximate thickness 150–250 ft.) Hard, well-bedded, flaggy, light olive-grey, calcareous siltstones with occasional thin limestone bands. These are the Lower Ludlow Shales of the *Monograptus tumescens* zone of Wood⁶ and this graptolite is the only common fossil.

Fossils *Chonetes lepisma* (J. de C. Sowerby), *Lingula lata* J. de C. Sowerby, *Monograptus tumescens* Wood (common and characteristic), orthoconic nautiloids.

Localities (a) Roadside exposure at Gorsty Farm (SO 4785 7355). (b) Exposures in steep wooded slope

above River Teme (SO 431 728), about half a mile north-west of Burrington Bridge.

(4) LOWER BRINGEWOOD BEDS (Approximate thickness 160–200 ft.) Irregularly bedded, flaggy, pale greyish-olive to greenish grey, calcareous siltstones, with limestone nodules. Large brachiopods, particularly strophomenids, are abundant. These beds have not previously been distinguished but have probably been included in the Aymestry Limestone.

Fossils *Atrypa reticularis* (Linnaeus), *Brachyprion* sp. nov., *Dalmanella orbicularis* (J. de C. Sowerby), *Gypidula lata* Alexander, *Leptaena rhomboidalis* (Wilckens), *Leptostrophus filosa* (J. de C. Sowerby), *Shaleria* sp. nov., *Sphaerirhynchia [Wilsonia] wilsoni* (J. Sowerby), *Strophonella euglypha* (Hisinger), *Strophonella funiculata* (McCoy), *Dalmanites vulgaris* (Salter), *Poleumita globosa* (Schlothheim), bryozoa.

Localities (a) Old quarry on south side of Ludlow–Wigmore road (SO 4825 7373), about 140 yards north-east of Mary Knoll House. (b) (SO 4940 7265) Sections 200 yards north-west of Sunnyhill Cottages.

(5) UPPER BRINGEWOOD BEDS (Approximate thickness 40–150 ft.) Hard, irregularly bedded, flaggy and nodular, greenish grey silty limestones or grey limestones, with thin shaly partings at intervals of several feet. The fauna is similar to that of the Lower Bringewood Beds, but strophomenids are less abundant, whereas *Conchidium knighti* and compound corals become common. These beds constitute the familiar Aymestry Limestone as seen at Aymestrey and View Edge.

Fossils *Atrypa reticularis* (Linnaeus) (common), *Conchidium knighti* (J. de C. Sowerby) (characteristically present), *Gypidula lata* Alexander, *Leptaena rhomboidalis* (Wilckens), *Sphaerirhynchia [Wilsonia] wilsoni* (J. Sowerby), *Strophonella euglypha* (Hisinger) (common), *Favosites* sp. (characteristically present), *Helolites* sp. (characteristically present), solitary corals, stromatoporoids (characteristically present), crinoid columnals.

Localities (a) Old quarry (SO 4851 7370) at north end of Mary Knoll. (b) East side of River Teme just south of Bow Bridge (SO 4306 7313).

(6) LOWER LEINTWARDINE BEDS (Approximate thickness 100 ft.) Flaggy, light olive grey, calcareous siltstones, with bands of shelly limestone which weather to dark yellowish-brown rottenstones. Brachiopods are abundant, but many species characteristic of the Bringewood Beds have disappeared (for example, *Conchidium knighti*, *Gypidula lata*, *Strophonella euglypha*), corals and stromatoporoids are also absent. These beds are roughly equivalent to the Daya or Mocktree Shales of Elles and Slater⁷.

Fossils *Atrypa reticularis* (Linnaeus) (common), *Camarotoechia [Rhynchonella] nucula* (J. de C. Sowerby), *Chonetes lepisma* (J. de C. Sowerby) (common), *Dalmanella orbicularis* (J. de C. Sowerby) (common), *Daya narcula* (J. de C. Sowerby) (common), *Leptaena rhomboidalis* (Wilckens), *Lingula lata* J. de C. Sowerby, *Shaleria ornatella* (Davidson) (common in the higher beds), *Sphaerirhynchia [Wilsonia] wilsoni* (J. Sowerby) (common), *Monograptus leintwardinensis* Lapworth (characteristically present).

Localities (a) Quarry at Sunnyhill Cottages (SO 4954 7253). (b) Old quarry (SO 4375 7307) at top of wooded scarp of Burrington Hays showing Lower Leintwardine Beds on Upper Bringewood Beds. (c) Deep roadside quarry (SO 4910 7399), about 1,050 yards east-north-east of Mary Knoll House, showing uppermost Lower Leintwardine Beds.

(7) UPPER LEINTWARDINE BEDS (Approximate thickness 5-20 ft.) Irregularly bedded, flaggy, light olive-grey, calcareous siltstones, with an abundant and most distinctive faunal assemblage. There are several trilobite species and an overlap of the brachiopod faunas characteristic of the lower and upper parts of the succession. Thin 'biscuity' dark yellowish brown layers, crowded with *Beurichia laevis* and *Chonetes grays* are characteristic of exposures in the western part of the district. This important division was not recognized by previous authors but appears to have been for the most part included in the *Dayia* or Mocktree Shales of Elles and Slater.¹

Fossils *Camarotoechia* [Rhynchonella] nucula (J de C Sowerby), *Chonetes striatellus* (Dalman), *Chonetes grays* (Davidson) (common in the west), *Dalmanella lunata* (J de C Sowerby), *D. orbicularis* (J de C Sowerby), *Leptaena rhomboidalis* (Wilkinson), *Shalera ornata* (Davidson) (common in the east), *Calymene neointermedia* R and E Richter (characteristically present), *Encrinurus* sp., Proetid trilobite, *Beurichia laevis* Klesow (characteristically present).

Localities (a) Small roadside exposure (SO 4925 7406) about three quarters of a mile east north east of Mary Knoll House. (b) Small old quarry (SO 4542 7370) above Forestry Commission track which leads from (SO 4595 7405) near Deepwood south wards, and then westwards across the wooded slopes of Bringewood Chase. Other small exposures by this track are at SO 4550 7371 and SO 4588 7374.

(8) LOWER WHITELIFFE BEDS (Approximate thickness 80 ft.) Irregularly bedded massive or thickly flaggy olive grey to dusky yellow calcareous siltstones with occasional calcareous nodules and with contorted siltstones at the top. Fossils are not abundant. Many of the brachiopods characteristic of the Leintwardine Beds have disappeared and mollusca have become important. These beds are the Lower Whiteliffes or Rhynchonella Flags of Elles and Slater.¹

Fossils *Camarotoechia* [Rhynchonella] nucula (J de C Sowerby) (common), *Chonetes striatellus* (Dalman) (small form commonest), *Dayia navicula* (J de C Sowerby) (common in certain beds only), *Fuchella* [Orthonota] amygdalina (J de C Sowerby), *Michelinoceras* [Orhoceras] imbricatum (Wahlenberg), *Serpulites longissimus* J de C Sowerby.

Localities (a) Roadside exposure (SO 4040 7413) just over three-quarters of a mile north east of Mary Knoll House. (b) Quarry (SO 4973 7247) about 300 yards east-south-east of Sunnyside Cottages with *Dayia navicula* fairly common. (c) Old quarry at western side of Hay Mill (SO 4348 7351) and exposures in south bank of River Tems east of the mill for about one-third of a mile.

(9) UPPER WHITELIFFE BEDS (Approximate thickness 100 ft.) Well bedded flaggy, light olive-grey to dusky yellow, calcareous siltstones with shelly lime stone bands. Fauna similar to that of the Lower Whiteliffes. Beds but brachiopods have become abundant. These are the Upper Whiteliffes or *Chonetes* Flags of Elles and Slater.¹

Fossils *Camarotoechia* [Rhynchonella] nucula (J de C Sowerby) (common), *Chonetes striatellus* (Dalman) (common), *Dalmanella lunata* (J de C Sowerby) (common), *Beurichia kloedeni* McCoy var. *terosa* Jones, *Fuchella* [Orthonota] amygdalina (J de C Sowerby), *Pteronitella cf. retroflata* (Wahlenberg), *Michelinoceras* [Orhoceras] bullatum (J de C Sowerby), *Serpulites longissimus* J de C Sowerby.

Localities (a) Whiteliffes (SO 5005 7415) on right bank of River Tems at Ludlow. (b) Exposures above eastern bank of River Tems south westwards from Downton Castle Bridge for example, at SO 4416 7411.

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EFFECT OF SOME NEUROMUSCULAR BLOCKING AGENTS ON MITOCHONDRIAL ENZYME SYSTEMS

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THE pyrolizidine alkaloids lasiocarpine and heliotrine have been shown¹ to block impulse transmission across neuromuscular junctions. These alkaloids also inhibit oxidations by pyridine nucleotide dependent dehydrogenases of liver mitochondria *in vitro*.² The same structural locus on the alkaloid molecule appears to be responsible for inhibition of impulse transmission and of mitochondrial oxidations. As the N-oxides of lasiocarpine or heliotrine affect neither transmission at neuromuscular junctions nor the activity of mitochondrial enzymes the inhibitory locus is likely to be the nitrogen atom of the cyclic nucleus. The neuromuscular blocking action of pyrolizidine alkaloids resembles the activity of d-tubocurarine in certain respects. d-Tubocurarine contains two quaternary nitrogen atoms as the

inhibitory centres and it was of interest to determine whether this alkaloid also inhibited mitochondrial enzyme systems. For similar reasons the effect on mitochondria of d-tre-1,10 phenanthroline ruthenium (II) perchlorate [Ru(phen)₂]⁺⁺, a complex ion³, was investigated.

Ru(phen)₂⁺⁺ has been shown to exert a curare like effect at the neuromuscular junction.⁴ This cation is a co-ordinately saturated metal chelate of high chemical stability and does not contain specific active groups or centres. Any biological activity which it may have is thus of a physical nature and is referable to the charge it carries.⁵

In common with lasiocarpine and heliotrine both d-tubocurarine and Ru(phen)₂⁺⁺ were found to inhibit *in vitro* the activity of mitochondrial enzyme

Table 1 INHIBITION OF L-MALATE OXIDATION AND EFFECT OF CO-FACTORS

| Time (min) | Interval oxygen uptake (μ l) | | | | | |
|--|-----------------------------------|---------------------------------------|---|----------------------|--|--|
| | Control | <i>d</i> -Tubocurarine 0.001 <i>M</i> | Ru(phen) ₃ ⁺⁺ 0.0005 <i>M</i> | Control + co factors | <i>d</i> -Tubocurarine 0.001 <i>M</i> + co-factors | Ru(phen) ₃ ⁺⁺ 0.0005 <i>M</i> + co factors |
| 10 | 45 | 42 | 45 | 51 | 54 | 57 |
| Side-arm contents tipped and equilibrated for 10 min | | | | | | |
| 10 | 39 | 27 | 21 | 54 | 48 | 48 |
| 20 | 24 | 9 | 9 | 42 | 30 | 30 |
| 30 | 21 | 6 | 7 | 42 | 27 | 30 |
| 40 | 18 | 0 | 0 | 42 | 30 | 30 |

System Adenosine monophosphate 0.001 *M*, magnesium sulphate 0.0067 *M*, potassium chloride 0.025 *M*, cytochrome *c* 0.00001 *M*, NaK phosphate buffer, pH 7.4, 0.0133 *M*, L-malate 0.01 *M*, water to 3 ml final volume, mitochondria equivalent to 100 mgm fresh liver added in 0.25 *M* sucrose, temperature 38° C, gas phase air, equilibration period 10 min, 0.1 ml 20 per cent potassium hydroxide in centre well to absorb carbon dioxide. Inhibitors and water (control flasks) added from side arms after 10 min incubation. Co factors diphosphopyridine nucleotide 0.0005 *M* and reduced glutathione 0.00067 *M* added in nicotinamide 0.04 *M*.

systems which require pyridine nucleotides for electron transfer. The oxidations of citrate, L-glutamate, α -oxoglutarate, L-malate and octanoate, all of which are dependent on pyridine nucleotide, are inhibited by *d*-tubocurarine and Ru(phen)₃⁺⁺ as well as by lasiocarpine and hehotrine. On the other hand, the activity of the succinoxidase system which does not require a pyridine nucleotide is increased in mitochondria suspended in 0.25 *M* sucrose by each of the agents.

Experimental results are recorded in Table 1 to show the concentrations necessary to produce inhibition of L-malate oxidation, the rate of development and degree of inhibition and the significant reversal of inhibition obtained by supplementing the reaction mixture with diphosphopyridine nucleotide, nicotinamide and reduced glutathione.

Clearly these agents inhibit mitochondrial enzyme systems by causing the loss or inactivation of pyridine nucleotides and, possibly, other respiratory co-factors. Such an effect could result from increased permeability of mitochondrial membranes allowing diffusion of soluble co-factors from the particles.

Mitochondrial permeability may be assessed spectrophotometrically by measuring at 340 m μ the rate of production of reduced diphosphopyridine nucleotide from diphosphopyridine nucleotide added externally to intact mitochondria oxidizing a diphosphopyridine nucleotide-dependent substrate^{6,7}. The rate of reduction of diphosphopyridine nucleotide is directly proportional to the permeability of the mitochondrial membrane to the passage of diphosphopyridine nucleotide into the particle. No effect of hehotrine, lasiocarpine, *d*-tubocurarine or Ru(phen)₃⁺⁺ on mitochondrial permeability could be demonstrated using this system. However, it was realized that the experimental conditions were very different from those obtaining in the system used for respiratory experiments.

Mitochondria re-isolated from a respiratory experiment in which they were subjected to 0.001 *M* *d*-tubocurarine or 0.0067 *M* lasiocarpine were found to be more permeable to the entry of diphosphopyridine nucleotide than incubated control mitochondria. More simply, it was possible to demonstrate an effect of the alkaloids on mitochondrial membrane permeability in the following manner. Mitochondria equivalent to 800 mgm of fresh rat liver were suspended in 5 ml of 0.25 *M* sucrose containing 0.01 *M* L-malate and 0.001 *M* *d*-tubocurarine or 0.01 *M* lasiocarpine and placed in an incubator at 37° C for 30 min, during which time the temperature of the reaction mixture rose to 32° C. The mitochondria were re-isolated by centrifugation after the addition of 35 ml ice-cold 0.25 *M* sucrose and resuspended in 0.25 *M* sucrose or water as required. Permeability of the mitochondria was

then assessed by the spectrophotometric method. Fig 1 shows that incubation in the presence of lasiocarpine or *d*-tubocurarine increases the permeability of mitochondrial membranes to the passage of diphosphopyridine nucleotide. The initial differences in optical density at 340 m μ of the curves in Fig 1 are due to reduction of diphosphopyridine nucleotide at different rates during the short time between adding the enzyme and taking the first reading. Suspension of mitochondria in water instead of 0.25 *M* sucrose abolishes selective semi-permeability of the membranes and also the effect of both the alkaloids.

Finally, it was possible to show that mitochondrial permeability increases rapidly under the oxidizing conditions of respiratory experiments and is present at the time oxidative inhibitions by the pyrazolidine alkaloids, *d*-tubocurarine or Ru(phen)₃⁺⁺ are expressed. The observation was made that each of these agents stimulated the oxidation of succinate

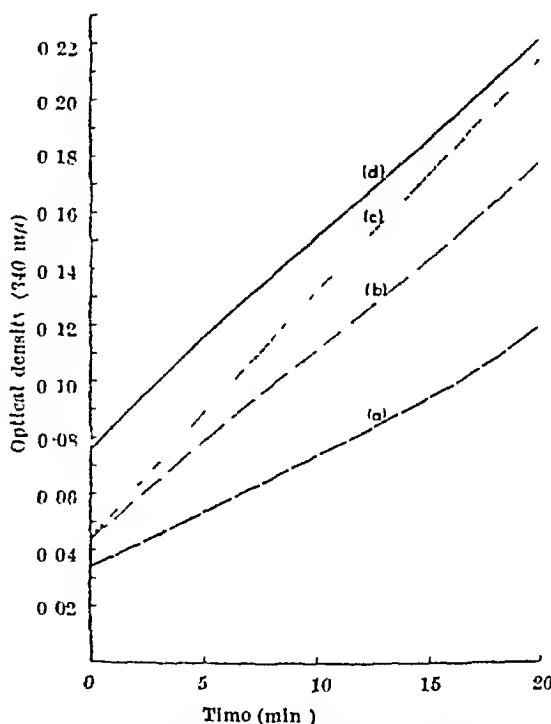


Fig 1 Reduction of diphosphopyridine nucleotide by liver mitochondria in 0.25 *M* sucrose. Mitochondria preincubated with (a) L-malate 0.01 *M*, (b) L-malate 0.01 *M* + *d*-tubocurarine 0.001 *M*, (c) L-malate 0.01 *M* + lasiocarpine 0.01 *M*, (d) no addition. System: NaK phosphate buffer, pH 7.8, 0.033 *M*, potassium chloride 0.025 *M*, magnesium sulphate (neutralized) 0.017 *M*, diphosphopyridine nucleotide 0.0015 *M*, potassium cyanide 0.0002 *M*, enzyme, 50 μ l 1 per cent mitochondria (rat liver) in 0.25 *M* sucrose, final volume 3 ml, gas phase air, temperature 22° C.

Table 2. EFFECT OF *d* TUBOCURARINE, LAIOCARPINE AND DIPHOSPHOPYRIDINE NUCLEOTIDE (DPN) ON SUCCINATE OXIDATION

| Time (min) | Interval oxygen uptake (ml) | | | | |
|------------|-----------------------------|-------------------------------|----------------------|-----|-------------------------------------|
| | Control | <i>d</i> Tubocurarine 0.001 M | Laiocarpine 0.0067 M | DPN | <i>d</i> Tubocurarine 0.001 M + DPN |
| 10 | 66 | 64 | 75 | 63 | 56 |
| 20 | 59 | 65 | 76 | 41 | 32 |
| 30 | 40 | 50 | 51 | 35 | 26 |

System As Table 1 with succinate 0.01 M as substrate and all flask contents in main chamber

by mitochondria in 0.25 M sucrose. This was thought possibly to be due to increased permeability of mitochondrial membranes allowing the loss of mitochondrial diphosphopyridine nucleotide and thus preventing the production of oxaloacetate which in low concentration inhibits succinate dehydrogenase specifically*. The suggestion received strong support from the lack of any effect of laiocarpine, heliotrine or *d*-tubocurarine on succinate oxidation by mitochondria in water, which would not be producing oxaloacetate. Conclusive evidence was obtained by the addition of diphosphopyridine nucleotide to mitochondria oxidizing succinate in the presence of each of the agents. Diphosphopyridine nucleotide added externally to intact mitochondria enters the particles slowly unless the permeability of mitochondrial membranes is increased. Succinate oxidation by mitochondria in 0.25 M sucrose was slightly inhibited by the addition of diphosphopyridine nucleotide alone but was rapidly and greatly inhibited by the combination of diphosphopyridine nucleotide and any one of the agents (Table 2). When mitochondria were suspended in water diphosphopyridine nucleotide produced maximum inhibition of succinate oxidation alone and laiocarpine, heliotrine or *d*-tubocurarine did not affect the rate of oxidation when added to systems with or without diphosphopyridine nucleotide. Similarly the addition of 0.0001 M Ca^{++} to mitochondria in 0.25 M sucrose stimulates succinate oxidation by increasing mitochondrial permeability and facilitates penetration of the particles and inhibition by added diphosphopyridine nucleotide.

Table 2 shows typical experiments with *d*-tubocurarine and laiocarpine, similar results were obtained with heliotrine and Ru(phen) $^{++}$. It is clear that each of the agents increases the permeability of mitochondrial membranes to the entry of diphosphopyridine nucleotide.

The effect of pyrrolizidine alkaloids, *d*-tubocurarine and Ru(phen) $^{++}$ on mitochondrial diphosphopyridine nucleotide is being investigated and will be reported elsewhere.

It is thus shown that these three types of chemically dissimilar compounds have actions in common on neuromuscular junctions and on liver mitochondria. At each site selective semi permeable membranes are involved. We suggest that the mechanism of action of the agents may be identical at the neuromuscular junction and on mitochondrial membranes and further, that, as the biological activity of Ru(phen) $^{++}$ is due only to the charge carried, the activities of pyrrolizidine alkaloids and *d*-tubocurarine may also be referable to the charge carried on the nitrogen atoms.

We wish to thank Dr. Price and Dr. Culvenor, of the Chemical Research Laboratories, for preparing the pyrrolizidine alkaloids, and Dr. Dwyer, of the National University, Canberra, who prepared *dl*-tris 1,10-phenanthroline ruthenium (II) perchlorate. We acknowledge gratefully the skilled and careful technical assistance of Miss Flint-Gallé and Miss Mann.

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EFFECT OF DIETARY FAT AND EXTENT OF BLOOD SAMPLING ON THE LEVEL OF PLASMA CHOLESTEROL IN THE RAT

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IN the course of an investigation of the effect of certain dietary fats on the plasma cholesterol level of the white rat, increases in the level of this substance were found which were at first attributed to the effect of dietary fat but which, on further study, were found to be due to the combination of this component and the frequency and extent of blood sampling.

Male white rats were placed on formula diets similar to those used by Beveridge et al. in studies on man. Fat supplied 28.4 and 58.5 per cent total calories, protein, 10.9 per cent. Plasma cholesterol determinations were made by the method of Sperry and Webb¹ modified to permit duplicate determinations on 0.1 ml of rat plasma. Blood samples were taken by tail section, using powdered heparin as the *in vitro* anticoagulant.

In Table 1 are shown the effects of varying dietary fat and blood sampling procedure on plasma cholesterol levels. In experiment 1, groups maintained on a high and a moderate fat intake were compared with those receiving their stock diet of 'Purina' fox chow. Blood samples of 2-3 per cent of total blood volume were taken from all groups on alternate days for the first 8 days and weekly thereafter. At the end of 35 days of feeding, the groups receiving corn oil showed a highly significant increase in plasma cholesterol, while those on fox chow remained unchanged. The group receiving a high fat intake

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Table 1 EFFECT OF DIETARY FAT AND EXTENT OF BLOOD SAMPLING ON PLASMA CHOLESTEROL LEVEL IN THE RAT

| Experiment No | Blood sampling procedure | Diet | Number of animals | Initial mean plasma cholesterol (mgm/100 ml) | Duration of test (days) | Final plasma cholesterol (mgm/100 ml) | Av group percentage change | P |
|---------------|--|------|-------------------|--|-------------------------|---------------------------------------|----------------------------|----------|
| 1 | Blood sample of 2 per cent blood volume taken on alternate days for the first 8 days and weekly thereafter | HC | 14 | 80.5 ± 6.0 | 35 | 96.5 ± 12.3 | +20.5 | <0.01 |
| | | MC | 14 | 75.7 ± 9.3 | 35 | 86.2 ± 9.0 | +13.5 | <0.01 |
| | | Chow | 14 | 76.4 ± 9.5 | 35 | 76.0 ± 7.8 | +0.3 | Non sig. |
| 2 | Blood sample of 0.5-1.0 per cent blood volume taken on first and final days only | HC | 30 | 64.8 ± 12.4 | 14 | 64.6 ± 12.4 | -0.3 | Non sig. |
| | | FF | 30 | 75.4 ± 9.4 | 14 | 70.2 ± 12.4 | -6.0 | Non-sig. |
| 3 | Blood sample of 1-1.5 per cent blood volume taken on alternate days for 6 days | HC | 20 | 73.7 ± 11.1 | 6 | 90.6 ± 10.7 | +31.1 | <0.01 |
| | | FF | 20 | 71.8 ± 11.7 | 6 | 78.8 ± 15.7 | +9.8 | Non sig. |
| 4 | Blood sample of 2.5-4 per cent blood volume taken on alternate days for 6 days | HC | 15 | 67.2 ± 14.3 | 6 | 150.0 ± 18.0 | +122.4 | <0.01 |
| | | FF | 15 | 67.7 ± 12.8 | 6 | 107.7 ± 27.2 | +59.0 | <0.01 |

Diets used HC, corn oil, 53.5 per cent cal, MC, corn oil, 28.4 per cent cal, FF, essentially fat-free, Chow, 'Purina' fox chow

demonstrated an increase of 20.5 per cent, while those on a moderate intake increased only 13.5 per cent during this period, the difference being highly significant.

This elevation in plasma cholesterol of the groups fed corn oil was paralleled by other groups receiving formula diets containing butter, beef dripping, coconut oil and corn oil supplemented with cholesterol to equal the concentration present in butter (not here reported). In each case the elevation in plasma cholesterol was dependent on the concentration at which the fat was fed and not upon the nature of the fat. Because of the consistency of the hypercholesterolemia with all fats examined and the gradation of response in proportion to the level at which the fats were supplied, it appeared certain that the increase in plasma cholesterol was dependent solely upon the presence of dietary fat.

However, repetition of the study in the second experiment, in which the group fed corn oil was compared with the more suitable control group consuming fat-free formula rather than fox chow, failed to reveal any change in plasma cholesterol after 14 days. The animals had blood samples of 0.5-1.0 per cent of total blood volume removed only at the start and conclusion of the test. The only difference in the conditions of the first two experiments that appeared to offer any rational basis of explanation for the apparently divergent results was the difference in the extent and frequency of blood sampling. This was, at first, regarded as unlikely, since no reports of hemorrhage causing a lipaemia in the rat similar to that described for the rabbit and guinea pig could be found in the literature.

However, in experiment 3, a group of rats fed a diet supplying 58.5 per cent of total calories in the form of corn oil was compared with a similarly matched group on a fat-free diet. Both were subjected to bleeding on alternate days for a period of 6 days, during which blood samples of 1-1.5 per cent of total blood volume were taken. The group on the high-fat ration showed an increase in plasma cholesterol of 31.1 per cent during this period, while those on the fat-free diet showed no significant change. An increase in the amount of blood taken to 2.5-4 per cent of total blood volume, in experiment 4, produced an increase in plasma cholesterol of 122 per cent in the animals on the high fat intake. Even animals on the fat-free diet showed an increase of 59 per cent.

It was now apparent that the hypercholesterolemia found in experiment 1 could not be attributed to an

uncomplicated response to dietary fat, but was the product of both dietary fat and the degree of hemorrhage to which the animals were subjected. Under conditions of low bleeding stress, a high fat diet, as in experiment 2, caused no change in plasma cholesterol. When bleeding was increased to 1-1.5 per cent of total blood volume on alternate days for 6 days (experiment 3), a high corn oil diet produced a significant increase in plasma cholesterol, although the animals on a fat-free diet and under the same conditions of bleeding showed no change. Thus the hypercholesterolemia is a combined effect of diet and hemorrhage. When bleeding stress was increased to 2.5-4 per cent of blood volume on alternate days for 6 days, highly significant increases in plasma cholesterol resulted in both the high fat and fat-free groups. These results, therefore, clearly indicate that the hypercholesterolemia due to severe hemorrhage does not depend solely on the presence of dietary fat although it is augmented by the latter.

This response of the rat to bleeding stress and dietary fat has not, to our knowledge, been previously reported. It is suggestive of the lipaemia of hemorrhage obtained in the rabbit^{3,4} and guinea pig^{5,6}. There is a difference, however, Spitzer⁷, on investigating the lipaemia produced in rabbits on a high-fat diet, found it necessary to bleed to 10-15 per cent of blood volume on successive days to elicit the response, and also found that the animal recovered in about the same time necessary to induce the hyperlipaemia. The rats were never bled more severely than 2.5-4 per cent of blood volume on alternate days to produce the hypercholesterolemia on high-fat diets, and from experiment 1 there is evidence that these elevations in plasma cholesterol are maintained for periods of time as long as 5 weeks after the period of severe bleeding.

Although no substantiated explanation of this phenomenon can be advanced at the present time, we wish to bring it to the attention of other workers in this field as a possible explanation of some of the conflicting reports on the effect of dietary fat on the plasma cholesterol level of the rat.

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NONHAEM IRON IN ERYTHROCYTES AS A PRECURSOR FOR HAEMOGLOBIN

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THE existence of nonhaem iron in erythrocytes from peripheral blood has long been a matter of dispute. The presence of iron receptors has been suggested by Walsh *et al.*¹ and Jandl *et al.*² have shown in experiments with radioactive iron that reticulocytes take up iron *in vitro* and that this iron is bound to the stroma and incorporated into haem. Recently, Bernard *et al.*³ and Lambrecht and Thimus⁴ have found nonhaem iron fairly constantly in erythrocytes from normal and pathological human blood as the difference between total iron and haemoglobin iron. The presence of nonhaem iron in the stroma of immature red cells in bone marrow has been demonstrated by electronmicroscopy.^{5,6}

The purpose of the present work has been to verify the existence of nonhaem iron in the stroma of normal mature red cells and demonstrate its significance in haemoglobin synthesis by means of *in vivo* experiments with radioactive iron.

A modification of the method of successive hemolysis used by Hillier and Hoffman⁷ for preparation of haemoglobin free red cell 'ghosts' for electron microscopy was chosen. The ghosts appeared greyish white, and no haemoglobin could be demonstrated spectrophotometrically but there was still a faint positive benzidine reaction.

Estimations of stroma iron were carried out on blood samples taken for ten successive days from a patient with recently diagnosed genuine hemochromatosis. The disease was mild and the patient may be regarded as hematologically normal. The iron contents of ghosts prepared from 10 ml of packed red cells ranged from 41γ to 125γ with an average of 70γ. A few determinations on ghosts

from normal humans and rabbits gave values within the above mentioned limits.

In order to estimate the significance of this stroma iron in haemoglobin synthesis this patient was given 8.5 μg iron 59 intravenously. Blood samples were taken daily, and after determination of the amount of stroma iron, this was electroplated on copper disks and the β radioactivity measured by a Geiger-Müller tube. As will be seen from Fig. 1, the specific activity of the stroma iron was higher than that of the haemoglobin iron on the first day after administration of iron 59, but lower on the following days quickly reaching constant values of about one third of the specific activity of haemoglobin iron. Owing to the very low counting rate on the first day it was deemed necessary to explore this early phase further.

Four female rabbits of the same age and weight were injected intravenously with about 10 μg iron 59 each. The animals were killed after 1, 2, 5 and 22 hr respectively and a sufficient amount of blood to provide 10 ml of packed erythrocytes was obtained from each animal. Stroma iron and radioactivity was determined as previously. The results appear in Table 1.

Table 1

| Hours after injection of iron-59 | Stroma iron in γ per 16 ml packed erythrocytes | Specific activity of stroma iron (c.p.m./mgm iron) | Specific activity of haemoglobin iron (c.p.m./mgm iron) |
|----------------------------------|--|--|---|
| 1 | 81 | 550 | 570 |
| 2 | 94 | 13,640 | 3,780 |
| 5 | 75 | 2,060 | 5,750 |
| 22 | 80 | 2,000 | 9,100 |

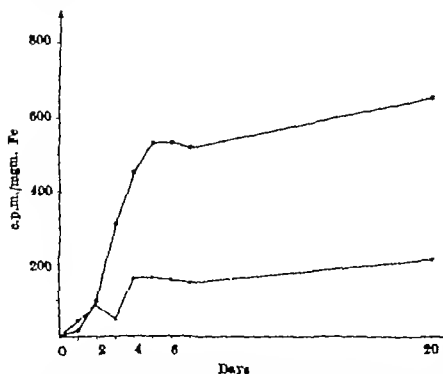


Fig. 1 Incorporation of iron-59 in haemoglobin and stroma iron in a patient with genuine hemochromatosis. O—O haemoglobin iron O—O nonhaem iron

There is a very high rate of incorporation in the stroma iron of the erythrocytes released during the first hours but already after 5 hr the specific activity of haemoglobin is higher than that of stroma iron. These findings strongly support the view that stroma iron acts as an intermediate between transport iron of plasma and haemoglobin.

That this transfer mechanism may be blocked artificially appears from the results of Bernard *et al.*³ and Jandl *et al.*², who show by means of iron 59 that there is practically no synthesis of haem *in vitro* in blood containing lead ions. That a similar blocking may be an important factor in certain anemias is seen from an experiment performed on a patient with severe anemia characterized after splenectomy, by a considerable amount of siderocytes in the peripheral blood. The anemia was probably of the type described by Deane *et al.*⁸. This patient was given 14.3 μg iron 59 intravenously and a week later the specific activities of stroma iron and haemoglobin iron were estimated. Despite the considerable period of time which had elapsed since the administration of iron 59 the specific activity of stroma iron was more

than four times higher than that of hæmoglobin iron, the specific activities being 1,660 c p m /mgm iron and 360 c p m /mgm iron, respectively. This strongly supports the view that blocking of the transport system of iron in the stroma of red blood cells may play an important part in this anaemia.

The chemical nature of the stroma iron is still unknown, but experiments which are in progress in this laboratory indicate that it may, at least in part, consist of ferritin.

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EXTREME SENSITIVITY OF GERMINATION AND PHOTOPERIODIC REACTION IN THE GENUS *CHENOPODIUM* (TOURN.) L.

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PLANTS of *Baeria chrysostoma*¹ and *Pharbitis nil*² are known to respond to photoperiod at a very early stage in growth. *Chenopodium rubrum* L. is particularly valuable as an experimental plant since floral initiation can occur very rapidly when seed is germinated under 8-hr short days in Petri dishes³. In addition, one photo-inductive short day may initiate floral formation (as shown in *Xanthium pennsylvanicum*⁴ and *Pharbitis nil*²), while, in germination, there are red/infra-red and red/blue reversal effects (as shown in lettuce^{5,6}). Furthermore, there is marked sensitivity to temperature in germination.

Detailed comparisons of flowering have been made between selections of four species of *Chenopodium*: (a) *C. rubrum* L., (b) *C. salinum*, Standley (syn *C. glaucum* var *salinum* (Standley) Boivin), (c) *C. glaucum* L. (syn *C. glaucum* L. var *glaucum* Aellen), (d) *C. album* L. Under 8-hr short days, with alternating temperatures of 15° C for 16 hr in darkness and 25° C for 8 hr in light of 1,200 foot-candles (fluorescent combined with incandescent), that is, 15–25° C, the least number of days from seed imbibition (on moistened filter paper in Petri dishes) to visible floral formation, has been, in species (a) 6, (b) 12, (c) 20, (d) 36. The corresponding minimum true leaf numbers were in species (a) 2, (b) 2, (c) 2–4, (d) 4. Alternating temperatures of 15–25° C to 20–30° C are optimal for floral initiation in these species. Floral initiation may occur under intensities as low as 150 foot-candles (fluorescent combined with incandescent), although less rapidly. Fig. 1a illustrates 100 plants of *C. rubrum* 17 days after imbibition under 8 hr short days, with light of 250 foot candles (fluorescent), alternating temperature 15–25° C, 90 per cent of the plants showed floral formation. Fig. 1b illustrates one of these plants when 21 days old, the two true leaves and four perianth members were very rudimentary, there were no stamens but the ovary produced a single viable seed after cross-pollination.

Nutrients markedly influence the amount of growth and floral formation, but the response is different between species. For example, under 8-hr

short days with light of 1,200 foot-candles (fluorescent combined with incandescent) and alternating temperature of 23–28° C, the minimum true leaf numbers of plants grown in Petri dishes, with water as compared with Hoagland's solution, were, in species (a) 2 versus 2, (b) 2 versus 4, (c) 2–4 versus 4–6, (d) 4 versus 9–10, respectively. Soil gave results similar to Hoagland's solution with an even greater leaf number occurring in *C. album*. The amount of floral formation was also proportionately much greater when nutrients were supplied, and stamen formation occurred even on some plants of *C. rubrum* (Fig. 1c). These results provide further evidence that the concept of minimum leaf number must be treated with circumspection⁷.

Wide differences in photoperiodic sensitivity between these species are shown under 20-hr long days or continuous light, when plants are grown in soil. *C. album* and *C. glaucum* will flower, although less rapidly than under short days. In contrast, *C. rubrum*, under 20-hr long days, at a temperature of approximately 24° C, has remained vegetative indefinitely (that is, at least 200 days, Fig. 1d). With increased age *C. rubrum* becomes increasingly sensitive to photoperiod and one photo-inductive cycle, that is, one 16-hr dark period following an 8 hr light period, may initiate floral formation—

Table 1. PER CENT GERMINATION OF (a) *C. rubrum*, (b) *C. salinum*, (c) *C. glaucum*, (d) *C. album*, IN DARKNESS AND UNDER 8 HR SHORT DAYS WITH CONSTANT AND ALTERNATIVE TEMPERATURES, 10 DAYS AFTER IMBIBITION

| Temperature | Darkness | | | 8 hr short days | | |
|-------------|----------|-----|-----|-----------------|-----|-----|
| | (a) | (b) | (c) | (a) | (b) | (c) |
| Constant | | | | | | |
| 35° C | 15 | 0 | 03 | 05 | 40 | 03 |
| 30° C | 5 | 0 | 00 | 05 | 80 | 100 |
| 25° C | 0 | 15 | 03 | 25 | 75 | 00 |
| 20° C | 5 | 0 | 43 | 5 | 40 | 80 |
| 15° C | 0 | 0 | 48 | 0 | 15 | 00 |
| 10° C | 0 | 0 | 10 | 0 | 0 | 23 |
| Alternating | | | | | | |
| 25–35° C | 25 | 15 | 03 | 100 | 00 | 08 |
| 20–30° C | 85 | 50 | 00 | 100 | 00 | 08 |
| 15–25° C | 05 | 15 | 05 | 100 | 75 | 75 |
| 10–20° C | 100 | 0 | 00 | 100 | 30 | 08 |

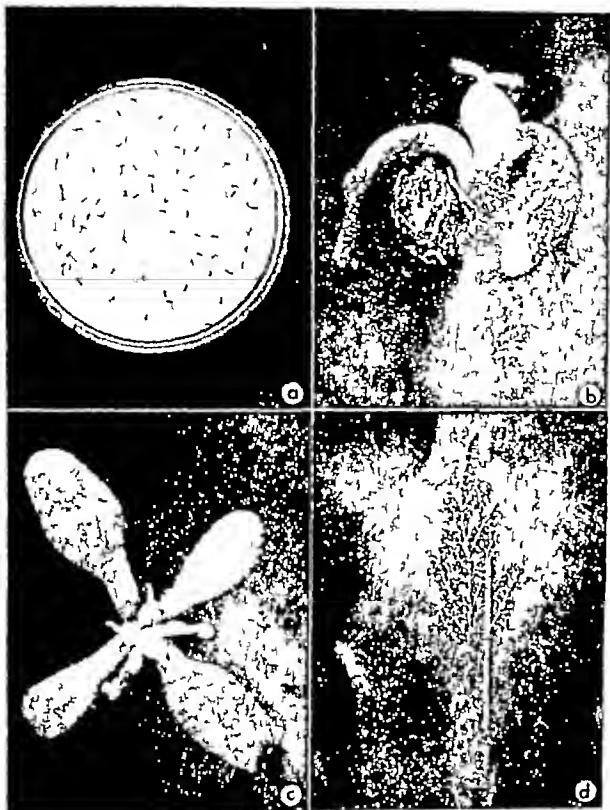


Fig. 1. *C. rubrum* L. a 100 plants 17 days old 0.8 cm tall 60 per cent flowering in 9 cm. x 2 cm Petri dish 8 hr short days 250 ft.-c (duor.) alternating temperature 13–25° C. b Flowering plant 21 days old from a original pericarp and testa 0.6 mm. diam still attached to cotyledon c Stamens and ovaries on plant grown with Hoagland's solution 8 hr short day, 1,200 ft.-c. (duor./incand.), alternating temperature 23–25° C original testa 0.6 mm diam. d Vegetative plant 200 days old 20 hr long days (scale 1 in rule)

especially if the prevailing light intensity is 2,000 foot-candles or more. With one photo inductive cycle, depending on age and treatment floral formation may be imperfect or delayed 6–8 weeks. Floral formation is increased in rate and amount with increase in the number of photo inductive cycles and under favourable conditions it may be visible microscopically in 3–4 days and macroscopically in 6–7 days.

C. salinum appears to be intermediate between *C. glaucum* and *C. rubrum* in sensitivity to photoperiod and, while some selections have flowered within about 120 days under 20 hr long days, others have remained vegetative indefinitely (that is, at least 200 days). Induction of floral formation in *C. salinum* can be accomplished with one photo inductive cycle—at an earlier stage of growth than in *C. rubrum*.

When sensitivity is evaluated by the amount of germination under different light qualities, energies, time sequences and temperatures, the species are again listed in order of sensitivity as (a) > (b) >

(c) > (d). Table 1 summarizes the percentage germination of non dormant seed under constant and alternating temperatures in darkness as compared with 8 hr short days (250 foot-candles—fluorescent). In continuous light, germination was similar to that under 8 hr short days. Germination of *C. rubrum* was negligible in darkness at constant temperatures < 35° C and under 8 hr short days at constant temperatures < 25° C. The lower alternating temperatures completely substituted for the light requirement in *C. rubrum* but not in *C. salinum*. Seeds of *C. rubrum* and *C. salinum* when exposed for 1 min. to white light of 50 foot-candles (fluorescent) 10 days after imbibition in darkness, germinated equally as well as under 8 hr short days. In darkness at a constant temperature of 25° C., transfer of seeds to 10° C for one 8 hr period, 10 days after imbibition, initiated 100 per cent germination of *C. rubrum* and 50 per cent of *C. salinum*.

In species (a)–(d) germination can be promoted by white or red and inhibited by blue or infra red radiation. In *C. rubrum*—the most sensitive species—at a constant temperature of 35° C., using appropriate filters and fluorescent combined with incandescent white light (1,200 foot-candles) 1 min of white or red light supplied 8 hr after imbibition may initiate 100 per cent germination while 1 min of blue or infra red radiation may completely inhibit germination. red/infra red and red/blue reversal effects are similar to those reported for lettuce*.

These and other unpublished results that will be reported elsewhere indicate that the genus *Chenopodium* offers valuable and diverse

material for experimental study. There is some evidence to support the postulation that 'weediness' of these species may be positively correlated with the amount of phenotypic 'plasticity' and with absence of sensitivity in germination and photoperiodic response. In order of distinction as weeds in Canada the species would be evaluated as *C. album* > *C. glaucum* > *C. salinum* > *C. rubrum*.

I am indebted to Dr H. A. Senn, director of the Plant Research Institute, for the availability of extensive controlled environmental facilities, and to Dr T. F. Cuddy of the Plant Products Division for the use of precisely controlled germination cabinets.

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REDOX POTENTIALS IN SOYBEAN NODULES DURING THE VEGETATIVE PERIOD

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THE attention of research workers is becoming more and more concentrated upon biochemical oxidation-reduction processes taking place during the fixation of molecular nitrogen. Rabotnova¹ established that redox potentials of leguminous root nodules are comparatively low, the rH -value being about 17–19. Fedorov², in his theory of nitrogen-fixation, also emphasizes the active role taken by various enzymatic systems under low rH -values. In connexion with these findings studies on the respiratory systems of rhizobia, nodules and leguminous plants require special attention. Bergersen³ found no substantial differences between the respiratory activity of cultivated rhizobia and bacteroides from nodules during their development. Allison, Ludwig, Minor and Hoover⁴ carried out respiration tests with nodules and leguminous plant roots and concluded that rhizobia in nodules are relatively inactive as regards respiration and carbohydrate consumption. The value of redox potential in nodules also represents an important condition for the activity of hydrogenase, which is regarded as having an essential part to play in the fixation of nitrogen. The role of hydrogenase in the fixation processes has been investigated by many authors, for example, Wilson, Burris and Coffee⁵ and recently Hamilton, Shug and Wilson⁶.

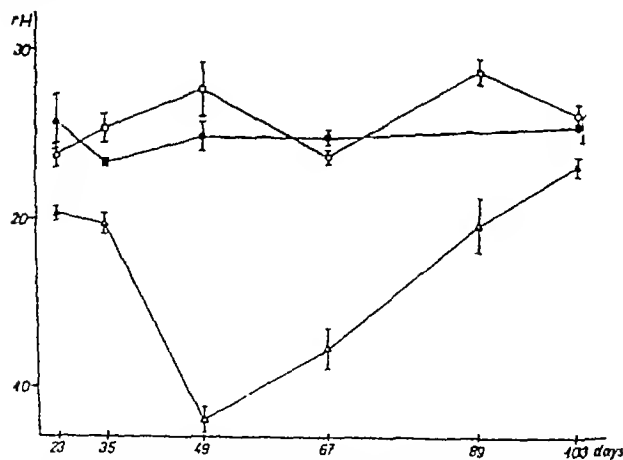


Fig 1 rH values in soybeans. \circ — \circ , stems, \bullet — \bullet , roots, Δ — Δ , nodules. Standard deviation \pm , abscissa, number of days after sowing.

In the present work the course of the redox potential and pH -value in stems, roots and nodules has been followed during the whole period of vegetation and related to the increase in the number and size of nodules. Both redox potential and pH -value have been measured in three replicate plants with platinum and antimony micro electrodes respectively, thrust directly into the plant organs. On each plant one nodule was chosen for the measurements. A saturated calomel half-cell was used for reference, the tests were carried out in the air. For greater simplicity in preparing graphs and easier comparison with other authors' results, the redox potential values

are expressed by means of an rH scale (Fig 1). As Hewitt⁷ reports reasons against using the term rH in biological systems such as these, the ranges of measured E_h and pH values are also quoted in the text.

The results of the rH field-tests measured in plants dug up at convenient intervals are presented in Fig 1. In the greenhouse similar results have been obtained with plants grown in sand with mineral nutrients containing 1/20 of nitrogen ratio. At suitable intervals the plants of single pots (3 plants per pot) were taken for potential measurements and estimation of nodulation and total nitrogen in plant material by the Kjeldahl method. Then the nitrogen fixation ratio in the glasshouse experiment could be calculated. Decrease of potential was observed in nodules of the same age as those in the field experiment.

Fig 2 shows the numbers and sizes of nodules in the field-experiment during the whole period of vegetation. Until the ripening of the plants, new pink nodules originated constantly under field, as well as under greenhouse, conditions. Their rH values were about 10 and their ability to fix nitrogen was high, as was proved by estimation of total fixed nitrogen content in each pot in the glasshouse and by the concentration of total nitrogen in single plant organs in the field. Nitrogen fixation and nitrogen content are given in Fig 3. Differently coloured nodules in various stages of development and with rH values differing by up to 13 units have been simultaneously found in the root system of one and the same plant, even on the roots of plants 103 days old. Thus, if the curve of rH values had to represent the actual course of the redox potential during the life of the nodule, it was always necessary to pick out for measurement only the oldest nodules in the root system of experimental plants. In the soybean root system in all our experiments nodule formation began very early, and always on the upper part of the main root. These first nodules grew very quickly and reached about $\frac{1}{2}$ in diameter and their content became pink during

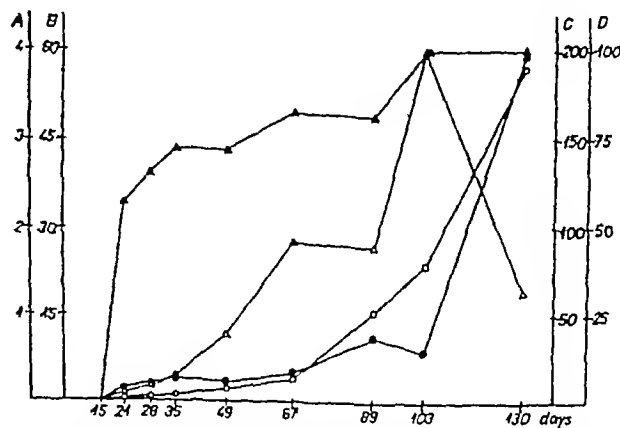


Fig 2 Formation and growth of nodules. A, \circ — \circ , volume of nodules on one plant (cc), B, \bullet — \bullet , number of nodules on one plant, C, Δ — Δ , average volume of one nodule (μ l), D, \blacktriangle — \blacktriangle , percentage of nodulation. Abscissa, number of days after sowing.

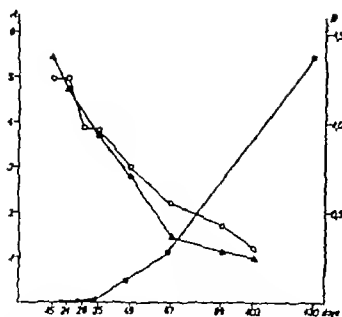


Fig. 3 Nitrogen fixation and nitrogen content in plants. A ○—○ percentage of total nitrogen in leaves of the field plants (inoculated △—△ controls B ●—● nitrogen (gm.) fixed per pot in glasshouse. Abscissa: number of days after sowing

the maximum decrease of potential, whereas other nodules scattered throughout the root system appeared and reached their largest size much later. The oldest nodules for the measurements could therefore be easily picked out according to their location, size, colour and also their consistence.

The tissue of the nodules differed from that of other parts of the plants not only in regard to its redox potential but also in pH value. During the period of low redox potential (about -200 mV), the pH of the pink nodules varied between 7.2 and 8.7, whereas in the roots and stems it was 5.9–6.0 (potentials about $+350$ mV). No differences were found between E_h and pH values measured in roots and stems of inoculated and control plants.

These results are evidence that the nodules on leguminous plants with quickly growing root systems originate on secondarily thickened parts of roots without root hairs and without primary cortex. The appearance of new active nodules is not limited by the advancing age of the host plant, almost up to the ripening of the fruits. Dif-

ferent values of redox potentials simultaneously measured in nodules of a single plant are in accordance with this observation. The rH values reflect only the physiological state and age of nodules irrespective to a large degree of the age of the host. When comparing the results plotted in Figs 1 and 3, we can see that a considerable fall of potential in the first nodules coincides with the beginning of nitrogen fixation observed in greenhouse and field tests. The differences in size and colour between the control and inoculated plants in the field were observed to run parallel with nitrogen content in leaves also from the seventh week after sowing.

A further interesting result is that the redox potential is, to a large degree, not conditioned by the size of the nodules. The size of nodules picked out for potential measurements in carrying out the field tests was about 200μ l and remained unchanged from the beginning of fixation until the plants ripened, the observations in the greenhouse were made on nodules of about a fifth that size, but with similar results as regards absolute values and development with time.

Very low values of potentials in nodules fixing atmospheric nitrogen are not opposed to the hypothesis that reduction of molecular nitrogen in nodules by hydrogen is catalysed by hydrogenases. The large differences between rH values in various soybean organs and in nodules is evidence of specific biochemical processes taking place in the nodules during the fixation of nitrogen and show that nodules cannot be regarded as ordinary organs of the plant, as might be deduced from the experiments on rates of respiration of nodules.*

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PHOTOREACTIVE PIGMENTS IN FLAGELLATES

Chromoprotein Pigments of Some Cryptomonad Flagellates

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THE cryptomonad flagellates are a little known group of organisms comprising both pigmented and apochlorotic forms. The pigmented forms are usually blue-green, brown, purple or red in colour and are capable of photosynthesis. Until very recently, nothing was known of the pigments responsible for these colorations—the only information on record before the present work* being a personal communication from Haxo and Wolken to Provasoli†, that *Rhodomonas lens*, a red cryptomonad,

contains a phycobillin-like pigment. The present communication describes water-soluble chromoprotein pigments from two blue-green cryptomonads, *Cryptomonas* sp. and *Hemiselmu virescens*, and a brown representative, *Cryptomonas ovalis* var. *palustris*. *Cryptomonas* sp., kindly supplied by Prof. E. G. Pringheim, was examined in 1953. This organism could only be grown in soil-water medium and was not available in sufficient quantity for more than the measurement of the absorption spectra of whole cells and crude extracts.

More extensive measurements have been made on the pigments of two other cryptomonads. *Hemiselmu virescens* obtained from Dr. Michael Droop, was grown on the synthetic medium 'DC' (ref. 4). Dense growth was obtained using light intensities of 1,000–1,500 lux at a temperature of 18° C. Cultures were grown for twenty days in 5 litre Fernbach flasks containing 1.5 l of medium. Optical densities of 2.5 were obtained by aerating the cultures.

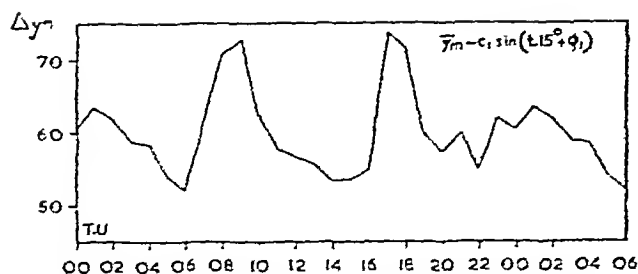


Fig. 1 Variations in $\Delta y_m = y_m - c_1 \sin(15t + \phi_1)$

- (2) that the 12, 8 and 4.8-hr periods have about the same amplitude and the same annual variation, (3) that the amplitude of the fourth harmonic is smaller in winter as compared with the other harmonic terms

However, harmonic analysis carried out on data for months taken individually shows that for the period of 1956-58 the winter maximum is higher for the fifth than for the third harmonic. It so happens that the second and fifth harmonics vary more or less linearly with solar activity, while that of the 8-hr period undergoes a linear increase to a maximum at sunspot number $R=130$ followed by a decrease. The behaviour of the amplitude of the 24-hr harmonic is more difficult to explain as it remains constant up to $R=150$ and then increases with constant high rate up to sunspot maximum. No solar effect is noted for the 6-hr period. It is doubtful whether this component has any physical significance.

Data, complete calculations and results will be published elsewhere.

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Temperatures in Polar Ice Caps

DECREASE in temperature with depth which was first observed by Sorge¹ in the top 20 m of ice at Eismitte in Greenland has since been confirmed for much deeper strata there^{2,3} and in Antarctica^{4,5}. Sorge thought that the negative temperature gradient could have been created by a secular rise in air temperature. Independent evidence exists for such a trend in Greenland but not in Antarctica⁶. Moreover, the much greater depth to which a steady decrease in temperature in the ice has now been traced would require a surface warming extending over very long periods. In these circumstances it seems necessary to consider first the effects of the warming of the ice-cap surface connected with the decrease in its height during the outward movement of the ice. By geometrical reasoning Robin⁷ deduced that in the absence of heat conduction this movement (of velocity v) coupled with a net surface accumulation \dot{z} leads to the temperature gradient:

$$\gamma_1 = -\dot{z}/v \quad (1)$$

where α is the surface slope and v the vertical gradient of the annual mean air temperature along the ice cap surface. A more complete treatment of the problem, taking into consideration heat conduction as well as advective temperature changes now shows the relation (1) to have a deeper significance.

The fuller treatment rests on the fact that, except near obstructions and the fringes of the ice cap, the

temperature gradients in the ice must be uniform over distances one or two orders of magnitude larger in the direction parallel to the surface ('horizontal') than normal to it ('vertical'). As a result the horizontal gradient does not contribute to the change of temperature with time, and when a co-ordinate system moving with the ice in the layer of annual mean surface temperature is considered the problem to be solved reduces to one of linear conduction. Due to net accumulation, the ice is continually moving downward while at the same time moving outward from the centre of the ice cap almost as a block, with the maximum shear concentrated close to the bottom of the ice⁸. Apart from the frictional heat released there, the horizontal movement of the ice then makes itself felt only by an increase in surface temperature with time. This constitutes the upper boundary condition of the problem which is governed by the relation

$$K \frac{\partial^2 T}{\partial z^2} + v \frac{\partial T}{\partial z} - \frac{\partial T}{\partial t} = 0 \quad (2)$$

where T is the temperature, z the depth, K the thermal diffusivity, and v the vertical velocity of the ice, equal near the surface to the net accumulation.

For the semi-infinite solid the solution of (2) for constant vertical velocity v and a constant rate of surface temperature change \dot{z} ($\dot{z} = \dot{z}$) has been given by Benfield^{9,10} who was concerned with the reverse process of cooling of rocks subject to lifting and denudation. For an ice cap with an initial linear temperature profile (of gradient A) the temperature gradient as function of depth z and time t is:

$$\gamma_2 = A \frac{1}{2} \left(1 + \frac{\dot{z}}{v} \right) \left[\operatorname{erfc} \frac{x - vt}{(4Kt)^{1/2}} + 2 \left(\frac{t}{-K} \right)^{1/2} \exp \left(-\frac{(x - vt)^2}{4Kt} \right) - \left\{ 1 - \frac{v}{K} (x - vt) \right\} \exp(vx/K) \operatorname{erfc} \frac{x + vt}{(4Kt)^{1/2}} \right] \quad (3)$$

It is of interest that independently of the initial gradient A the expression (3) reduces to Robin's form (1) not only for $K \rightarrow 0$ (vanishing heat conduction) but also for any K when $t \rightarrow \infty$. This is linked with the fact that the only linear solution of (2) has the form¹¹

$$T = \dot{z}(t - x/v) \quad (4)$$

Numerically it is found that with conservative assumptions ($A=0$, $K=38 \text{ m}^2/\text{year}$, $\dot{z}=5 \times 10^{-4} \text{ C/year}$ corresponding to $V=10 \text{ m/year}$, $\alpha=5 \times 10^{-3}$, $\dot{z}=1^\circ \text{C}/100 \text{ m}$, $v=10 \text{ cm/year}$) 5×10^3 years or a movement of 50 km suffice to create negative temperature gradients varying only in the range 77 per cent and 51 per cent of the limiting value (1) of $-0.5^\circ \text{C}/100 \text{ m}$ between the surface and 400 m depth. These gradients are of the order of those observed^{2,3}. A systematic investigation of (3) for other values of its parameters is under way.

The existence of the limiting gradient (1) is due solely to the vertical movement of the ice. Without this the temperature gradient has the form¹²:

$$\gamma_2 = -\dot{z}(t/K)^{1/2} 2 \operatorname{erfc} (x/(4Kt)^{1/2}) \quad (5)$$

which for any finite depth z increases indefinitely as $t \rightarrow \infty$. This makes it doubtful as to whether without vertical motion the assumption of steady heat-flow conditions from the start⁴ can be justified for this problem.

In the uppermost layers of the ice complications arise from the variation of density with depth, while lower down a decrease in the vortical velocity may have to be taken into account. These effects are now being studied by means of numerical integrations, on the digital computer *Csiris* at the University of Melbourne, which will also facilitate the introduction of a finite ice thickness and of more complicated boundary conditions, equivalent to combinations of climatic change and irregular ice movement.

This work was suggested by Dr P. Loewe and has had the benefit of his advice as well as that of Mr Malcolm Mellor and Prof J. C. Jaeger.

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Two Cases of Triple Fission of Uranium-235

TSEEN et al.¹ pointed out for the first time in 1946 the possibility that uranium 235, when bombarded with thermal neutrons may sometimes divide into three fragments, two heavy and the other one with a mass of around 32. The same kind of event has also been seen by others² but in other cases it was not observed.³

We have found two cases (Figs 1 and 2) among a series of photographic plates loaded with enriched uranium that were irradiated in the thermal column of reactor BR 1 at Mol in Belgium, in these plates we looked for the light particle which in some cases is omitted during uranium fission⁴ but in these two events from their aspects and type of ionization, it was clear that the third track could not be an alpha particle. These facts are in accord with results

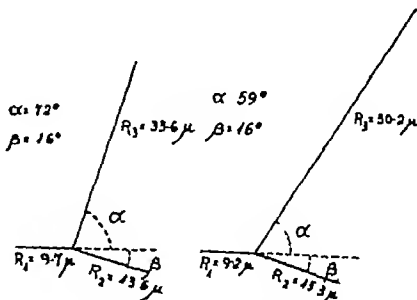


Fig 3

Fig 4

Figs. 3 and 4. Scheme in space of the ranges and angles of the two triple fission events.

obtained by Carvalho of the Centro Brasileiro de Pesquisas Físicas (private communication), who has found ternary fissions giving a light fragment of mass greater than 4 in studying the photo-fission of uranium 238 by 15 MeV photons. We have checked that each of these events lies in its own plane as would be expected since they were produced by thermal neutrons. Figs 3 and 4 show the arrangement of these events in their own planes. By application of the laws of conservation of mass and momentum the mass and energy of each fragment have been evaluated.

To dismiss the possibility that the process was due to ordinary fissions in which one of the two heavy fragments has collided with nuclei of the emulsion we have checked each event by calculating the factors

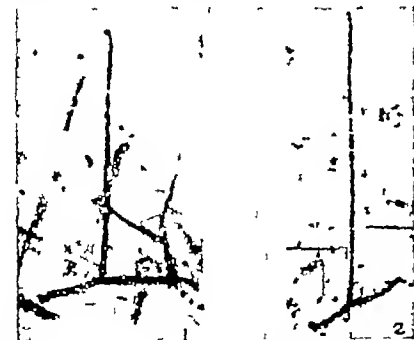
$$a = \frac{M_1}{E_1} = \frac{\sin(\beta + 2\alpha)}{\sin \beta} \quad (1)$$

$$b = \frac{E_2}{E_1} = \frac{\sin^2 \alpha}{\sin \beta \sin(\beta + 2\alpha)} \quad (2)$$

in which M_1 is the mass of the fragment which is supposed to collide with the nuclei E_1 and E_2 are the respective energies of those particles after the collision, α and β are the angles in Figs 3 and 4. M_1 can only be the mass of one of the nuclei contained in the emulsion (hydrogen, carbon, nitrogen, oxygen, bromine, silver and uranium) and these possible values when substituted in (1) will give the allowed values of M_1 . We know that the masses remain between 65 and 170 a.m.u., and in this way we can eliminate those which do not fulfil that condition. We calculated the energy E_1 for the nuclei the masses of which fulfil condition (1) by means of the range-energy curve⁵, from these values and equation (2), we found the possible energy for the fission fragment E_2 , which must remain between 30 and 130 MeV (ref 3). As in our two cases neither event fulfilled these conditions we must conclude that we were actually confronted with two fissions of U 235 produced by thermal neutrons.

In Table 1 our results are compared with those of other workers.

These three fissions were found among 350 000 ordinary binary fissions which have been observed so far, but we are proceeding with the examination of



Figs. 1 and 2. Photomicrograph of two triple-fission events found in uranium-235 loaded plates irradiated with thermal neutrons.

TABLE 1

| Author | M_1 (amu) | M_2 (amu) | M_3 (amu) | E_3 (MeV) | E_{total} (MeV) |
|------------------------------|----------------|----------------|----------------|----------------|----------------------|
| Tsien <i>et al</i> (ref 1) | 127 ± 13 | 77 ± 8 | 32 ± 5 | 47 ± 2 | 162 |
| Perfilov (ref 2) | 62 | 113 | 60 | — | — |
| | 127 | 77 | 32 | — | — |
| Wollan <i>et al</i> (ref 5)* | 133 | 89 | 14 | 110 ± 20 | 243 |
| Dutta (ref 2) | 166 | 43 | 30 | — | 200 |
| Our observations | 150 ± 13 | 74 ± 13 | 12 ± 2 | 35 ± 7 | 166 ± 33 |
| | 169 ± 13 | 55 ± 13 | 11 ± 2 | 40 ± 10 | 187 ± 36 |

Calculated by us using the observations published in ref 5

the plates. Naturally, owing to the very low probability of this phenomenon, our measurements cannot be of high accuracy.

We thank the staff of CEN, of Mol, and especially Mr Beets for his assistance and for helping with the radiation and development of plates used in this investigation. We are also very grateful to the microscopists of our laboratory, Miss Amelia Agustín and Miss Paz Gutiérrez, for their patient collaboration in the scanning and measurement work.

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Current Fluctuations in the Oxide Cathode

DURING some work here on the relation between the conduction and emission mechanisms in the oxide cathode (assumed an excess electronic semi-conductor) we have come across slow but marked fluctuations in the values of both currents when these were measured simultaneously for certain values of the field applied to the anode. Further, over the range of temperature explored, a threshold at about $1,100^\circ\text{K}$ was indicated, which is well above the temperature at which 'p' type conduction has been suspected, generally, the current fluctuations become more and more compensatory in the sense that an increase in one occurs simultaneously with a decrease in the other, till at $1,250^\circ\text{K}$, the marked field periodicity shown in the diagram takes place. Above this temperature, the fluctuations are much larger for certain field values and the correlation less pronounced, but the general character of the form of the curves is maintained.

The experimental arrangement involved the insertion of three platinum probes into the barium oxide/strontium oxide matrix (approximate equimolecular proportions) between which the conduction current was measured, these served as cathodes and supplied the emission current to a spiral nickel anode which surrounded them. As is well known to users of these emitters, their past history is important when trying to explain their behaviour under any particular set of conditions, in the present instance, thermal activation by flashing at progressively higher and higher temperatures between 980°K and $1,400^\circ\text{K}$.

for various times was carried out and measurements of (conduction) drift recorded before a quasi-stable equilibrium was established. In order to disturb this as little as possible, it was decided to take 'spot' readings throughout all the subsequent simultaneous measurements of conduction and emission currents.

The current as shared by the emission and conduction processes is furnished by those electrons, which, through activation, either thermally or by drawing space current, or, using both techniques, pass from the impurity-level into the conduction band of the oxide, in this case the impurity-level consists of the excess barium atoms which are held substitutionally at vacant oxygen lattice sites. It would be expected on simple grounds that the division of the available electrons would be a function of the applied fields, the impedance of the respective paths (along and perpendicular to the emitter) and the mobilities. In such a complicated situation as exists in the matrix when the fields are crossed as in the present measurements the smooth variation which might otherwise be expected, gives rise to the series of maxima and minima recorded at specific field values. At high fields there can even be reversal of direction (also facilitated by working at higher temperatures). In the case of the conduction current the envelope of the maxima falls and then rises, that of the minima continually falls. This strange behaviour may be attributed to various causes. In order that there may be flow in and out of the solid it is generally held that the electrons have to pass through or over the crystallite boundaries surrounding the pores; these may be contaminated with a layer of barium; also the path through the pores will not be an easy one in

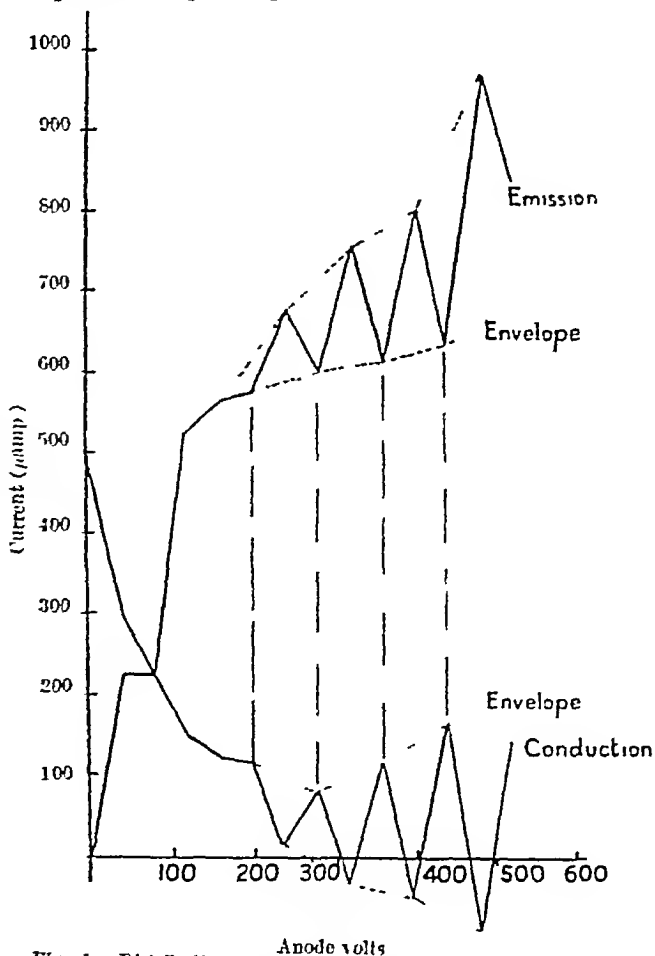


Fig 1 Distribution of conduction electrons in excess semi-conductor BaO/SrO at 1250°K

the presence of an electron space charge and we have consequently very different and variable impedances throughout the motion. The existence of a fluctuating space charge combined with one produced by positive ions (produced in the electrolysis) could give fluctuating space charge clouds when recombination takes place in the rather specialized geometrical structures involved. These effects would be more pronounced as the temperature increased to the point at which ionic conduction became important. One can visualize a fluctuating effect of this kind arising through lack of equilibrium in the intervals between observations, (of the order of a few seconds) thus involving a decay with a time constant of the same order of magnitude; this picture is consistent with results obtained under pulsed conditions (μsec pulses) by ourselves and also by other workers in this field.

We hope to publish these results in full at a later stage of the work.

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Radar Echoing Area Polar Diagrams of Birds

As part of an investigation into the sources of unidentified radar point echoes, or 'angels', we have been measuring the echoing area polar diagrams of birds using a high resolution X band radar. This radar, which is horizontally polarized, is capable of measuring equivalent echoing areas as low as 2×10^{-4} sq metre with an accuracy better than ± 1 db and of detecting even smaller radar targets. Each bird in flying position but with wings closed and legs retracted, was fixed to a nylon cord. The nylon cord was held vertically between ground and an aerial line suspended between two towers. Typical azimuth polar diagrams for three birds are shown in Fig. 1. Each pattern was made with the aerial of the radar fixed in elevation and bearing, while the bird was rotated in bearing about a point at the centre of its body. The rate of rotation of the specimen and the time constant of the equipment provide a smoothing factor over approximately 10° in azimuth. The smoothing factor provides satisfactory 'averaging' and removes the fine lobe structure. The spacing between radar and bird was chosen to give an even illumination of the rotating bird. The birds were placed at heights which coincided with the radar aerial elevation angle of approximately 18° , an arrangement which ensured a low side lobe background and consequently optimum radar sensitivity. The bird echoing areas were evaluated by comparison with standard metal spheres.

The echoing area polar diagrams, taken in azimuth, for a domestic pigeon (*Columba domestica*), a starling (*Sturnus vulgaris*) and a house sparrow (*Passer domesticus*) are shown in Fig. 1. Only half the diagram is shown, the other portion covering bird aspects from 180° to 360° in azimuth, is a mirror image of the diagram in Fig. 1. Maximum echoing areas occur between 65° and 115°

Table 1 MAXIMUM AND MINIMUM ECHOING AREAS

| Specimen | Aspect | | |
|---------------|----------------------|----------------------|----------------------|
| | Broad-side (sq m) | Head (sq m) | Tail (sq m) |
| Pigeon | 1.0×10^{-4} | 1.1×10^{-4} | 1.0×10^{-4} |
| Starling | 2.5×10^{-4} | 1.8×10^{-4} | 1.3×10^{-4} |
| House sparrow | 7.0×10^{-4} | 2.5×10^{-4} | 1.8×10^{-4} |

in bearing that is when the birds are broadside-on to the radar. The minimum areas coincide with tail on and head-on positions of the bird with respect to the radar beam. Principal maximum and minimum echoing areas for the three birds are given in Table 1.

Measurements were then made on the effect of the feathers and the contribution of the wings to the echoing area. A pigeon was plucked the feathers and body being measured separately. The echoing area of the feathers, packed into a thin polythene bag was approximately 5×10^{-4} sq metre when viewed from the direction presenting maximum area to the radar. The plucked bird was also measured and it produced a similar diagram to that shown for the bird in plumage. A rook (*Corvus frugilegus*) was measured in the broadside position and gave a peak echoing area of 2.5×10^{-4} sq metre. The bird, with outstretched wings was then fixed with its body parallel to the nylon cord and peak echoing areas of back and belly views were measured. These outspread wing views of the bird were similar in peak echoing area and differed from the broadside measurement by less than 5 per cent.

We gratefully acknowledge the help of our colleagues at the Royal Aircraft and Royal Radar Establishments and to Mr I M Hunter, of the Royal Aircraft Establishment who proposed the experimental measuring system.

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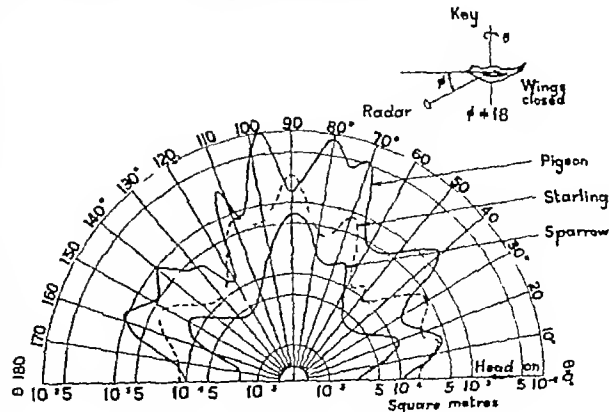


Fig. 1 Echoing area polar diagrams in azimuth at X band

CRYSTALLOGRAPHY

Intermolecular Distances and Diamagnetic Anisotropy in Crystals as Measures of the Polarity of Benzene and Borazole Substituents

THE structures of 1,3,5-trichlorobenzene and of B₃N₃H₃Cl₃ have been analysed, and although not isomorphous they are in many respects very similar^{1,2}. Both are nearly layer structures. The direction cosines of the molecular axes *L* (along one Cl-Cl direction) *M*, and *N* (normal to the ring) are as follows (at 20°C)

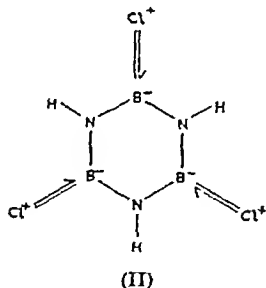
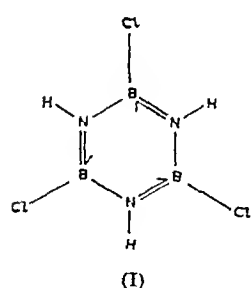
| | | | | | | |
|--|----------------------|---------|----------------------|---------|----------------------|---------|
| | <i>L_a</i> | +0.0368 | <i>M_a</i> | -0.9070 | <i>N_a</i> | -0.4232 |
| C ₆ H ₃ Cl ₃ | <i>L_b</i> | +0.9965 | <i>M_b</i> | +0.0058 | <i>N_b</i> | +0.0838 |
| | <i>L_c</i> | +0.0758 | <i>M_c</i> | +0.4193 | <i>N_c</i> | -0.9021 |
| | <i>L_a</i> | 0 | <i>M_a</i> | -0.8862 | <i>N_a</i> | -0.4632 |
| B ₃ N ₃ H ₃ Cl ₃ | <i>L_b</i> | 1 | <i>M_b</i> | 0 | <i>N_b</i> | 0 |
| | <i>L_c</i> | 0 | <i>M_c</i> | +0.4632 | <i>N_c</i> | -0.8862 |

The intramolecular distances are

| | |
|---|--|
| C ₆ H ₃ Cl ₃ | B ₃ N ₃ H ₃ Cl ₃ |
| Mean Cl-Cl 5.354 Å | Mean Cl-Cl 5.498 Å |
| Mean Cl-C 1.711 Å | Mean Cl-B 1.753 Å |
| Mean C-C 1.387 Å | Mean B-N 1.415 Å |

Both molecules are plane to within the limits of experimental error, and the rings are regular hexagons to within 0.04 Å in bond-lengths, and 2.5° in bond-angles.

Coursen and Hoard² have argued, on the basis of the above bond-lengths, that B trichloroborazole shows no evidence for any reduction in the double-bond character of the ring in favour of a large contribution from a structure of type II such as was suggested by Wiberg³ and supported by the spectral studies of Rector, Schaeffer and Platt⁴.



If the intermolecular distances are compared, however, it will be seen that in spite of the close similarity in the structures, there is an unexpected difference in the nearest Cl-Cl', Cl-H' and H-H' distances in the two structures.

| | | |
|--|--------|------------------------------|
| C ₆ H ₃ Cl ₃ | Cl-Cl' | 3.628, 3.650, 3.749, 4.042 Å |
| | Cl-H' | 2.963, 2.968, 2.984 Å |
| | H-H' | 2.647 Å |
| B ₃ N ₃ H ₃ Cl ₃ | Cl-Cl' | 4.020, 4.054, 4.247, 4.301 Å |
| | Cl-H' | 2.484, 2.524 Å |
| | H-H' | 2.810 Å |

The implication of this would seem to be that both Cl and H atoms are charged in the trichloroborazole molecule, with a corresponding reduction in the double-bond character of the ring, in spite of the short B-N distance, that is, that there is a larger contribution from (II) than would be expected on the basis of intramolecular distances only.

That the borazole ring in this structure has considerably less double-bond character than has the benzene ring is also supported by measurements of the

diamagnetic anisotropy, made by Mrs E. W. Toor⁵. These lead to a molecular anisotropy of $\Delta K = 18 \times 10^{-6}$ as compared with 60×10^{-6} for benzene. The corresponding measurements on C₆H₃Cl₃ have not been made, but those on the isomorphous C₆H₃Br₃ give $\Delta K = 47 \times 10^{-6}$. From this it would seem that there is some reduction in the aromatic character of benzene also on substitution. The only other partially substituted benzene derivative for which both an accurate structure analysis and diamagnetic susceptibilities are available is 1,4-C₆H₄O₂, for which $\Delta K = 40.5 \times 10^{-6}$. It would be very desirable indeed to have more measurements on such compounds and also to be able to compare intermolecular distances in cases where the packing seems to depend more on Cl-Cl', H-H' and Cl-H' than on C-C', C-Cl' or C-H' distances.

It may even be possible to determine whether substituent atoms are charged positively or negatively, by forming mixed crystals with compounds of known electronic constitution and observing the resulting intermolecular distances.

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Influence of the Size of the Halogen Atom on the Difference between Lattice Constants of Copper dipyridine dichloride and dibromide

In verifying the validity of Peyron's and Torgensen's rule in organic halogen complexes of copper, Serator¹ found that a compound intermediate between CuPy₂Cl₂ and CuPy₂Br₂ exists. Crystallographic studies of these compounds were based on the crystal structure of CuPy₂Cl₂, which has been solved by Dunitz². We have solved the crystal structure of the bromine derivative³.

CuPy₂Br₂ and CuPy₂Cl₂ have very similar structures. Both are monoclinic (space group *P*2₁/*n*) with octahedral co-ordination of halogens and nitrogens around copper atoms, the co-ordination octahedra, with shared edges, are oriented in the direction of the growth axis of the needle-formed crystals. The difference between these compounds lies in the position of halogens, the orientation of the symmetry elements with respect to the lattice vectors and, of course, in the values of the lattice constants (Fig. 1).

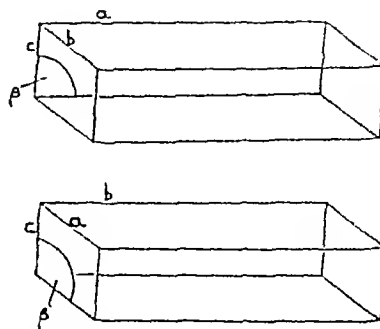


Fig. 1. A comparison of the lattice constants of CuPy₂Cl₂ and CuPy₂Br₂. Top, CuPy₂Cl₂, *P*2₁/*n*, *a*, 17.00 kX, *b*, 8.50 kX, *c*, 3.87 kX, β , 91°52'. Bottom, CuPy₂Br₂, *P*2₁/*n*, *a*, 8.30 kX, *b*, 17.72 kX, *c*, 4.04 kX, β , 96°.

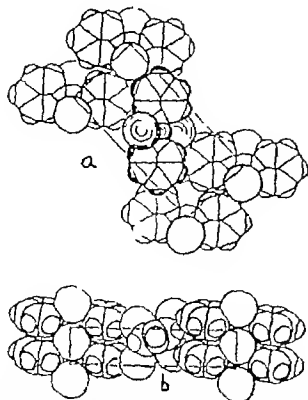


Fig. 2. (a) Arrangement of the molecules of CuPy_2Br_2 in the projection along the c -axis. (b) Projection of the same structure perpendicular to the c -axis

When the lattice constants are compared it is interesting to note that the substitution of bromine lengthens the largest and smallest lattice constants but shortens the intermediate one. We have observed a similar effect with copper ethylenediamine dichloride and dibromide for which $a=6.81$, $b=5.78$, $c=8.32$ kX, $\beta=93^\circ 50'$ and $\alpha=7.00$, $b=6.04$, $c=8.29$ kX, $\beta=96^\circ 72'$ respectively.

The differences can be explained by the use of the van der Waals radii for atoms and groups of atoms. Fig. 2a illustrates the arrangement of the molecules in the crystal structure of CuPy_2Br_2 in projection along the c -axis. Fig. 2b the projection of the same structure perpendicular to the c -axis. Fig. 2a shows that the structure is close packed with the pyridine ring close to the halogens of neighbouring molecules. The angle between the molecule axis and the longest basic vector is $\varphi=43.5^\circ$ in $\text{Cu}_2\text{Py}_4\text{Br}_4$. By substitution of a bromine for a smaller chlorine, space between the pyridine rings and halogens is freed, and in order to conserve close packing it is inevitable that the neighbouring molecules will close up and that the molecular axis will change its alignment. (In the case of the chlorine derivative the value of this angle is $\varphi=46.4^\circ$). As a consequence the longest lattice distance is shortened and the middle one lengthened.

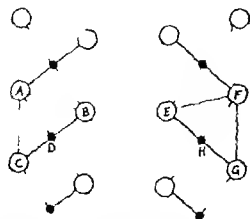


Fig. 3. Arrangement of halogens and copper atoms. Left: $\text{Cu}_2\text{Py}_4\text{Cl}_4$. $AB=3.75$ kX ($2R_{\text{Cl}}=3.60$), $AD=3.03$ kX ($2R_{\text{Py}}=2.28$), $AC=3.87$ kX ($D_{\text{Cu}}=5.70$), $2R_{\text{Cl}}=3.60$. Right: $\text{Cu}_2\text{Py}_4\text{Br}_2$. $EF=3.06$ kX ($2R_{\text{Py}}=3.00$), $EH=2.44$ kX ($R_{\text{H}}=3.17$ kX), $FG=4.04$ kX ($2R_{\text{Br}}=3.00$, $D_{\text{Cu}}=5.70$). For construction the following data have been used: covalent radii $r_{\text{Cu}}=1.14$ kX, $r_{\text{Cl}}=0.99$ kX, $r_{\text{Br}}=1.30$ kX, van der Waals radii $R_{\text{H}}=1.95$ kX, $R_{\text{Cl}}=1.80$ kX, thickness of aromatic molecule $D_{\text{Py}}=5.70$ kX.

The causes which influence the value of the lattice constant c are illustrated in Figs 2b and 3. In the case of the chlorine derivative $c=3.87$ kX, which is nearly equal to the thickness of the aromatic molecule (3.70 kX) whereas twice the van der Waals radius of chlorine is only 3.60 kX. In the case of the bromine derivative, however $c=4.04$ kX, which is greater than the thickness of the aromatic molecule but is nearly equal to twice the van der Waals radius of bromine. The lattice constant c of the chlorine derivative is thus defined by the thickness of the aromatic molecule, whereas in the case of the bromine derivative it is the van der Waals radius of bromine. It is probably the tilting of the plane of pyridine rings relative to the basic vector c that affects the value of the monoclinic angle.

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RADIOCHEMISTRY

Effect of Gamma-Radiation on the Synthesis of Methanol over Zinc Oxide

THE semiconducting oxides for example zinc oxide, nickel oxide and vanadium pentoxide form an important class of heterogeneous catalysts. It is well known that the catalytic activity of these materials is closely linked with their ability to act as either electron sources or sinks. Since radiation is able to modify the electrical properties of semiconductors, it is to be anticipated that it will also have a significant effect on the catalytic activity of the metal oxides.

The reaction chosen for study in the present work was the synthesis of methanol from carbon monoxide and hydrogen over a zinc oxide catalyst. At temperatures where the reaction proceeds at a reasonable rate the equilibrium favours carbon monoxide and hydrogen. The standard free energy of the reaction becomes negative only below 150°C , whereas the reaction is rapid only above 350°C . It is apparent that if radiation were capable of activating the catalyst at lower temperatures, the reaction would be greatly facilitated. Since it was desired to induce reaction at low temperatures where the equilibrium is favourable for the synthesis of methanol it was not necessary to use the high pressures 200 atm. of the industrial process. A 3:1 mixture of hydrogen and carbon monoxide was used at a total pressure of 1 atmosphere, and the reaction vessel and circulating system were constructed of glass.

Of the catalysts investigated (both pure zinc oxide and zinc oxide admixed with chromium oxide) only one was active at temperatures below 250°C , and this was used in studying the effect of radiation. The catalyst was prepared by the decomposition of zinc carbonate in air at 300°C . The zinc carbonate was made from 'AnalaR' materials.

The reaction vessel was in the form of an annular cylinder with the tube containing the source of radiation along its axis so that the catalyst could be

CHEMISTRY

Concentration by Ion Flotation

It has been found possible to concentrate inorganic ions from aqueous solutions, even if very dilute, by a flotation technique. The principle depends upon the use, as a collector, of a surfactant ion, of charge opposite to the ion to be floated. The surfactant must be introduced in such a way that it exists as a simple ion, not as a micelle. This means that the concentration of the surfactant should not be allowed to exceed the critical micelle concentration, but, also, as soaps have a tendency to age on standing, the soap should be freshly prepared in alcoholic solution, or, preferably, dissolved in a non-polar solvent, such as petrol ether, which is evaporated off, followed by immediate solution in ethyl or isopropyl alcohol. By bubbling a gas, usually air, into the solution, through a fine gas distributor, an extended air-water interface is produced. The surfactant tends to concentrate at the bubble, so orientated that the polar head carrying the charge is on the water side of the water-air bubble interface. There is an attraction between it and the charged ion in the solution, which seems more marked if the ion is polyvalent. The collector and ion are carried to the surface by the bubble, where a froth or scum is produced, depending on whether there is excess surfactant or not. As the froth drains and the bubbles break, the concentration of the collector-ion product increases to form, ultimately, a characteristic scum, often coloured, of insoluble soap, which can be easily removed.

Provided the charge on the surfactant ion is opposite to that of the ion to be floated, the nature of the surfactant is not critical, though some specificity has been noted in that some ions are better floated by longer chain compounds, as these produce more insoluble soaps with the ions. For floating anions, which include the complex metal anions, the surfactant must be cationic and could be a quaternary ammonium salt, one radical of which is about C_{16} or above, such as didodecyl-dimethyl ammonium chloride or lauryl pyridinium chloride, or it could be an amine salt such as dodecylamine chloride. The quaternary ammonium salts have the advantage that being salts of strong bases they can be used in alkaline solution. For floating cations, the collector must be anionic and could be sodium laurate, palmitate or the sodium salt of sulphated fatty alcohols. As the fatty acid soaps are hydrolysed in acid solution, they are best reserved for alkaline solution, and for slightly acid solutions, the sodium salts of alpha sulphaalkyl acids are suitable.

The technique is very wide in its applications. Among others, the following anions have been floated: ferrocyanide, ferricyanide, cobalticyanide, platinum-chloride, fluoroborate, uranyl sulphate anion, chromate, vanadate, molybdate, argentocyanide, silicate, polythionate. The following cations have been floated: cupric, cuprammonium, nickel, nickelammonium, cobalt, cobaltammonium, aluminium, zinc, manganese, calcium, barium, strontium, vanadyl, uranyl, thorium.

By introducing the collector in small doses, the technique allows for selective concentration, the most strongly adsorbed ions being concentrated in preference to the less strongly adsorbed. A striking example of this is the separation of cobalticyanide ions the

irradiated at the highest possible intensity. With the 380-curie cobalt-60 source in the irradiating position, the catalyst received a dose of 2.5×10^{19} eV gm⁻¹ hr⁻¹. Apart from the reaction vessel, furnace and gas pre-heater, the apparatus was outside the radiation shield. Premixed carbon monoxide and hydrogen were circulated by an all-glass circulating pump, and the resulting products were condensed in traps maintained at -195°C .

Analysis of the products showed that besides methanol, methane and carbon dioxide were also formed. The selectivity of the catalyst for the synthesis of methanol was improved by working at temperatures below 260°C . The effect of radiation was examined by introducing the cobalt-60 source during a thermal run.

No effect of radiation was observed at temperatures above 250°C or below 175°C , the results of three experiments between these temperatures are shown in Table 1.

Table 1

| Temp ($^\circ\text{C}$) | Rate (methanol) ml | | NTP/lhr Difference | <i>G</i> (molecules of methanol per 100 eV) |
|---------------------------|--------------------|------------|-----------------------|--|
| | Unirradiated | Irradiated | | |
| 223 | 0.18 | 0.24 | 0.06 | 0.58 |
| 204 | 0.103 | 0.200 | 0.097 | 0.83 |
| 201 | 0.036 | 0.144 | 0.108 | 1.01 |

The value of *G* is calculated from the number of methanol molecules per 100 eV of γ -energy absorbed in the zinc oxide of weight 11.2 gm. The effect of radiation is shown to be quite small and is masked at higher temperatures. Since the lower temperature limit for the effect of radiation is very close to that for normal thermal catalysis, it is apparent that irradiation of the catalyst does not greatly influence the normal reaction mechanism. Thus participation of holes seems unlikely, since these are not present in unirradiated zinc oxide, which is an *n* type semiconductor.

The amount of carbon dioxide formed also increased under irradiation, but to a lesser extent than the yield of methanol. The maximum value of *G* obtained for carbon dioxide was 0.56 at 201°C .

There seems little doubt that the observed increase in the rate of formation of methanol over irradiated zinc oxide may be ascribed to direct participation of electrons freshly produced by radiation. At this temperature, both hydrogen¹ and carbon monoxide² are adsorbed as ions, so that energetic electrons may be expected to influence adsorption and reaction rates. The value of *G* obtained is consistent with this view if we assume that about 20 per cent of the electrons induced by irradiation are effective in promoting catalytic reaction and that about 20 eV are required to free one electron.

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¹ Gubokawa, Y., and Toyama, O., *J. Phys. Chem.*, **60**, 833 (1956).

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concentration of which is of the order of mgm./l from a solution containing anionic uranium, the maximum concentration being approximately 1 g/l. This case is interesting, because in the uranium industry in South Africa, cobalticyanide ions are adsorbed on the anion exchangers, which are used to concentrate the uranium anions, and the adsorption is so powerful that they cannot be eluted off, thus constituting a resin poison. It is the same more powerful forces that are responsible for the preferential flotation of the cobalticyanide ions. Thus there is a superficial parallel between this new technique and that of ion-exchangers, the difference being that in ion-exchange the adsorption is at a stationary solid-liquid interface, whereas in ion flotation, the adsorption is at a mobile liquid gas interface.

There are certain precautions that have to be taken. First, it must be stressed that the collectors must be in the molecular state and not in the aggregated micellar form. This is important, because if micelles should be present, the ions will be adsorbed on them, producing stable colloids that have no tendency to float and are not easily disintegrated. This is why it is advisable to use freshly prepared solutions of the collector. Some apparent failures in applying the technique were traced to the use of solutions that had been standing for a long time. As the critical micelle concentration is very much less for the longer chain surfactants it is advisable to use the shortest ones that will give a sufficiently insoluble soap. A second precaution that must be taken arises from the fact that should the froth or scum be allowed to return under the surface, there is a danger of it being peptized by excess surfactant to form a stable colloidal solution. This is because larger aggregations of free soap have different properties from single molecules adsorbed at an interface. This difficulty is avoided by ensuring that the bubbles are very small and not violent enough to disrupt the surface froth vigorously, and also by the continuous removal of the froth as it is formed. Technically, this will present no difficulty. The temperature must not be allowed to rise above the melting point of the soap that is formed, as if it does a liquid film is formed which breaks the froth and introduces unnecessary problems in collection.

In recovering values from solution there still remains the problem of processing the ion soap product formed. Each case would need to be considered on its merits. If the product is much more valuable than the reagent, it could be recovered by ignition and destruction of the collector. A second method would involve the solution of the soap in alcohol and the precipitation of an insoluble salt of the metal ion regenerating the soap. An example of this is the solution of the quaternary ammonium ferrocyanide soap in absolute alcohol to which alcoholic potassium hydroxide is added. Potassium ferrocyanide is precipitated and the quaternary ammonium hydroxide remains in solution and can be reconverted to the chloride by addition of hydrochloride. Another method is the solution of the soap in a non polar solvent such as benzene and an extraction with strong acid. This can be applied to copper laurate. On extraction with hydrochloric acid, cupric chloride enters the aqueous phase and lauric acid remains in the benzene.

Apart from a possible advantage in illuminating a

filtration and the advantage that it offers a new and alternative procedure for separations, the technique has the special merit that it can handle very dilute solutions, concentrations of parts per ten million being by no means the lower limit. This means that in addition to application in the extractive metallurgical field especially when dealing with low grade materials, there are possibilities in the chemical manufacturing industry for purification and in the recovery of wastes or by products. It also has possibilities as an analytical technique, where it would be a convenient way of collecting trace material, or collecting ions from very dilute solution ranging the changes on ligands pH, and choice of that are not easily determined by other means. By ringing the changes on ligands pH, and choice of surfactant collector, a wide range of separations becomes possible. Because it offers a clear-cut means of distinguishing anions from cations and also because it can collect the ions selectively, the technique should offer a useful tool for determining unequivocally, the nature of the chemical species present in kinetic or equilibrium studies. It might also offer a convenient way of collecting samples for geological prospecting based on the sampling of rivers for dissolved metals.

Because ions can be concentrated from very dilute solutions, the recovery of values from the sea can for the first time be considered as an economic possibility. It is recognized that a wide variety of elements exist in the sea albeit in very low concentrations. Hitherto the movement of the large bulk of water has presented an insurmountable obstacle to economic recovery of these elements. In ion flotation, however it is only bubbles that have to be moved and the volume of sea to be stripped can be increased by increasing the depth at which the bubbles and collectors are introduced. It has been calculated based on approximate figures that if a curtain of bubbles is introduced from a pipe 100 m. long, sunk to a depth of 100 m., in an area where a current of 3 knots flows, the quantities of materials in the volume swept by these bubbles in an hour would range from 27,500 kgm. of aluminum, through 50-500 kgm. of copper and 150 kgm. of uranium to 300 gm. of gold. If a reasonable fraction of this could be collected and carried to the surface it might become of economic, if not of strategic, importance. Limited to beaker experiments it has not been possible to work at such dilutions but it has been found possible to collect copper from solutions only 100 times more concentrated than the sea.

There is a possibility of using the technique in reverse to solve some sewage effluent problems, particularly the foaming nuisance of dodecylbenzene sulphonate. The addition of aluminum ions to the solution changes the foam to an easily handled scum, and in the same way, ferrocyanide ions can be used to remove any cationic soaps that may have escaped into effluents.

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Hydrogenolysis of Carbon-Oxygen Bonds in some Aromatic Compounds by Electrolysis

WE have examined the reduction of anthraquinone and 9 10-diacetoxy-anthracene to 9 10-dihydroanthracene and xanthinol to xanthene by controlled potential electrolysis on a mercury cathode in dimethylformamide, phenol being present as proton donor in the experiment on the quinone. We have not previously encountered a report of carbon-oxygen scission brought about by such means.

Anthraquinone gives a small polarographic wave in dimethylformamide at -2.15 V (versus mercury pool anode)¹, which in the presence of phenol (mole ratio 2-15) increases in height and is resolved finally into two waves, each of height equivalent to the addition of two electrons². 9 10-Diacetoxy- and diethoxy-anthracene even in the absence of a proton donor give waves whose total height is equivalent to the addition of four electrons, and in the presence of phenol the total height increases still further^{1,2}. Once any of these compounds is reduced to a derivative of 9 10-dihydroanthracene one would not expect further reduction, since the products contain two unconjugated benzene rings which are not normally reducible at the dropping mercury electrode before the decomposition potential of the supporting electrolyte. A similar situation arises in the polarography of xanthone, this gives a third wave in addition to the two associated with the reduction of the carbonyl group⁴, which increases in height as phenol is added². Moreover, xanthinol gives a reduction wave of potential close to that of the third wave of xanthone.

In order to identify the reactions responsible for these unexpectedly large wave heights, we have electrolysed anthraquinone (1 gm + 10 gm phenol in 400 ml), 9 10-diacetoxyanthracene (0.63 gm in 150 ml), and xanthinol (1 gm in 250 ml), using 0.1 N tetraethylammonium iodide in dimethylformamide as supporting electrolyte. Reduction took place on a stirred mercury cathode whose potential (measured against a small mercury pool reference electrode) was controlled at -2.15 V, for further details of apparatus and technique see ref. 3.

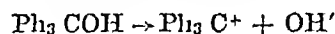
The total consumption of electricity corresponded to the addition of 8-10 electrons to the quinone and 6 to the diacetate. In both cases the current fell less rapidly than exponentially, suggesting that either a slow non-electrochemical reaction intervenes between steps of the reduction, or one of the electron transfer steps is unusually slow.

After the current had fallen to a few milliamperes the solutions were diluted with water and the products extracted with chloroform. In the anthraquinone experiment the extract afforded a 60 per cent yield of 9 10-dihydroanthracene (identified by melting-point, mixed melting-point, and infra-red and ultra-violet spectra), and a 10 per cent yield of a dark purple solid. The latter gave a green solution in hot alcohol, from which purple crystals deposited on cooling. Its infra-red spectrum resembled that of a mixture of anthraquinone and phenol (a donor-acceptor complex?), but its two polarographic waves were at less negative potentials than those of anthraquinone in the presence of 1 molecule of phenol (-0.16 and -0.65 V compared with -0.32 and -0.75 V). The product of reduction of 9 10-diacetoxyanthracene gave a 60 per cent yield of 9 10-dihydroanthracene, identified as before. The product of reduction of xanthinol was identified as xanthene by mp and mixed mp

(recovery 30 per cent, but much of product accidentally lost).

Phenanthraquinone and 1 4-naphthaquinone were also reduced electrolytically in the presence of phenol, the electricity consumption corresponding to the addition of about 10 and 6 electrons respectively. However, in neither case could a definite product be obtained. The material yielded by phenanthraquinone was phenolic, that given by the naphthaquinone oxidized rapidly in the air during working up, so that it was probably also phenolic. It appears therefore that neither of these quinones lost any major part of their oxygen by reduction, in any case with these compounds the large electron uptake can be accounted for by reduction of the aromatic nuclei.

It will be noted that the three compounds found to suffer carbon-oxygen scission can all be regarded as derivatives, or convertible to derivatives, of diphenyl carbinol. Triphenyl carbinol is notable for its ease of reaction with negatively charged ions such as halide, and the reaction often proceeds by prior ionization⁵.



Diphenyl carbinol has a similar but less marked tendency to yield a carbonium ion. Thus the substances now found to lose oxygen by reduction are of the type known to lose hydroxyl ions comparatively readily. However, benzhydrol (diphenyl carbinol) itself shows no wave even in the presence of phenol, evidently the further activation provided by a hydroxy-methylene or an oxygen bridge is necessary for scission of oxygen to be fast enough to be detected polarographically.

The removal of hydroxyl from xanthinol can only be a direct nucleophilic displacement reaction, since the atom from which it is detached is saturated. Hydroxyl or acetate ions could be displaced from the anthraquinone derivatives in the same way once the nucleus had been reduced to the 9 10-dihydro condition. But here there is an alternative dissociation of OH^- or OAc^- from the incompletely protonated dihydroanthraquinone structure. Thus in Fig. 1 ($R = \text{H}$ or OAc)

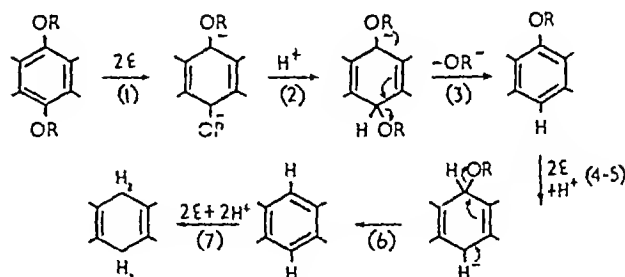


Fig. 1

(for simplicity, charges are shown localized on particular atoms). This alternative is made possible by the existence of the stable intermediates formed in steps (3) and (6). Its feasibility clearly depends on the rates of these dissociations, which in turn will be determined by the structure of the rest of the molecule, it is clearly less in the phenanthraquinone reaction since *ortho* quinonoid structures would be involved, the diphenyl carbinol structure is absent, and the centre ring has less aromatic character than it has in the linearly condensed isomer.

We have observed some loss of oxygen from solvent extracts of coal on electrolytic reduction in dimethylformamide in the presence of phenol, which we

attribute to reactions of the type discussed above, this will be reported elsewhere

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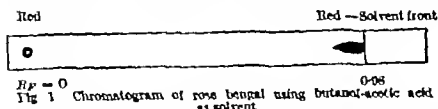
The British Coal Utilization Research Association,
Leatherhead
July 14

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Paper Chromatographic Separation of Components of Rose Bengal Labelled with Iodine-131

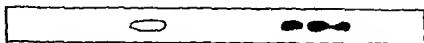
Rose bengal (tetraiodotetrachlorofluorescein) is labelled with iodine 131 is used in medicine to test hepatic function. The most used tests are those of Bland and Nordsyke¹ and Taplin, Meredith and Kade². In both tests it is assumed that the dye, injected endovenously is eliminated only by the liver. Experiments on the elimination of the dye were made with labelled rose bengal supplied by a well known laboratory specializing in radio pharmaceuticals³. The study showed that the elimination curve could be resolved into two exponential curves. This suggests that the dye is not eliminated only by the liver, perhaps because the dye is not a single chemical substance. Stowe, Delprat and Weeks⁴ have directed attention to the fact that the liver only eliminates rose bengal when it has eight halogens, that is when it is the pure chemical compound tetraiodotetrachlorofluorescein.

We attempted to separate the components of the dye by paper chromatography. One-dimensional chromatograms were run using a mixture of butanol and acetic acid (20 per cent) as solvent. Two components were identified, one with R_F zero and one with R_F 0.98 (Fig. 1). By the count-rate the amount of



substance with R_F zero was found to be 18 per cent of the amount of substance with R_F 0.98. The original red colour of the dye usually fades on chromatograms developed with butanol acetic acid. The colour is restored by exposing the strip to ammonia vapour. A parallel chromatogram was run with the same solvent, adding potassium iodide to the rose bengal to calculate the R_F for free iodide, the iodide spot was identified with lead acetate with R_F 0.1. The spot was not radioactive indicating that no exchange took place with the rose bengal.

Ishida *et al.*⁵ using ethanol ammonia as solvent, found an R_F value of 0.60 for rose bengal. We tried a mixture of 25 per cent ethanol, 5 per cent ammonia 1 made up with 70 per cent water as solvent and found that by running the chromatograms and allowing the solvent to drip from the end of the strips, the spot at R_F 0.60 resolved into three red spots, all active (Fig. 2). With this same mixture as solvent an active colourless spot with R_F 0.35 was always found, it is not free iodide, which had R_F 0.05 with the same solvent.



R_F 0.35
Fig. 2 Chromatogram of rose bengal using ethanol-ammonia as solvent

Two-dimensional chromatograms were run with butanol acetic acid and ethanol ammonia. Four active components were found: one colourless and three others with the original colour of rose bengal. Separations by paper column chromatography, with these solvents are being carried out in order to separate the four components for injection and to follow the elimination of each component.

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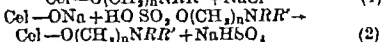
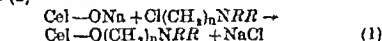
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15 Anion Exchangers Based on Cellulose

A SERIES of anion exchange derivatives of cellulose has been prepared and characterized. The preparative technique was based on the reaction of alkali cellulose with organic halides and sulphates. This is a well known method for preparing cellulose ethers¹, and by choice of suitable reagents produces ion exchangers. A reaction of this type can be represented by equations (1) and (2).



The chloro compound is the most frequently used halide, n being generally 1 or 2 and R and R' being hydrogen or alkyl, aryl etc., radicals.

In the above equations anion exchangers are produced and the alkali cellulose is represented by $\text{Cel}-\text{ONa}$. Whilst the various views on the structure of this adduct need not be discussed here, free alkali is always present in the reaction mixture. Experimental difficulties arise from the competition for the other reacting agent between the alkali cellulose and this free excess alkali. The choice of the most suitable reagent is governed largely by the reactivities of the haloamines and amine hydrogen sulphates. In this work all the reagents were prepared (and purified if necessary) in the laboratory to eliminate side effects introduced by the use of commercial materials. In any event, many of the compounds are not commercially available, and methods had to be developed for their syntheses. In general, this was achieved by reacting the requisite monoalkanolamine with either thionyl chloride to yield the chloroalkyl amine² or fuming sulphuric acid to give the sulphate derivative³.

A series of anion exchangers (1-9) was prepared by reacting alkali cellulose with the following compounds: chloroethylamine (1) chloroethylamine

thylamine (2), chloroethyldiethylamine (3), chloroethyldiisopropylamine (4), and the following hydrogen sulphates aminoethyl (5), dimethylaminoethyl (6), diethylaminoethyl (7), diisopropylaminoethyl (8), di-2 ethylhexylaminoethyl (9)

The following illustrates the preparation of the anion exchanger using chloroamines 20 gm of purified wood cellulose were mercerized with 80 gm of 20 per cent sodium hydroxide solution and to the mixture 50 gm of 50 per cent aqueous chloroethyldiisopropylamine solution was added. The thoroughly dispersed mixture of reagents was heated at 105°C for 60 min, after which it was washed and cycled with acid and alkali. It was finally washed free of excess electrolyte.

A typical reaction employing the sulphate compound was as follows. A 10 gm sheet of cellulose was steeped in a solution of 5 gm sodium hydroxide and 10 gm diethylaminoethyl hydrogen sulphate in 19 gm of water, and heated at 100°C for 60 min. It was then washed and cycled with acid and alkali. Finally, it was washed free of soluble electrolyte.

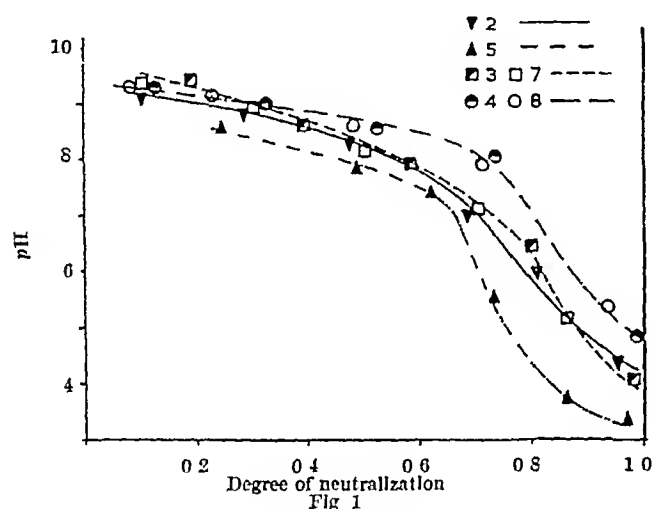


Fig 1

Figure 1 gives the titration curves obtained by the equilibration technique, using hydrochloric acid as the titrant in presence of 0.1N potassium chloride solution. It can be seen that the preparations gave products of varying basicity and exchange capacity. A general feature of the results is the independence of the extent of substitution on the size of the functional group until the ethyl hexyl derivative is reached, which is apparently excluded from the cellulose phase. This is scarcely surprising considering the interstitial spacing of the individual cellulose chains, even after mercerisation of the polysaccharide. Discussion of the swelling must of necessity be incomplete, because of variations in mercerisation, which lead to differences in the breakdown of the crystalline regions of the cellulose. Thus the intracellular capillaries which sorb water by purely physical forces (as opposed to water associated with the exchange sites of the polyelectrolyte) will be disturbed and varying amounts of water retained. Nevertheless, it can be seen that the nitrogen content and functional group play a dominant part and, as expected, the larger the aliphatic side chain of the amine the less the swelling. The titration curves show that the two preparative routes lead to similar exchangers, dependent on the amino groups only, and a characteristic feature is the absence of any indication

| Derivative | Nitrogen content % | Calculated | Experimental (at pH 5) | Equilibrium swelling (water content in %) |
|------------|--------------------|------------|------------------------|---|
| 1 | 0.14 | 0.10 | — | — |
| 2 | 0.48 | 0.34 | 0.33 | 65 |
| 3 | 1.50 | 1.14 | 1.06 | 69 |
| 4 | 0.07 | 0.09 | 0.09 | 59 |
| 5 | 1.31 | 0.94 | 0.72 | 70 |
| 6 | 0.17 | 0.12 | — | 58 |
| 7 | 0.89 | 0.04 | 0.56 | 63 |
| 8 | 0.75 | 0.54 | 0.53 | 57 |
| 9 | 0.00 | 0.06 | — | 57 |

of polyfunctionality, which fits the ideal equations of this reaction and makes these exchangers particularly useful. An important feature in the application of these ion exchangers is their hydroxylic nature, which affects the affinities, equilibria and kinetics of exchange, the investigation of these properties is in progress.

Thanks are due to my colleagues Mr B N Brook and Mr R C Parsons for experimental work and the Directors of Messrs W and R Balston, Ltd, for permission to publish.

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BIOCHEMISTRY

Reversal by Acetylcholine of the Inhibition by Thyroxine of Oxidative Phosphorylation in Guinea-pig Heart Sarcosomes

THE inhibitory effect of thyroxine on oxidative phosphorylation of mammalian mitochondria was demonstrated by Lardy and Feldott¹, and Maley and Lardy².

In the course of experiments carried out in this laboratory on the effect of several autopharmacological drugs and synthetic compounds of quaternary ammonium on oxidative phosphorylation of heart sarcosomes, it was found that acetylcholine, besides showing a stimulatory effect on oxidative phosphorylation of α -ketoglutarate by heart sarcosomes shows a very clear effect on the reversal of the inhibition of oxidative phosphorylation by heart sarcosomes caused by thyroxine.

Guinea-pig heart sarcosomes were prepared in sucrose (0.32 M)—versene (0.001 M) adjusted to pH 7.5 with sodium hydroxide isolation medium according to the method of Cleland and Slater³. Assays of respiration and phosphorylation were carried out in 2-ml volume in a medium containing sucrose (0.32 M), potassium chloride (0.018 M), phosphate buffer (0.018 M at pH 7.5) and sarcosomes (approximately 2.6 mgm protein), the other additions are indicated in the figures.

Respiration and oxidative phosphorylation were assayed polarographically by the method of Chance and Williams⁴. An oxygen electrode apparatus according to Davies and Brink⁵ was used, assembled with an electrode of the rotating type according to

Kolthoff and Laitinen* (The oxygen electrode used in this work was built at Prof. Britton Chance's laboratory, Johnson Foundation for Medical Physics, University of Pennsylvania, to whom we are indebted.)

Thyroxine inhibition of oxidative phosphorylation of a tightly coupled preparation as heart sarcosomes, shows a very definite effect on the respiratory control of the preparation. Thus, addition of thyroxine on the system containing the medium, α ketoglutarate and sarcosomes, causes an uncoupling of oxidation and phosphorylation with the consequent decrease of the respiratory control coefficient. Further addition of acetyl choline, however, causes a complete reversal of the inhibitory effect of thyroxine bringing back the respiratory control to the preparation which behaves again as a tightly coupled preparation. Thus, it seems that thyroxine and acetyl choline are typical biochemical antagonists. On the other hand we failed to demonstrate any adrenaline effect on oxidative phosphorylation of heart-muscle sarcosomes—a probable indication that at this level adrenaline and acetyl choline do not act as antagonists.

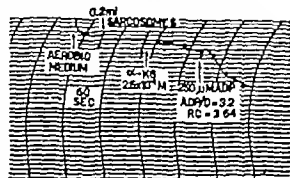


Fig. 1. Polarographic assay of respiration and oxidative phosphorylation in guinea pig heart sarcosomes. The recorder is one of an Esterline-Angus type.

Fig. 1 shows a control experiment which can be analysed from left to right. To the air saturated medium (240 μM oxygen) containing 1.8 ml of solution containing sucrose (0.32 M), potassium chloride (0.018 M), and phosphate buffer (0.018 M, pH 7.5) 0.2 ml of a sarcosome suspension was added followed by the addition of a ketoglutarate (2.5 — 10⁻⁴ M). With the addition of 250 μM of adenosine diphosphate, there was an acceleration phase of respiration ('active state' or state 3) and the respiration was increased 3.04 fold. As the preparation was tightly coupled, it showed a very clear respiratory control. After the adenosine diphosphate becomes depleted the respiration decreased by a factor of 3.64. The ratio of adenosine diphosphate, to oxygen, in this experiment was 3.20.

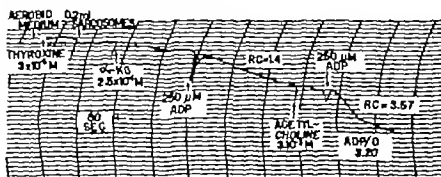


Fig. 2. Polarographic assay of the effect of thyroxine and acetyl choline on oxidative phosphorylation of guinea pig heart sarcosomes.

Fig. 2 shows an experiment where sarcosomes were pre incubated with thyroxine (3.0 × 10⁻⁵ M final). After successive additions of medium, thyroxine, sarcosomes suspension and a ketoglutarate, 250 μM of adenosine diphosphate was added. It can be seen that now there is a very neat uncoupling of phosphorylation

and oxidation with the preparation showing a poor respiratory control. This step was followed by the addition of 10 μl of a 0.61 M solution of acetyl choline, which by its turn was followed by the addition of 250 μM of adenosine diphosphate. Then the respiration was again stimulated and the rate of respiration was increased 3.57 fold during the active state which was followed by a very neat decrease of the respiration by a factor of 3.28. Thus, the preparation regained its respiratory control and came back to the quiescent state after the depletion of the phosphate acceptor behaving again as a tightly coupled preparation.

Thus, it seems that acetyl choline is able to restore the normal oxidative phosphorylation properties of a guinea pig heart sarcosome which was pre incubated with thyroxine and inhibited by it.

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Separation of Prealbumins by Starch Gel Electrophoresis

SEPARATION of complex protein mixtures can be achieved by electrophoresis in starch gels¹⁻³, the resolving power of which can be further increased by substituting for the routinely employed borate buffer a discontinuous system of buffers^{4,5}. Smithies has recently improved the resolution by applying serum directly into wells cast in the gel and performing the electrophoresis with the gel in the vertical position⁶.

I wish to report on results obtained with this last technique in which starch hydrolysed (Connaught Medical Research Laboratories, Toronto) was used in conjunction with the discontinuous system of buffers for the preparation of the gels. Subjecting normal and pathological human sera to electrophoresis in such gels for 5–8 hr at 6 V/cm, several protein zones were detected in front of the albumin instead of the two usually present⁷. This result was not, however, satisfactorily reproduced in every experiment since the separation of the protein entities occurs ahead of the albumin on a very narrow area of the gel.

This region is governed by the distance between the front of the albumin and the high voltage gradient of the discontinuous system of buffers, the latter being constantly visible as a migrating brown line. In general but within certain limits the longer the distance between the two, the better the resolution of any protein migrating faster than human albumin. The distance differs with starches of various origins and its measurement provides a simple and effective means of assessing any starch with respect to this property. In some the distance may equal the length of the whole electrophoretic pattern in others it may

ANIMAL PHYSIOLOGY

Evidence for Phosphatidic Acid as the Sodium Carrier

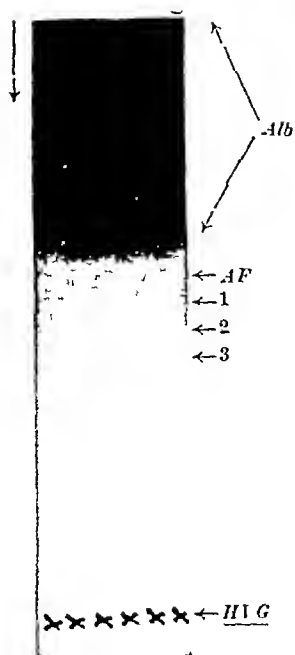


Fig 1 Photograph of a vertical starch gel electropherogram. Figure shows anodic portion of the albumin (*Alb*), distribution of the prealbumins and position of the high voltage gradient (*HVG*). Zone 1 is the acidic α_1 -globulin, zone 2 is prealbumin A, zone 3 is a new prealbumin. The distance between the albumin front (*AF*) and the high voltage gradient measure 2.5 cm after 5½ hr at 6 V/cm

measure only 0.5 cm. By mixing two starches in varying concentrations, the effective area can be adjusted at will.

The optimal conditions for normal human sera were established by preparing the gels from starch-hydrolysed (final concentration 11 per cent), and Baker's starch (lot No. 8072, final concentration 2 per cent), and conducting the experiment at room temperature under standard conditions given above. Fig 1 demonstrates a typical result obtained with normal serum. Three protein zones are present ahead of the albumin. The fastest has not been previously recognized. It was present in very low concentration in every one of the 35 normal individuals screened. The protein migrating immediately ahead of the albumin belongs to the acidic α_1 -globulin and was previously identified as a single zone^{2,7}. However, in certain sera this zone can be separated into two. The intermediate protein zone is prealbumin A^{2,8}.

Since even greater multiplicity of prealbumins has been observed through studies on sera and urines of nephrotic children (Poulik, Zuelzer, and Meyer, in preparation), no attempt is made to classify the new components until their classical electrophoretic relationships are firmly established.

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THE mechanism of active transport of ions is one of the basic problems of cell physiology. For example, most cells extrude sodium against a concentration gradient, and the system which brings this about has been termed the 'sodium pump'. The biochemical mechanism of the 'sodium pump' has remained a mystery. In view of the fact that the turnover of certain phosphatides is concerned in the active extrusion of organic molecules from endocrine and exocrine glands¹, we have recently investigated the possibility that this turnover may also be involved in the secretion or active transport of sodium ions. The salt glands of marine birds are particularly suitable for studying this problem, since they are capable of secreting an apparently² pure solution of sodium chloride in concentrations as high as 0.84 M. Furthermore, the secretory activity of the gland can be stimulated by cholinergic agents. The secretion of sodium chloride by the salt gland is normally regulated by the activity of that branch of the facial nerve (cholinergic) which innervates it, and which in turn appears to be regulated by osmoreceptors.

Incubation of slices of the salt gland of either the Black-footed or the Laysan albatross with acetylcholine plus eserine led to a marked increase over controls in the incorporation of phosphorus-32 into phosphatidic acid (fifteen-fold) and a smaller increase (three-fold) in incorporation into phosphoinositide. There was a comparatively slight increase in incorporation of phosphorus-32 in phosphatidyl choline and phosphatidyl ethanolamine. These results are shown in Table 1. There was very little incorporation of phosphorus-32 into phosphatidyl serine under these conditions. The stimulation of phosphatidic acid turnover was far greater than has been observed in any of the other tissues studied. It is likely that at least a part, if not all, of the stimulation of incorporation of phosphorus-32 into phosphoinositide in the salt gland is secondary to the stimulation of this incorporation into phosphatidic acid, since phosphatidic acid appears to be one precursor for phosphoinositide synthesis³. The relatively slight stimulation of incorporation of phosphorus-32 into phosphatidyl choline and phosphatidyl ethanolamine may also be a secondary effect—a small part of the pool of each of these phosphatides may be derived from phosphatidic acid or one of its breakdown products. It is very improbable that the stimulation of incorporation of phosphorus-32 into phosphatidic acid by acetylcholine could have been a secondary effect, since the other phosphatides failed to show a similar response and the incorporation of phosphorus-32 into the acid-soluble phosphate ester fraction, seven minute acid hydrolyzable phosphorus (adenosine triphosphate), phosphoprotein and nucleic acids was not stimulated.

From these results it appears likely that phosphatidic acid is the sodium carrier, according to the mechanism postulated recently for the transmembrane transport of hydrophilic substances generally⁴. For the secretion of sodium the postulated mechanism is as follows. Phosphatidic acid is formed by diglyceride kinase⁴ from diglyceride and adenosine triphosphate at the inner surface of the luminal membrane. Sodium combines specifically with phosphatidic acid by ionic linkage. (The specificity of

Table 1 PHOSPHATIDE TURNOVER IN THE SALT GLAND OF THE ALBATROSS IN RESPONSE TO ACETYLCHOLINE

| Concentration of acetylcholine† | Phosphatidic acid | | Phosphatidylcholine | | Phosphatidyl ethanolamine | |
|---------------------------------|-------------------|---------|---------------------|---------|---------------------------|---------|
| | Control | ACh† | Control | ACh† | Control | ACh† |
| 10 ⁻⁴ M | 13 000 | 100 000 | 32 100 | 102 000 | 85 000 | 113 000 |
| 10 ⁻³ M | 11 700 | 137 000 | 31 800 | 87 000 | 74 000 | 105 000 |
| 10 ⁻² M | 10 800 | 163 000 | 27 800 | 83 500 | 78 400 | 110 000 |
| 10 ⁻¹ M | 12 200 | 185 000 | 34 400 | 83 500 | 87 600 | 104 000 |

Slices of the salt gland were incubated in bicarbonate saline with added glucose (1 mgm./ml.) and sodium dihydrogen phosphate labelled with phosphorus-32 for 2 hr. at 37°C. After incubation the tissues were ground with sand, and the phosphatides were isolated as described elsewhere (ref. 1).

† Corrected to a specific activity of 10⁴ counts per minute per μ m phosphorus for the inorganic phosphorus in the medium.
‡ Fucose sulphate (10⁻⁴ M) was added with acetylcholine.

phosphatidic acid for sodium is likely to be determined by a particular protein with which phosphatidic acid is probably loosely combined at the inner surface of the membrane. A good analogy is a coenzyme which has no specificity for the substrate but which participates directly in the enzyme-catalyzed reaction.) The sodium salt of phosphatidic acid, which is lipid-soluble, diffuses across the lipid membrane, where it is hydrolyzed by phosphatidic acid phosphatase⁴, forming diglyceride and disodium phosphate. The hydrophilic sodium is discharged into the aqueous lumen. The lipophilic diglyceride diffuses back to the inner surface of the membrane where the cycle is repeated. The enzymes, diglyceride kinase and phosphatidic acid phosphatase, have been shown to be present in the membranous fraction of a cell free preparation from brain tissue and evidence has been presented that these are the enzymes involved in the increased turnover of phosphatidic acid in response to acetylcholine.⁴

The increased turnover of phosphatidic acid in the salt gland on stimulation with acetylcholine offers a possible explanation for the similar effect observed in brain cortex slices and in brain microsomal membranes.⁴ Along with depolarizing the postsynaptic membrane, acetylcholine may activate the sodium pump which extrudes sodium from the nerve following its influx during depolarization.

Based on the fact that they form lipid-soluble salts with cations several workers⁵ have suggested that phosphatides including phosphatidic acid may be cation carriers. However, until now no direct biochemical evidence has been obtained for this.

We are grateful to Dr Sidney R. Galler U.S. Office of Naval Research and Lieut. Comdr Glenn A. Wilson, for providing us with albatrosses, and to Prof. Hubert Frings for advice on their care. This work was supported by grants from the United States Public Health Service, Cerebral Palsy Research and Educational Foundation, Eli Lilly and Co. and the Wisconsin Alumni Research Foundation.

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Reflex Inhibition of Intestinal Motility

SINCE the classical study of intestinal motility by Bayliss and Starling¹ it has been generally assumed that the parasympathetic and the sympathetic components of the autonomic nervous system exert a central, reciprocal control of the activity of intestinal smooth muscle. Thus, sympathetic fibres, running in the splanchnic outflow, should convey centrally induced inhibitory effects. Exactly how this inhibitory influence is brought about in reflex excitations of the sympatho-adrenal system is, however, not known in detail. At least four principally different modes of action may be considered:

(1) Specific, inhibitory sympathetic fibres in direct contact with the intestinal smooth muscle, according to the classical conception.

(2) A local 'overflow' of the adrenergic transmitter, released at the intestinal vasoconstrictor nerve endings.

(3) Local chemical changes induced by the neurogenic reduction of the blood flow to the intestine.

(4) Hormones from the suprarenal medulla, released by splanchnic nerve activation.

Experiments were performed on cats anaesthetized with nembutal or chloralose urethane. Parasympathetic reflex influences were excluded by acute vagotomy. Intestinal motility was measured by means of a continuous recording of the luminal changes in an intestinal segment, isolated *in situ* but with intact nerve and blood supplies. The venous outflow from this segment was continuously recorded by a closed optical drop recorder connected to an ordinate writer. Arterial blood pressure was measured from one of the femoral arteries.

Reflex inhibition of the intestinal motility was induced in the following different ways: (a) occlusion of the carotid arteries, (b) graded withdrawal of blood, (c) electrical or mechanical stimulation of the splanchnic nerve, (d) distention of other, isolated parts of the intestine. In the course of these procedures for inducing reflex inhibition of the intestinal motility the effects of adrenalectomy and of sympathetic denervation of the intestinal segment on motility and blood flow were studied. These inhibitory effects were compared with the effects obtained by graded electrical stimulation of the splanchnic nerves by intravenous infusions of catechol amines and by mechanical reductions of the intestinal blood supply.

It was found that inhibitory responses induced by carotid occlusion, by withdrawal of blood or by stimulation of afferent somatic nerves were not influenced by postganglionic sympathetic denervation of the intestine. Inhibitory responses, however, were not obtained after adrenalectomy or when the venous blood from the adrenals was diverted from the general circulation.

By re-infusion of the adrenal venous blood thus collected, an intestinal inhibition appeared, which was essentially identical with that obtained when the adrenal circulation was intact.

As long as the adrenal glands were intact, direct splanchnic stimulation induced an almost maximal intestinal inhibition at frequencies as low as 1-2 impulses per second. The latency of the onset of this inhibition corresponded to the circulation time from the adrenal glands to the intestine. Contrary to this delayed, but pronounced inhibitory response, the intestinal vasoconstriction obtained by splanchnic stimulation was always prompt. After exclusion of the adrenal glands splanchnic stimulation still induced a prompt vasoconstrictor response but it was now in general necessary to use frequencies above 8-10 impulses per second to induce significant intestinal inhibitions. At these frequencies, however, an 'overflow' of the adrenergic transmitter from the vasoconstrictor fibre endings is known to take place^{2,3}. The inhibitory response to splanchnic stimulation, obtained with high frequencies after exclusion of the adrenal glands, thus appears to be a consequence of the vasoconstrictor fibre activation, confirming recent findings by Celander^{4,5}. This inhibition seems to be caused by the 'overflow' of transmitter, and/or by the mere reduction of the intestinal blood supply.

In striking contrast to the delayed intestinal inhibitions seen on direct stimulation of the splanchnic nerves at 'physiological' frequencies or in the above-mentioned types of reflex sympathetic activations, which appears to be predominantly a consequence of the adrenal medullary secretion, a prompt and intense intestinal inhibition occurred regularly on distention of another, isolated part of the intestine. The rapidity of the onset of this latter inhibition had all the characteristics of a direct, neurogenic mechanism. The same type of inhibition was easily reproduced also by direct stimulation of the nerve fibres from the distended intestinal segment.

To sum up, the intestinal inhibitions seen on reflex activation of the sympatho-adrenal system appear to be predominantly a consequence of the secretion of catechol amines from the adrenal medulla. Even the small blood concentrations obtained at fairly low sympathetic discharge rates are capable of inducing a maximal intestinal inhibition.

A full report of this work will appear in *Acta Physiologica Scandinavica*.

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² Bayliss, W. M., and Starling, E. H. *J. Physiol.* 24, 99 (1899).

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liver¹⁻⁵. Perfusion experiments carried out on rat liver furnished numerous valuable data concerning the mechanism of storage⁴.

We have now succeeded in elaborating a method by which the phenomenon of storage may be investigated *in vitro* on excised connective tissue membranes. This procedure is much simpler than organ perfusion as several samples can be studied simultaneously. The greatest disadvantage of the perfusion technique is that the liver parenchyma represents a bulky ballast which interferes with the biochemical and pharmacological analysis of the function of storage. In the case of the connective tissue membranes, no such interference occurs.

For the mounting of the connective tissue membrane a clamp-like device is used, made of 'Perspex' or 'Polystyrol' sheets which are pressed together by means of a rubber band. At the end of the sheets a round hole 12.5 mm in diameter is cut. On pressing two buttons the sheets open so that the connective tissue membrane may be slipped between them, and if the buttons are then released the membrane will be fixed in the frame. To make sure that the membrane cannot slip out of the sheets and collapse, one of the sheets is provided with a rubber ring which fixes the membrane firmly.

The dorsal hair of the rat is removed and the animal killed with ether. The skin of the lumbar region is cut on both sides and stripped from below upwards to the middle of the dorsum. In this region, with a few strokes of the scissors, it is always possible to isolate suitable subcutaneous membranes a few square centimetres in area. While an assistant expands the membrane with pincers, the open plastic device is cautiously pushed forward and a relatively homogeneous part of the membrane is fixed in the round aperture. Afterwards the membrane preparation is separated with scissors and immediately immersed in the pre-warmed fluid in the incubating vessel. Of course, care must be taken that the membrane does not dry up in the course of preparation. It is still easier to insert the omentum into the device by simply expanding it with pincers and slipping it between the two plastic sheets.

The preparation enclosed in the frame is put into a glass vessel into which 20 ml of the colloid mixture to be examined is introduced. The stopper is provided with an air tube. The vessel is immersed in a water-bath, the temperature of which is controlled with an electric thermostat-regulator. In the subsequent experiments it was always adjusted to 38° C. A shaker keeps the vessels in motion at a rate of 10 oscillations per min.

The experiments have shown that the histiocyte system of connective tissue is able to store colloids *in vitro*. Moreover, if the medium is of suitable composition, the cells function so well that the storage activity is scarcely less than that which can be observed in the living organism.

Perfect pictures of the storing were obtained with diluted serum. Not only rat serum, but also foreign serum, is able to elicit the function of the histiocytes. The following mixture proved to be adequate: 10 ml cattle serum, 10 ml Ringer solution, 0.1 gm glucose. Good results were also obtained with human and horse serum. If 15-25 mgm colloidal gold or 10 mgm colloidal silver were introduced into this mixture, then after 5-6 hr the histiocytes were packed with red and brown storage granules, respectively (Fig. 1). The above quantities relate to commercial preparations which were stabilized with protecting colloids.

A Method for *in vitro* Investigation of the Colloid-storing Function of Histiocytes

ONE of us has shown as early as 1929 that the characteristic function of the reticulo-endothelial cells, namely, the granular storage of colloidal substances, can also be studied in surviving tissues¹. The Kupffer cells store colloidal gold, silver or carbon in large quantities if these substances are perfused in a suitable solution through the portal system of the isolated

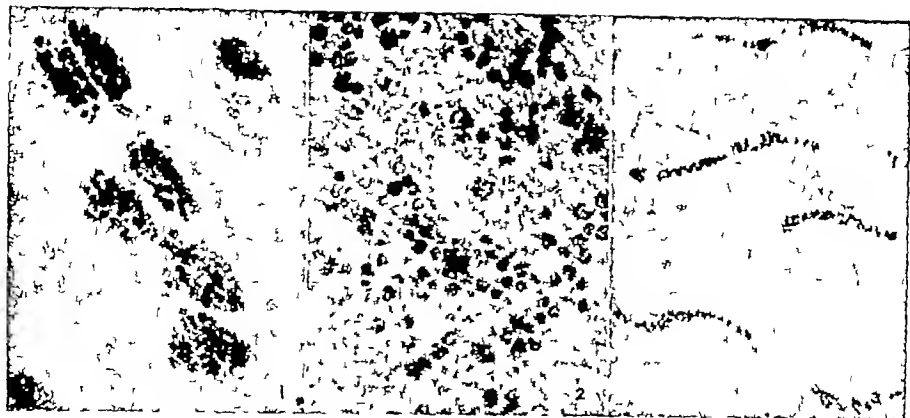


Fig. 1. *In vitro* induced colloidal gold storage in subcutaneous connective tissue histiocytes of the rat, 6-hr stage, methanol fixation.

Fig. 2. Storage experiment *in vitro* with colloidal silver. Granular accumulation in the reticuloendothelial cells of a milk spot in the omentum of the rat, 6-hr incubation, methanol fixed preparation. Low power view.

Fig. 3. *In vitro* induced storage of colloidal gold in human subcutaneous connective tissue. The characteristically shaped histiocytes were examined within 7 hr with red granules.

The diameter of the particles was about 100A and 200A respectively. In the omentum membrane, beside the histiocytes of the stroma, numerous cells of the milk spots were also crowded with metallic granules (Fig. 2).

We not only succeeded in inducing the storage of colloidal metals but also that of macromolecular substances. For example, the connective tissue membrane was kept for 6 hr in the following mixture: 2 ml of a 5 per cent solution of polyvinyl pyrrolidone (molecular weight 35,000), 8 ml of Ringer solution, 10 ml of cattle serum, 0.1 gm of glucose. By means of the ammonium sulphate potassium periodate potassium iodide reagent^{3,4} suitable for the demonstration of vinyl polymers in tissues it could be established that the histiocytes contain numerous polymer granules stained brown. If instead of the pyrrolidone compound polyvinyl alcohol (molecular weight 50,000) was used the histiocytes were crowded with granules which showed with iodine the bluish black reaction characteristic of polyvinyl alcohol. If pectin (molecular weight 35,000) was used as macromolecular substance in a final concentration of 0.5 per cent the histiocytes were crowded with pectin granules exhibiting an intense blue colour by supravital staining with new methylene blue.

Successful storage experiments were also carried out with human subcutaneous connective tissue obtained in connexion with surgical manipulations. The histiocytes readily store colloidal gold in 50 or 20 per cent cattle serum diluted with glucose Ringer solution. Elongated spindle or band-shaped histiocytes are characteristic of human tissue (Fig. 3).

Rat histiocytes function excellently in a fluid medium containing exclusively artificial ingredients. The following medium was applied: 30 mgm sodium caseinate, 100 mgm glucose, 20 ml Ringer solution, 20 mgm colloidal gold. After 6 hr, an abundant

accumulation of gold could be observed in the histiocytes.

The experiments provide evidence that for the observation of storage the contribution of only two factors is necessary: inorganic electrolytes and a suitable hydrophilic colloid. The latter need not be serum protein but can also be another foreign colloid. The liver perfusion experiments also prove that, beside serum proteins, casein, gelatine, or even gum arabic may elicit storage in the Kupffer cells.⁴

It is to be hoped that the method described will be useful for the investigation of the storage phenomenon because it provides a unique possibility for the examination of the effects of different physico-chemical and biochemical factors and various drugs on the process of storage.

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'Supercarbia' in the Anæsthetized Dog

ALMOST a hundred years ago Bert¹ showed that carbon dioxide inhaled in concentrations of 30-50 per cent could cause respiratory failure in the unanæsthetized dog. In subsequent years many anæsthetists and others have become convinced that retention of carbon dioxide can cause respiratory depression and even apnoea in man but few have recorded their observations.^{2,3} Studies in unanæsthetized man are difficult and dangerous, but it was shown that, in one subject, the inhalation of 30 per cent carbon dioxide caused respiratory arrest probably as a result of convulsions precipitated by the effects of the hypercapnia.⁴ What evidence there is, all points to the fact that concentrations of carbon dioxide in excess of 50 per cent cannot be inhaled without causing respiratory failure.

In order to study further the alleged paralyzing effect upon respiration of high concentrations of carbon dioxide we progressively raised the concen-

tration of this gas in the mixture (carbon dioxide + oxygen + anaesthetic) inhaled by dogs anaesthetized with a barbiturate, cyclopropane or halothane. Convulsions did not occur (presumably because of the anaesthetic) but respiratory arrest occurred at inhaled carbon dioxide concentrations varying from 23 to 55 per cent (180–440 mm mercury arterial carbon dioxide tension) depending upon the anaesthetic agent used and its concentration. It was then possible, by ventilating the animal artificially, to increase the inhaled concentration of carbon dioxide to 60–80 per cent (above which level hypoxia might supervene) without serious cardiovascular effects (normal arterial and venous pressures, normal cardiac rhythm). If administration of the anaesthetic was then discontinued (which was possible because at such high concentrations carbon dioxide itself acts as an anaesthetic agent) the animal would resume regular, though slow, spontaneous respiration at a minute volume similar to that during the control period and sufficient to maintain full oxygenation of the arterial blood. The arterial carbon dioxide tension in this stage ranged from 550–670 mm mercury.

We have maintained dogs in this state (which might be called 'supercarbia') for 1 hr or more without any significant change in blood pressure or the electrocardiogram. It has also been possible to return dogs to a normal carbon dioxide tension (the anaesthesia having been resumed at the appropriate moment).

These results would suggest that prolonged severe carbon dioxide retention does not necessarily arrest respiration and may not in itself be deleterious to the circulation, if the effects of the anaesthetic agent and the convulsions can be eliminated. The lethal limit of high levels of carbon dioxide, uncomplicated by these factors, would seem to depend largely, if not solely, upon the hypoxia which must accompany the inhalation of carbon dioxide in concentrations in excess of 80 per cent.

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¹ Bert P. 'Pression barométrique' 1087 (Paris, 1878)

² Scurr, C. F. *Brit Med J*, 1, 505 (1954)

³ Gray, T. C., Fenton, E. S. N., *Brit Med J*, 1, 820 (1954)

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PLANT PHYSIOLOGY

Nature of the Olefines produced by Apples

DURING the past few months, we have been using gas chromatography for the routine analysis of ethylene in air samples from fruit stores (unpublished results, see also *Nature* of September 26, p. 995). A long column is used in order to separate the ethylene from other hydrocarbons of low boiling-point, and under our experimental conditions, using a flame ionization detector, the lower limit of detection for ethylene in a 0.5 ml sample of air is about 0.3 $\mu\text{g}/\text{m}^3$. This represents a sensitivity at least 1,000 times greater than we obtained with a katharometer detector used previously. In order to detect other hydrocarbons which might be produced by apples in much smaller quantities, large samples of air from apple stores were passed through a U-tube

fitted with a sintered plate or filled with glass wool and cooled in liquid oxygen. The condensates were then liberated on to the chromatography column.

The experimental conditions were as follows. Detecting and recording system: the output from two flame ionization detectors¹ (fed from blank and analytical columns) was amplified by a d.c. current amplifier². The output of this was recorded on a 3-mV potentiometric recorder. Eluent gas: hydrogen and oxygen from cylinders were controlled to a pressure of 28 mm mercury above atmospheric by Edwards VPC1 controllers and mixed in equal proportions. Column: 5 mm bore, length 7.3 m, packed with Johns Manville C22 firebrick 36–60 mesh range, impregnated with liquid paraffin in the weight ratio 100:30.

Under these conditions, in which butane emerged 58 mm after the air peak, the retention volumes, relative to butane, of the authentic compounds which covered the relevant range, and were available to us were: methane, 0.01; acetylene, 0.03; ethylene, 0.04; ethane, 0.07; propylene, 0.22; propane, 0.27; propyne, 0.28; cyclo-propane, 0.47; formaldehyde, 0.48; methyl propane, 0.62; methyl propene, 0.81; 1-butene, 0.83; butane, 1.0; trans-2-butene, 1.12; cis-2-butene, 1.23; dimethyl ether, 1.28. Large concentrations of carbon dioxide gave a negative peak at 0.02.

In a typical experiment with Edward VII apples stored on a half-ton scale in steel cabinets³, air from the store was drawn into a 200-ml gas sampling tube and expelled slowly with mercury through a U-tube immersed in liquid oxygen.

In Table 1 are shown the calculated rates of production of the more volatile compounds obtained from Edward VII apples in three environments and identified by their behaviour on a liquid paraffin column. In each case the ethylene figure was obtained separately from an analysis of a 0.5-ml gas sample. Experiments with a single apple were done in order to apply more stringent conditions than were possible with our normal storage methods. The apparatus used was all glass, without grease, and the air supply was admitted to the apple after passing through a U-tube containing activated carbon and immersed in liquid oxygen. From the apple the air was passed directly into the cooled trap.

Table 1

| | 400 kgm apples, gas mixture 0.5 per cent carbon dioxide in air at 3°C ($\mu\text{g}/\text{m}^3/\text{kgm/hr}$) | 400 kgm apples, gas mixture 8.0 per cent carbon dioxide at 3°C ($\mu\text{g}/\text{m}^3/\text{kgm/hr}$) | One apple aerated for 1½ hr at 11°C (ppm/kgm/hr) |
|-----------|---|--|--|
| Acetylene | 1 | 0.5 | 20 |
| Ethylene | 7,000 | 4,000 | 27,000 |
| Ethane | 0.5 | — | — |
| Propylene | 0.5 | 0.5 | 9 |
| Propane | 4 | 3 | 7 |

Four different columns containing liquid paraffin, di-nonyl phthalate, tritolyl phosphate and $\beta\beta'$ -oxydipropionitrile as stationary phases were used. In passing through this series, there is a progressive acceleration of saturated in relation to unsaturated hydrocarbons. However, the presence of excessive quantities of ethylene in the analytical mixture and the fact that in columns of similar length the components of the mixture move progressively faster through columns packed with the later phases of the series, made it difficult to obtain confirmatory evidence

from runs with stationary phases other than liquid paraffin. Peaks corresponding to methyl propane and butane were detected on all four columns, while propane was detected on all except the α -xy dipropionitrile column.

Apples are not unique among plant organs in producing a variety of hydrocarbons. Dormant potatoes have recently been shown to yield a similar range of compounds (Burton, IV G, and Meigh, D F, unpublished results). Whether the minute quantities of substances that are produced have any significant role in apple metabolism remains to be found.

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McWilliam I G and Dewar R A *Nature* 181 760 (1958)

Lovell J E *J Chromatogr* 1 35 (1958)

Meigh D F *J Sci Food Agric* 7 590 (1958)

Maintenance of Semipermeability of Plant Cell Membranes in the Absence of Metabolic Energy Supply

It is generally believed that the semipermeability of cell membranes is closely associated with the living functions of the cell. According to Harvey¹ "Selective permeability becomes the surest test to distinguish the living from the dead, holding where all others fail. It can truly be said of living cells that by their membrane ye shall know them."

In the results to be presented below we would like to show:

(1) That under certain special conditions cells can maintain their semipermeable properties while their energy supply is drastically cut down, or even when all the energy supplying processes are abolished and the cells can be regarded as non living.

(2) That these special conditions are to some extent connected with electrostatic phenomena.

The experiments were carried out with thin slices of red beet root (*Beta vulgaris*) 200–400 μ thick, corresponding to 1–3 layers of cells. The slices were washed in aerated tap water for at least 24 hours. The degree of semipermeability of the membrane was estimated by following the appearance of red pigment in the external solution. Most of the results reported here, as will be seen, were all or none effects. In order that the external solution in the case of control samples should be completely colourless only freshly dug beetroots were employed.

When the slices were placed in 0.01 M sodium fluoride solution under a nitrogen atmosphere, the red pigment started to leak out after 7–9 hours, and after 24 hours there was no pigment left in the tissue. Slices thus treated for 24 hours did not evolve detectable amounts of carbon dioxide when placed in Warburg respirometers at 30° C, and thus according to the present state of our knowledge were without energy supply. Now if magnesium nitrate or sulphate in concentration of 0.1 M was present in the medium together with the sodium fluoride from the start of the experimental period, no leakage was observed even after 7 days. No evolution of carbon dioxide could be detected under these conditions (Exactly similar results were obtained if, in addition to sodium fluoride, the medium contained 10⁻² M sodium oxyanide and 5 \times 10⁻⁴ M 2,4-dinitrophenol). If the slices were at

this stage transferred to higher concentrations of the salts, for example, 0.4 M, plasmolysis could be observed under the microscope. A return to the turgid state was brought about by replacing the 0.4 M solution with 0.1 M solution. The semi permeability of the membranes of 'non living' cells had thus been maintained in the presence of the magnesium salts. If these slices were transferred to distilled water instantaneous leakage occurred.

Further experiments investigated whether leakage could be prevented by the presence of other salts. Sodium chloride, sulphate and iodide were found to be efficient at concentrations of about 0.06–0.8 M. Since some divalent cations are precipitated by sodium fluoride, this substance had to be omitted in subsequent experiments. Prolonged anaerobiosis alone however caused considerable leakage and this could be entirely prevented by the addition of many salts for example calcium, lead and cobalt nitrates or manganese sulphate etc., all in concentrations of 0.1 M.

2,4-dinitrophenol, the best known uncoupler of phosphorylation, also induces leakage of red pigment. When the inhibitor was applied in concentration of 5 \times 10⁻⁴ M at pH 5.5 and at 30° C leakage started after 4–6 hours. It could be entirely prevented by including 0.1–0.2 sodium or potassium chlorides or 0.05 M magnesium or cobalt nitrates, in the original media. If slices which had been treated with 2.4 dinitrophenol for 12–16 hours, in the absence of salts were rinsed and transferred to distilled water leakage continued at about the same rate for several hours. But if they were transferred instead to the salt solutions indicated above the leakage ceased at once.

It is reasonable to conclude that changes in semi permeability are due to some reversible changes in the physical state of some macromolecular structure in the membrane. When energy is supplied by metabolism the non leaky state is maintained. But this is also achieved by high concentrations of salts. A relevant property of these concentrated salt solutions may be the screening of charges. That implies that we are dealing with electrostatic phenomena. Another indication that this is the case is the effect of pH on the system. When slices were placed for 48 hours in a graded series of 0.02 M phosphate buffers, in the presence of 0.01 M sodium fluoride and under a nitrogen atmosphere, all the red pigment leaked from the tissues at all pH's from 2.5 to 5.0. Leakage was less complete at pH's 6.0 and 7.0. At pH's 8.0, 9.0 and 10.0 no leakage occurred. The maintenance of semi permeability at high pH, contrasting with the heavy leakage at low pH, may be interpreted as showing that when the structure is negatively charged the membrane is non leaky, whereas when positively charged it leaks. It is premature to envisage a model for the mechanism by which the living cell controls the physical state of the membrane, but there are grounds for assuming that this is achieved by means of the direct action of adenosine triphosphate on some membrane component.

These experiments, and their interpretation, will be discussed more fully elsewhere.

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¹ Harvey L. V. In foreword to 'The Permeability of Natural Membranes' by H. Davson and J. F. Danielli (Cambridge University Press 1952).

tration of this gas in the mixture (carbon dioxide + oxygen + anæsthetic) inhaled by dogs anæsthetized with a barbiturate, cyclopropane or halothane. Convulsions did not occur (presumably because of the anæsthetic) but respiratory arrest occurred at inhaled carbon dioxide concentrations varying from 23 to 55 per cent (180–440 mm mercury arterial carbon dioxide tension) depending upon the anæsthetic agent used and its concentration. It was then possible, by ventilating the animal artificially, to increase the inhaled concentration of carbon dioxide to 60–80 per cent (above which level hypoxia might supervene) without serious cardiovascular effects (normal arterial and venous pressures, normal cardiac rhythm). If administration of the anæsthetic was then discontinued (which was possible because at such high concentrations carbon dioxide itself acts as an anæsthetic agent) the animal would resume regular, though slow, spontaneous respiration at a minute volume similar to that during the control period and sufficient to maintain full oxygenation of the arterial blood. The arterial carbon dioxide tension in this stage ranged from 550–670 mm mercury.

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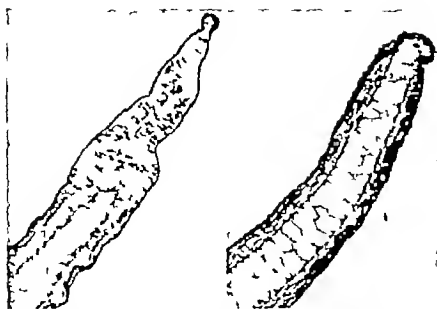


Fig. 1 a Regeneration blastema in control axolotl tadpole. b absence of regeneration blastema in axolotl tadpole treated with β -mercaptoethanol (1/300)



Fig. 2 a Control regeneration blastema (Planaria). b absence of regeneration blastema after treatment with β -mercaptoethanol (Planaria)

than in the controls. Cytochemical studies suggest that mercaptoethanol inhibits and that dithiodiglycol stimulates ribonucleic acid synthesis.

Regeneration of the head in planarians. In the case of planarians also, β mercaptoethanol (M/300) completely inhibits regeneration and even blastema formation (Fig. 2a and b). Again dithiodiglycol has, if anything, a stimulatory effect on regeneration.

In conclusion, our experiments suggest that increase in the —SH content of the cells by the addition of β mercaptoethanol inhibits morphogenetic movements in regenerating organisms as well as in developing embryos. Dithiodiglycol, on the contrary, has usually a stimulatory effect on morphogenesis. The action of mercaptoethanol—ethylglucosamine, an —SH-containing substance which presumably does not penetrate into the cells leads to developmental abnormalities. Taken together, these facts suggest that a biochemical system (the nature of which has still to be studied) involving —SH and —SS— groups plays a key role in morphogenetic processes.

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July 14

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⁴ Brachet J *Exp. Cell Res. Supp.* 6: 78 (1958)

Shell and Siphon Regeneration in *Macra stultorum* Linne (Lamelliibranchiata)

THE study of quantitative collections of dead shells belonging to the lamelliibranch *Macra stultorum* Linne, for the year classes of 1953–1957 on the Dogger Bank, is yielding valuable information on the mortalities exerted by several classes of predators. The chief ones which are recognizable from the dead shells are the drilling prosobranch *Natica poliana* Forbes and the asteroids *Asterias rubens* Linné and *Astropecten irregularis* (Pennant). The prosobranch drills a hole through the shell and presumably feeds through this hole. The actual method of its feeding has not been described although its method of drilling has received considerable attention. Turner¹ lists a full bibliography on the drilling mechanism. Very occasionally live *Macra* are caught, and more rarely their dead shells, bearing an incompletely pierced bore hole. It is presumed that the *Natica* was interrupted in its meal through itself being attacked by a larger predator. Even more interesting are some very rare instances of *Macra* having sealed over the incomplete bore holes on the inside, with an outgrowth of the nacreous layer. We have noticed such seals in both living and dead (at the time of collection) bivalves, in individuals ranging from 4 to 31 mm. Fig. 1 shows a typical sealed bore hole. The area covered by the seal is very much larger than the bore hole itself. This may be explained by the fact that, as has been observed, sand enters through the bore hole and irritates a large area of the mantle membrane. Wasteful killing of very young *Macra* by very young *Natica* seems to be indicated by shells which bear up to five bore holes and still contain flesh.

Oysters are able to seal off the perforations made by *Urosalpinx cinerea* Say. Dr D. A. Hancock has kindly directed my attention to his observations². He thinks the falling temperatures might have caused the oyster drills to abandon the attack. Oysters perforated with a hand drill completely sealed off the holes in 9–14 days at 7–11 °C when kept in tanks.

Shell regeneration does not exhaust the *Macra* response to a reprieve, for it may outgrow a size at which fishes (plaice, dab) are capable of eating the whole bivalve. This size, of course, depends on the size of the attacking fish, and the field data have provided a tentative relationship for the sizes of the largest *Macra* which plaice of a given size can consume. When feeding in a field of *Macra* which are above the "escape size", the fish take only the

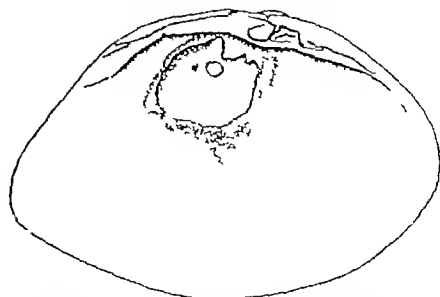


Fig. 1. A valve of a *Macra* pierced but not killed by a *Natica*. The bore-hole was afterwards sealed off by the secretion of nacreous material (Scale 5 mm)

bivalves' siphons. That this injury is not always mortal for the *Macra* is shown by the large number of regenerating stages among *Macra* above 20 mm long—up to 10 per cent of some samples. A first experimental attempt at inducing the regeneration of siphons, and so to build up a time-scale for the various stages of regeneration, failed through lack of sufficient live *Macra* to carry the experiment through. In eleven days no growth had taken place, but the cut edges had healed perfectly.

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¹ Turner, H. J. *Ecol.* 34 (1), 222 (1953)

² Hancock, D. A. *Fish Invest.* Series II, xxi (10) (1959)

Light Regulation of Coat-Shedding in a Tropical Breed of Hair Sheep

BREEDING activity in sheep in temperate climates is predominantly controlled by the photoperiod. The mechanism governing sexual activity in tropical sheep has not yet been elucidated. During current studies of this problem Persian Blackhead ewes were exposed to an experimental light regime similar to that used to induce oestrus in Suffolk ewes at Cambridge, England, namely, 14 hours dark, 4 hours light, 2 hours dark and 4 hours light¹. Results regarding sexual activity were inconclusive but the coats of the treated ewes grew long, dense and shaggy. The coats of control ewes were sleek and short. Managerial conditions other than the light treatment were identical for the two groups of ewes.

In further studies, Persian Blackhead rams were maintained in pens roofed with 'Windowlite', a translucent plastic which reduced the light entering the pens. After four months in the pens coat-growth was markedly affected and the coat was long, tousled and dense. Persian Blackhead rams maintained under natural lighting during this period had short, sleek coats. The comparative coats of rams maintained in the pens for eight months and rams allowed free-range during the daytime over the same period of the year, are shown in Fig. 1.

Wool growth in sheep and normal cyclic coat shedding of *Bos taurus* cattle in the tropics are subject to photoperiod control^{2,3}. Yeates has shown that an experimentally imposed photoperiod similar to that of equatorial regions eliminates the natural coat cycle of European cattle and tends to keep them in a thick heat-retaining coat⁴. Although cyclic coat shedding in *Bos taurus* cattle in the tropics is also hampered by low nutrient intake⁵ the penned rams received sufficient food to gain $\frac{1}{2}$ -1 lb per week in live-weight.



Fig. 1 (a) Persian Blackhead ram maintained on natural lighting, (b) kept in a pen with reduced lighting.

These independent observations suggest that the growth of, or failure to shed the hair, was due to a qualitative or quantitative interference with the normal photoperiod at this latitude (17° 50' S).

Although it has been suggested that the annual fluctuation in the tropical photoperiod may be too small to effect control of reproductive activity in sheep⁶ it is of note that a physiological mechanism sensitive to light changes exists in a breed of sheep indigenous to the tropics.

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A Possible Role of Indoleacetic Acid Oxidase in Crown Gall Tumour Induction

THE necessity of auxin for the transformation of incipient tumour cells to fully altered tumour cells has been demonstrated by Braun and Laskaris¹ and by Klein and Link². Both groups demonstrated that decapitated plants inoculated with an avirulent strain of *Agrobacterium tumefaciens* would develop crown gall tumours if their cut surfaces were smeared with a lanolin paste containing a plant growth hormone (indole-3-acetic acid), but not if these cut surfaces were smeared with lanolin alone. The action of indole-3-acetic acid was demonstrated to be on the tissues and not on the bacteria, as the latter did not become virulent as a result of exposure to indole-3-acetic acid.

The bacteria themselves have generally been assumed to be the source of the extra auxin required for the transformation of incipient to fully-altered tumour cells. However, attempts to find correlations between auxin production by the bacteria and their virulence have yielded inconclusive results³. This communication will present evidence that the extra indole-3-acetic acid needed for transformation may not be bacterial in origin but may in fact be due to a decreased destruction of auxin in the tissues infected with virulent bacteria.

Sunflower plants were selected for uniform height (70 cm), stem width and general appearance. An apical section was cut just below the internode that had last fully expanded, this internode was usually between 15-18 cm long. The leaves and apical internode were then removed, and the section was washed in undiluted 'Clorox' (a commercial preparation of sodium hypochlorite) to which a small amount of detergent had been added. The washed sections were then dipped into absolute alcohol, flamed, and allowed to cool in a sterile Petri dish. The now-sterile internode was cut horizontally into five sections, each about 2.5 cm long. Each section was then split longitudinally into two sub-sections, and each sub-section implanted basal end up in a tube of White's medium without added auxin. These cultures were grown in a 25° C controlled-temperature room for two days, after which the contaminated sections, if any, were discarded. Inoculations were made on the second day.

after placing in culture by smearing the cut surfaces with a 48 hr culture of *A. tumefaciens*. One set of sub-sections was inoculated with a virulent strain, the other set of sub-cultures with an avirulent strain. On the day of inoculation and on five successive days the sub-sections of an entire internode were separately cut into slices and assayed for indole 3 acetic acid oxidase.

Indole 3 acetic acid oxidase determinations were run by the method of Lipetz and Galston⁴. 450–500 mgm of slices were placed in 10 c.c. of a reaction mixture containing 10^{-4} M indole 3-acetic acid, Mn^{++} and 2,4-dichlorophenol buffered at pH 6.1. At time zero, and at selected intervals afterwards, aliquots were removed from the reaction mixture and assayed for residual indole 3 acetic acid with Salkowski reagent in a Klett colorimeter equipped with a 540 mμ filter. Klett readings were converted to μgm of indole 3-acetic acid with the aid of a standard curve prepared with indole 3 acetic acid solutions of known concentrations.

In the series inoculated with the virulent IIBV7 strain and IIBNF6 avirulent strain a significant depression in the comparative levels of indole 3 acetic acid oxidase was observed on the second day after inoculation with the virulent bacteria. These results are presented in Table 1. Similar experiment per

Table 1. DIFFERENCE IN μGM OF INDOLE 3-ACETIC ACID OXIDIZED PER GRAM TISSUE IN 4 HOURS BY PARALLEL TISSUE CULTURES INOCULATED WITH VIRULENT AND AVIRULENT STRAINS OF *A. tumefaciens*

| Day after inoculation | Virulent—Avirulent | Significance (t test)* |
|-----------------------|--------------------|------------------------|
| 0 | -1.0 ± 2.2 | n.s. |
| 1 | +0.6 ± 4.6 | n.s. |
| 2 | -23.0 ± 6.7 | 2 per cent |
| 3 | -8.6 ± 7.4 | n.s. |
| 4 | +1.9 ± 6.5 | n.s. |
| 5 | -2.5 ± 6.0 | n.s. |

n.s. = not significant at the 5 per cent level

formed using the virulent A 6 and the avirulent A 66 strains were more erratic, and therefore inconclusive.

The extra indole-3 acetic acid necessary for complete tumour induction may thus be a product not of the bacteria, but of the infected tissues whose indole 3 acetic acid-destroying system has been inhibited. The drops of indole-3 acetic acid oxidase levels in tissues inoculated with virulent strains might thus be one factor involved in the transformation of incipient tumour cells to fully altered tumour cells and the avirulence of some strains of *A. tumefaciens* may be due to their inability to initiate this inhibition of indole 3 acetic acid oxidase.

I am indebted to Dr. A. W. Galston for advice and encouragement, and to Drs. A. C. Braun and T. Stoner for cultures of *A. tumefaciens*. This investigation was supported by pre-doctoral fellowship OF 7607-O of the National Cancer Institute, Public Health Service. It constitutes a portion of a doctoral thesis presented to the Graduate Faculty of Yale University.

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ENTOMOLOGY

Chemical Changes Associated with Diapause in the European Corn Borer, *Ostrinia nubilalis* (Hbn) (Lepidoptera: Pyralidae)

INDUCTION of diapause, at 65° F. in the European corn borer, *Ostrinia nubilalis* (Hbn) requires that last instar larvae be exposed to photoperiods of 9 h to 14 h of light a day for about 3 weeks. Initiation of diapause is then marked by cessation of feeding, a sharp reduction in oxygen consumption and failure to pupate when placed in an environment favouring completion of development.¹ Our interest in the physiology of diapause prompted a search for other changes associated with its induction. This communication reports differences in the amino acid composition of diapause and non-diapause borers.

Larvae were reared as described earlier.² Larvae that did not undergo diapause were obtained by withdrawing them from the stock culture 3 or 4 days after the moult to the last instar; they were deprived of food for 3–6 hr before analysis. Larvae in diapause were obtained by manipulating photoperiod and temperature; they were tested after they had been stored in diapause for two months at 38° F. Ninhydrin positive substances were separated by two dimensional partition chromatography. The squash technique described by Fox³ and Robertson⁴ was used. A single head provided sufficient material for good resolution in the developed chromatogram. The head was cut from the larva and immediately crushed in the lower left corner 1 in. from the edges, of Whatman No. 1 chromatography paper, 12.5 or 10 in. square. The crushed head was removed and the spot dried at room temperature. The paper was developed 12 in. in the first direction with *n*-butanol acetic acid, and water, in the proportions 4:1:1, and 12 in. in the second direction with 80 per cent aqueous phenol. The colours were developed with 0.1 per cent ninhydrin in isopropanol. In some cases proline was located by spraying with 0.3 per cent ninhydrin. Compounds were identified by comparing chromatograms with those of known amino acids and, in some instances, by co chromatography with individual amino acids.

Fig. 1 A and B, shows tracings of representative chromatograms, run simultaneously. The substances named in Fig. 1 were found in head squashes of both diapause and non diapause borers. Separation of valine, methionine, and tryptophan was poor but generally adequate to establish their identities. Arginine, not shown in Fig. 1, was present in both groups as a diffuse spot in the area bounded by spots 5, 7, 8 and 9. Not detected were ornithine, β alanine, taurine, hydroxyproline, and sarcosine. Larvae not in diapause differed from those in diapause in having at least one unidentified, slow running spot not present in the latter. This is spot X of Fig. 1B. In some chromatograms, partial division of spot X and differences in colour between its parts suggested that two compounds might be present. The chromatographic difference persisted even after ethanol extracts of larva had been washed with chloroform, evaporated, and boiled under reflux with 6N hydrochloric acid for 20 hr. The unknown, therefore, is probably not a peptide. A second difference between diapause and non-diapause larvae was the much higher concentration of proline in the former. Analyses were carried out to determine the differences arise during or after the diapause. Spot X was found in 41

¹ Braun A. C. and Laskowski T. *Proc. U.S. Nat. Acad. Sci.*, **28**, 463 (1942).

² Klein R. M. and Link G. K. *Proc. U.S. Nat. Acad. Sci.*, **38**, 1066 (1952).

³ Locke, S. B. *Baker A. J. and Duggar B. M. J. Agric. Res.* **59**, 510 (1959).

⁴ Lipetz, J. and Galston, A. W. *Amer. J. Bot.* **46**, 193 (1959).

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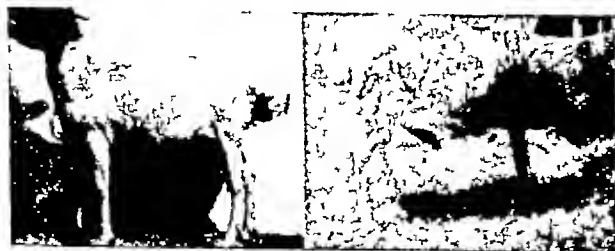


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believed to be the same as his 'Funduszellen', types (c) and (d) being the 'Mündungszellen'.

The type IV alveoli (Fig 1A and B) are found in adult males only, scattered amongst type III. They are composed of a number of similar cells, type (g) which become filled with purple staining granules after the tick starts to feed.

A more detailed description of the salivary alveoli and of the changes which they undergo during the life cycle of the tick will be published at a later date.

I am indebted to Mr M Ulrich of the Photographic Department, South African Institute for Medical Research, for the photomicrographs.

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June 22

¹ Bonnet M. A. C. R. Acad. Sci. 142 296 (1906)

² Douglas, J. R. *Univ. Calif. Pub. Ent.* 7 297 (1913)

³ Robinson L. J. and Davidson, J. *Parasitol.* 6 217 (1913)

⁴ Nordenskiöld E. *Zool. Anz.* 28 476 (1905)

BACTERIOLOGY

Bacteriophage Typing Applied to Strains of *Brucella* Organisms

SURFACE antigens usually limited to one taxonomic group are the main factors determining the bacteriophage specificity of bacterial species¹. By such sensitivity, species of *Salmonella* can be distinguished² and the degree of sensitivity is used for typing strains of *S. typhi*^{3,4} and strains of other bacteria⁵.

Brucella phages were discovered only after rigorous search⁶ and they have apparently not yet been described in detail. A *Brucella* phage grown on strain 19 *Brucella abortus* in a shake flask culture has now been found to be active on cultures of *Br. abortus* laboratory strains, but not on *Br. melitensis* and *Br. suis*. This phage was obtained by growing a single plaque taken from the end point dilution of a phage suspension kindly supplied by Dr A W Stablesforth from Weybridge England.

The phage produces irregular plaques of small diameter, the smallest only being recognized as spots in the bacterial mot on 'Albumin' agar. These spots and the edges of the plaques appear to consist of extremely rough colonies of the *Brucella* strain attacked.

The technique found most practical is as follows. A 72 hr aerated liquid culture of phage is cleared by centrifugation at 3,000 r.p.m. for 75 min and the supernatant heated at 60° C for 60 min to destroy any remaining bacteria. The phage suspension is stored at 4° C and serially diluted ten fold before use. The phage dilutions are spotted on dry 'Albumin' agar plates by means of a 1 mm diameter platinum loop. After drying the spots are covered with a suspension of young cells taken from surface culture and made up to a density of approximately Brown's tube 1 in a diluent of distilled water containing 0.1 per cent (w/v) carboxy methyl-cellulose. The 0.02 ml dropper pipette is used for depositing the suspension over the site of the phage spot. After standing in the dark for 1 hr the plates are incubated at 37° C in inverted position for 24 hr or longer and if necessary in an atmosphere of 10 per cent carbon

TABLE 1
DIFFERENTIAL SUSCEPTIBILITY
Titration of *Brucella* Bacteriophage

| Phage dilution | M 1631 | A 544 | S 1230 | A 510 | Br Sh Sem |
|-----------------|--------|-------|--------|-------|-----------|
| Un diluted | — | +++ | — | +++ | — |
| 10 ¹ | — | +++ | — | +++ | — |
| 10 ² | — | +++ | — | +++ | — |
| 10 ³ | — | ++ | — | ++ | — |
| 10 ⁴ | — | + | — | + | — |
| 10 ⁵ | — | — | — | — | — |

++++ confluent lysis

+++ plaques and spots

++ spots

+ few than 5 spots

~ no phage activity

dioxide. An example of the results is given in Table 1.

Here it was found that *Br. melitensis* strain 1631 and *Br. suis* strain 1230 which are World Health Organization reference strains were completely resistant as was also a stock culture of a local *Brucella* variant isolated from sheep semen.

The aerobic *Br. abortus* strain 19, and the carbon dioxide dependent *Br. abortus* strain 544 which is a World Health Organization reference strain were equally susceptible to the phage.

These results show that phage typing may have important taxonomic and possibly also epidemiological value in the field of *Brucellosis* research.

Acknowledgments are due to Dr R A Alexander, director of veterinary services, for permission to publish this report and to Mr P V Mulders for technical assistance.

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¹ Burnet, F. M. *Brit. J. Exp. Path.* 3 121 (1952)

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Induction of Phage Formation in the Lysogenic *Escherichia coli* K-12 by Mitomycin C

MITOMYCIN C, a newly isolated antibiotic is receiving special attention because of its antineoplastic activity as well as its selective inhibitory action on the synthesis of bacterial deoxyribonucleic acid¹. It has also been observed that the impaired deoxyribonucleic acid synthesis of cells of *Escherichia coli* B treated with mitomycin C can be promptly restored by infection with the bacteriophage T2². These properties suggested that this antibiotic could induce the development of active phage from the prophage state in lysogenic bacteria, since they are similar to ultra violet effects. This communication concerns the lytic process of *Escherichia coli* K-12 induced by mitomycin C added externally.

Cells growing in salts glucose synthetic medium were harvested at the logarithmic phase of growth resuspended in a similar fresh medium in the presence of various concentrations of mitomycin C, and incubated at 37° with vigorous aeration. The cells were taken at intervals and measured photometrically at 600 mμ. The amount of mitomycin C per ml, was 10⁻⁵ to 10⁻⁷ g/ml.

the same rate as in the control culture during the first 90 min, though later it stopped (Fig 1). With 0.5 or 1 μgm of mitomycin C per ml of medium, the turbidity increased normally for about 60 min and then suddenly began to decrease. After shaking for 2 hr the incubation medium became almost clear with only some cell debris present. The viable cell count was 2.4×10^4 per ml compared to 4×10^9 per ml in the control culture. In the presence of higher levels of mitomycin C (5–10 μgm per ml), the increment of optical density was observed for only 30 min, after which it ceased. It was also found that the addition of chloramphenicol at the beginning of incubation prevented the lysis caused by mitomycin C whereas its addition at 45 min after the start of incubation had no effect on the lytic process in the presence of the antibiotic.

The appearance of the growth-curve in the presence of mitomycin C coincides almost exactly with growth-curves observed after the induction of lysogenic bacteria with appropriate doses of ultra-violet³ or chemical agents^{4,5}. Therefore an investigation was undertaken in order to see whether the lysis of the cells is due to the development of active (?) phage. The bacterial lysate obtained after a 2-hr exposure to 1 μgm mitomycin C per ml was plated on a λ -sensitive bacteria, *Escherichia coli* C 600. It was found that 3×10^9 phage particles were released into the medium compared to 1.7×10^7 in the control culture (the yield of phage was about 200 times greater than that of the spontaneous control). Fig 2 shows a one-step growth-curve of λ -phage liberated by *Escherichia coli* K-12 after induction with 1 μgm of mitomycin C per ml. In this experiment a growing culture of *Escherichia coli* (O.D.₆₆₀ = 0.175) was incubated with vigorous shaking in the presence of antibiotic for 10 min. After dilution (10^5 and 10^7) the incubation was continued, and samples were taken at intervals for plating on a λ -sensitive bacteria. The first phage particles appeared in the medium at the end of a latent period, at which time lysis of the culture began. Another experiment indicated that *Escherichia coli* W 1485 (a non-lysogenic strain) was not lysed in the presence of any amount of mitomycin C. This observation provides additional evidence to support the conclusion indicated above.

These results show that mitomycin C can induce the development of active phage in the lysogenic

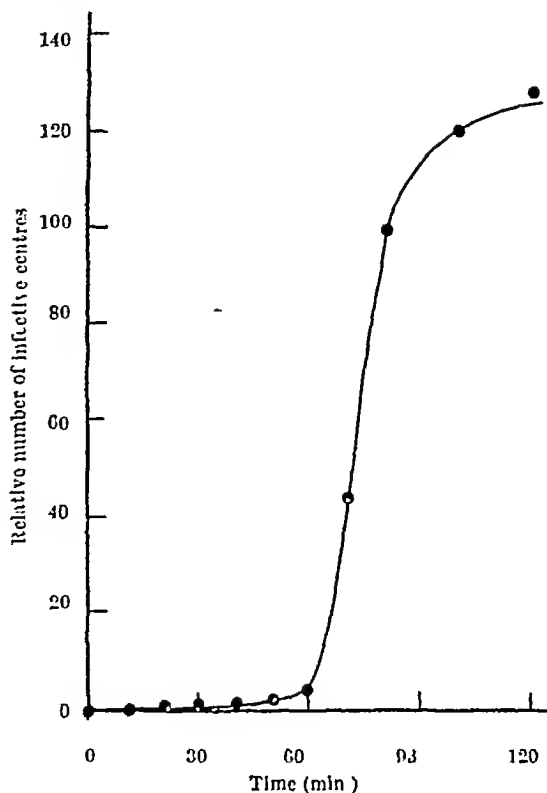


Fig 2 Induction of phage production in *Escherichia coli* K-12 by mitomycin C

strain of *Escherichia coli* K-12. This antibiotic therefore produces many of the results characteristic of ultra-violet irradiation.

We wish to express our appreciation to Prof H Kikkawa for his interest and encouragement in this work, and to Dr S Shiba of this University for a generous supply of mitomycin C.

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Specific Inhibition of Antibody Formation During Immunological Paralysis and Unresponsiveness

FAILURE of antibody to appear in the serum following large doses of antigen has been reported under varying sets of conditions. In normal adult mice, a life-long state of 'immunological paralysis' can be induced by the administration of a sufficient amount of pneumococcal polysaccharide¹. This antigen is known to persist for at least a year, and it

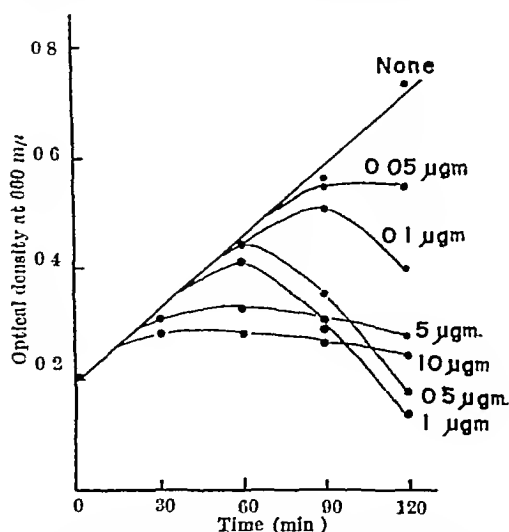


Fig 1 Change in turbidity of the culture of *Escherichia coli* K-12 incubated in the presence of various concentrations of mitomycin C

Table 1

| Group | No of Mice | Antigen Injected | Route of Inoculation | Days of Infection* | Day of Death | Animals with A/B titre | Serum A/B at Death | Antibody† cells/mm |
|--------------|------------|---|--|--------------------|--------------|------------------------|--------------------|--------------------|
| A (neonatal) | 14 | 0.5 mgm./gm. dry fluid bovine serum albumin + weekly dose of alum-precipitated bovine serum albumin | Subcutaneous + intraperitoneal alter- nately | 1-60 | 50 | 0/5 | + | 0 |
| | | | | 1-66 | 70 | 0/4 | + | 0 |
| | | | | 1-66 and 63** | 0 | 0/3 | + | 0 |
| B (adult) | 12 | same | same | 75-79 | 78 | 0/5 | + | 0 |
| | | | | 35-75 | 81 | 0/2 | + | 0 |
| | | | | 35-75 and 82** | 80 | 0/5 | + | 0 |
| C | 16 | 2 mgm. alum precipitated bovine serum albumin | Subcutaneous | 55-56 | 61 | 14/16 | 0 | 18.3 |
| D | 0 | 500 µgm. Type II pneu- monococcal polysaccharide | Intraperitoneal | 50 | 70 | | | 0†† |
| E | 0 | 1 µgm. Type II pneu- monococcal polysaccharide | Intraperitoneal | 56 | 70 | | | 0.22 |

* Numbers cited refer to age of animal in days per animal. †† One questionable cell.

** 2 mgm. alum precipitated bovine serum albumin administered. † Mean value using 3-10 slides.

may either continuously neutralize antibody as it is formed or it may inhibit the actual synthesis of antibody.² These alternatives may be used to explain the more temporary immunological unresponsiveness inducible in adult rabbits with massive injections of purified proteins.³ However, when the same protein antigens are administered during foetal or neonatal life subsequent antibody formation is inhibited for longer periods.^{3,4} Apparently the neonatal cells possess a different order of sensitivity to inhibition. It is not clear whether this inhibition is dependent upon the continuous presence of antigen, but there is a correlation between increasing dosage and prolongation of unresponsiveness.⁵

If antigen constantly neutralizes antibody as it is formed, immunofluorescent methods should detect cells containing antibody in the lymphoid organs of such paralyzed or unresponsive mice. However, inhibition of a more fundamental nature would be implied if no positive cells could be found. Our evidence indicates in fact that no demonstrable antibody formation takes place in mice either made unresponsive to bovine serum albumin or paralyzed with pneumococcal polysaccharide.

Experiments with both bovine serum albumin and pneumococcal polysaccharide type II were undertaken with both large and small doses of antigen. Swiss white non inbred mice were used. Animals were injected subcutaneously and intraperitoneally with 500 µgm./gm./day of bovine serum albumin a dose shown previously by Dixon and Maurer⁶ to be large enough to prevent the occurrence of an immune disappearance rate in adult rabbits. Individual animals were bled from the tail and assayed for anti bovine serum albumin by Boyden's hemagglutination method.⁶ Antigen was determined by hemagglutination inhibition a serum level of 0.1 µgm./ml. of antigen nitrogen being detectable. The spleens of the animals were quick frozen and sectioned in a cryostat. Three to ten sections per animal were examined by immunofluorescence for cells containing antibody using the appropriate controls.⁷ The number of these cells per section was counted and the area of each section estimated from measurements made with a stage micrometer.

The results shown in Table 1, were striking. No cells containing antibody were found in either adult or neonatal mice at intervals following the cessation of daily large injections of bovine serum albumin. Moreover an additional dose of 2 mgm. of alum precipitated bovine serum albumin to some members

of these groups likewise failed to provoke a detectable cellular response. Control animals given only alum precipitated bovine serum albumin (group C) responded with antibody titres which reflected in general the appreciable numbers of cells containing antibody visible in their spleens (Table 2). (The single control mouse failing to respond also had no detectable antibody in sections of its spleen.)

The axillary lymph nodes were also examined in a few animals. No positive cells were found in group A. In group C the density of antibody-containing cells in the lymph node was about threefold greater than in the spleen. The lack of correlation between serum titre and numbers of cells in the spleens of some animals recorded in Table 2 may have been due to the differing contribution made by various organs in individual cases.

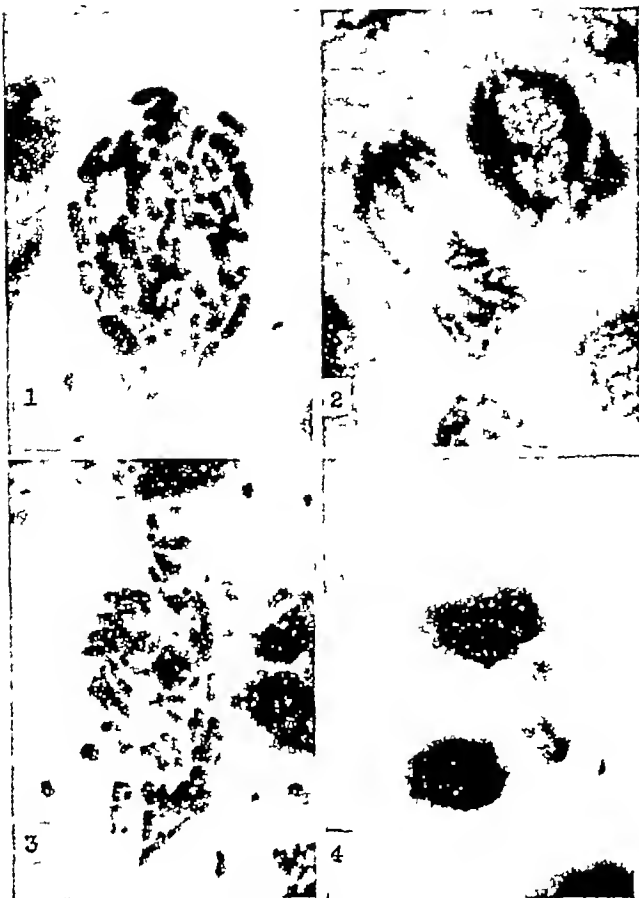
This inhibition of the formation of antibody to bovine serum albumin was specific because it did not interfere with a concurrent secondary cellular response to 20 Lf of diphtheria toxoid administered to a few animals during the massive injection of bovine serum albumin. More recent observations suggest that a dose of bovine serum albumin fifty times less or 10 µgm. daily is equally inhibitory to specific antibody formation. Oddly enough although diphtheria toxoid is a good antigen in mice 10 µgm. daily doses failed to produce unresponsiveness.

In the experiments with pneumococcal polysaccharides II, the doses used were those known to result in immunity or paralysis in mice¹ no titrations of pneumococcal antibody were carried out. No cells containing antibody could be detected in the spleens of mice given the larger dose of polysaccharide (group D). However positive cells were visible in the spleens of mice immunized intraperitoneally with

Table 2. CELLS CONTAINING ANTIBODY FOUND IN INDIVIDUAL MICE*

| Group C—bovine serum albumin | | Group E— pneumococcal polysaccharide II |
|------------------------------|------------------------|---|
| No. of Cells | Reciprocal Serum Titre | No. of Cells |
| 2,347 | 320,000 | 62 |
| 1,070 | 5,120 | 23 |
| 890 | 10,000 | 17 |
| 841 | 40,000 | 6 |
| 323 | 1,250 | 2 |
| 267 | 1,560 | 1 |
| 370 | 2,660 | |
| 228 | 20,000 | |
| 174 | 10,000 | |
| 0 | <10 | |

* Calculated on the basis of ten sections of spleen.



Figs 1-4 Effect of the extract of *Alstonia scholaris* on the root-tip of *Allium cepa* showing polyploid metaphase stickiness, diplochromatid appearance and laggings and fragments respectively ($\times c. 2,700$)

11 days continuous treatment in 25 per cent of the stock solution. Tumours were formed about 1 cm behind the growing apex of the root and were elongated.

Cytological examination showed most of the cells to be in a resting state, and divisions were noted in only 8-10 per cent of the cells. Irregular division, like fragmentation, lagging, stickiness of the chromosomes was frequent. 2-3 per cent of the cells showed polyploid chromosome numbers. Metaphase and anaphase chromosomes appeared to be shortened and swollen. The diplochromatid appearance, as characteristic of colchicine treatment, was evident. The cells of the tumour showed extreme elongation.

It may be noted that Bailey² has reported chromosome swelling and stickiness following treatment with hydrochloric acid and sodium hydroxide in high concentration. Whether the very low concentration of these two chemicals used for extraction here can be responsible for stickiness and characteristic swelling, was checked by control experiments with bulbs kept in these chemicals alone. No effect, however, was noted.

It is clear therefore that this extract is capable of including tumours and polyploidy in plant cells. The tumour production involves mainly cell elongation and polyploidy rather than rapid rate of division in all planes.

I am grateful to the Ministry of Education, India, for awarding me a National Research Fellowship, during the tenure of which the present work was carried out. I am also thankful to Dr I. Banerji, head of the Department of Botany and to Dr A. K.

Sharma, lecturer in charge, Cytogenetics Laboratory, University of Calcutta, for facilities provided for carrying out the work.

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¹ Takenaka, Y. *Ann. Rep. Nat. Inst. Genet. (Japan)*, 5, 69 (1955)
² Bailey, P. C., *Cytologia*, 21, 292-299 (1956)

Genetic Control of Tryptophan Peroxidase-Oxidase in *Drosophila melanogaster*

BUTENANDT¹, BEADLE² and EPHRUSSI³ have shown that kynurenine synthesis occurs in insects and that in *D. melanogaster* the gene 'vormillon' (*v*) controls kynurenine formation. Tryptophan oxidation to kynurenine was extensively studied in mammal liver by Knox and Mehler⁴, who showed that two enzymes are involved in this two step reaction: tryptophan peroxidase-oxidase and kynurenine formamidase. Since the mutant *v* contains a normal amount of the latter enzyme⁵, it was thought that the first step of tryptophan oxidation, which leads to formylkynurenine, is in some way affected by this mutation. No direct demonstration of enzyme control by the *v* gene has been given up to now; workers have tried unsuccessfully to demonstrate that tryptophan is metabolized *in vitro* by *Drosophila* extracts⁶. A very low content of tryptophan peroxidase-oxidase and the relative inadequacy of the methods of enzyme assay, account probably for these results. Only recently activity of tryptophan peroxidase-oxidase was recognized in an insect—the meal-moth *Ephestia kuehniella*⁷, and quantitative determinations were made by measuring the fluorescence of chromatographically separated spots. This communication deals with the genetic control of tryptophan peroxidase-oxidase in *D. melanogaster* studied by means of a very sensitive method.

Flies were reared on standard corn meal agar medium at 25° isolated within a few hours after emergence and transferred into vials containing fresh medium, where they were kept for 6 days. The flies were homogenized for enzyme assay in a Potter homogenizer in four volumes (w/v) of a cold solution of 0.014 M potassium chloride and 0.0025 M sodium hydroxide. The crude extracts were then centrifuged at 12,000 g for 30 min. and the clear supernatant used directly. All the operations were performed at 0°. Incubation mixtures were prepared according to Knox⁸ and contain 1 ml. of enzyme extract, 2 ml. of phosphate buffer 0.1 M pH 7 and 0.3 ml. of 0.03 M L-tryptophan; for the blank preparation the amino-acid was omitted. The vials were incubated at 37° in an atmosphere of air and the reaction was stopped by the addition of 1 ml. of 20 per cent trichloroacetic acid. After filtration, kynurenine was determined by the Bratton-Marshall method⁹; the tubes were stored at 0° for 14 hr. before reading at 560 mμ in a Beckman DU spectrophotometer. The molar extinction coefficient of the diazotized kynurenine is at this time maximum ($\epsilon = 28,500$). The filtrates were also used for paper chromatography, in order to identify the products of the reaction.

After incubation of enzyme extracts of wild-type flies an appreciable amount of a diazotizable substance is formed, which has an absorption peak at 560 mμ when subjected to the Bratton-Marshall reaction. This compound was identified with kynurenine by comparison of the characteristic reactions

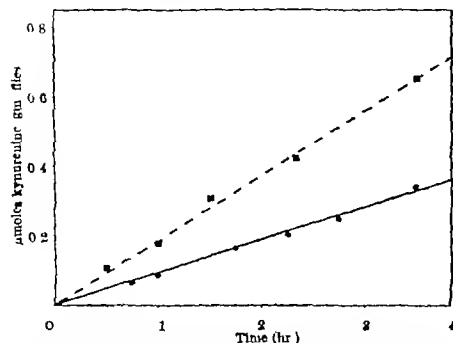


Fig. 1 Time course of tryptophan oxidation by *Drosophila melanogaster* homogenates in air and in oxygen atmosphere. Solid line, air atmosphere; dotted line, oxygen atmosphere. Two homogenates with different activity were used.

Activity = amoles of kynurenine formed in 1 hr by 1 gm. of flies
Table 1 AROMATIC AMINE FORMED BY HOMOGENTIS OF *Drosophila melanogaster* INCUBATED WITH 1 TRYPTOPHAN DETERMINED BY THE BRATTON AND MARSHALL METHOD

| Strain | Mean activity \pm standard error | No. of determinations |
|-----------------------|------------------------------------|-----------------------|
| wild type | 0.131 \pm 0.013 | 7 |
| <i>v</i> ¹ | 0.014 \pm 0.002 | 6 |
| <i>v</i> ² | 0.010 \pm 0.002 | 6 |

(Ehrlich, ninhydrin) and R_f values given by the pale blue fluorescent spot, found in chromatograms, with those given by a sample of pure kynurenine. The systems butanol acetic acid water (4:1:5) propanol 1 per cent ammonium (2:3), potassium chloride 20 per cent sodium citrate 4 per cent, formic acid 5 per cent methanol benzene butanol water (2:1:1), were used for chromatography.

Kynurenine formation was determined at successive time intervals and shown to be proportional to time for many hours, the results of such an experiment are illustrated in Fig. 1. The incubation in an atmosphere of pure oxygen increases the rate of the reaction by a factor of 1.2, the addition of 0.01 M sodium diethylthiocarbamate inhibits quite completely the reaction. The tryptophan peroxidase-oxidase activity of wild type *D. melanogaster* flies and of two *v* mutants was determined.

As shown in Table 1 the *v* strain homogenates produce at a very slow rate a diazotizable compound but no kynurenine could be found in chromatograms obtained from incubation mixtures of these strains. It seems therefore probable that the *go* controls the synthesis of the tryptophan peroxidase-oxidase and that the mutant strains lack this enzyme. A similar situation was observed in the mutant *a* of *Ephestia kuehniella*⁴.

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GEOGRAPHY

Effects of the Water Hyacinth (*Eichornia crassipes*) in the Nile Valley

THE presence of *Eichornia crassipes* (water hyacinth) in the Nile has already been reported¹. Since then its presence in force has been noted in the River Sobat, but its spread downstream in the White Nile is being checked at Jebel Aulia Dom, some 47 km south of Khartoum.

Fish is an important item in the diet of the peoples living on the banks of the infected rivers. *Eichornia* has interfered, in some cases seriously, with fishing. The mats formed by the plant along the river banks exceed 10 m in depth in many parts of the White Nile, while numerous side channels are choked up with the weed. The Nilotics, the largest single group of peoples affected have three main methods of fishing—with basket, line and spear. This growth seriously hinders the use of baskets and lines as these are always used from the banks. Thus there has been a relative increase in the proportion of fishing by spear from canoe. Perhaps the Nilotics will begin to use basket and line from canoes. However the riverbank growth pushes the canoes out of the shallows where it is easier to paddle into the main current. In several areas there have been reports of less fish than in the past. This may be due to *Eichornia* restricting breeding grounds, but it seems more likely to be a measure of the increased difficulty of fishing.

The interference with navigation by paddle steamers in the Nile has already been referred to¹. The plant also interferes with local navigation by small craft, such as the Nilotic ombato canoe and dug out. These primitive boats are unable to hug the shallows where the current is slackest if much *Eichornia* is present along the banks and are forced out into the main stream where paddling is more difficult. At the same time the number of possible landing places is reduced and time and labour have to be spent in keeping clear the small village landing places.

In most areas the effect on animal dry season grazing appears negligible. In some areas where this grazing, exposed by the falling rivers usually called 'toch' in the Nilotic regions of the Sudan, is limited it is possible that the powerful *Eichornia* may restrict the growth of other more valuable forage grasses, whilst also it makes it more difficult for cattle to drink in safety from crocodile infested rivers. An interesting situation is to be found in the lower Sobat. Here the river is choked with the result that the grazing exposed by the falling river is of very narrow extent. The cattle grazed near the river bank during the rainy season are taken towards better pastures along the White Nile during the dry season after the river has begun to fall. The most difficult time for animals along the lower Sobat is during the early dry season after the grass brought by the rains has dried up and before the Nile pastures are ready. At this period of the year *Eichornia* in spite of its low grazing value, provides a welcome source of green matter for the cattle.

Another possibility which could prove serious to the economy of the Sudan is that *Eichornia crassipes* might appear in force in the canals of the various pump schemes. So far this has not happened though many have had to employ labour to clear out the pump intakes. An increase in costs of production however small is serious in the present state of the world market for long staple cotton.

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So far the presence of *Eichornia crassipes* in the Nile has not proved disastrous, though it is making the already hard lives of some of the more primitive river-side inhabitants a little harder. So far it has proved advantageous in only the lower reaches of the River Sobat.

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¹ *Nature*, 182, 538 (1958)

STATISTICS

Estimation of Linear and Non-linear Structural Relations

THE problem considered by Wayman¹ is one example of a wide class of problems which have given rise to a large body of literature in recent years. Lindley² has reviewed the field, and thirty subsequent papers are listed by Barton and David³. Of particular importance is the estimation of non-linear structural relationships. Several methods for estimating the unknown parameters are available, we outline below a method which will often give estimates of nearly optimal accuracy.

We suppose the observations to consist of n pairs (x_i, y_i) with

$$x_i = X_i + u_i, y_i = f(X_i) + v_i \quad (i = 1, 2, \dots, n) \quad (1)$$

where the function $f(X)$ contains unknown parameters to be estimated and where the variances σ_u^2, σ_v^2 of u_i, v_i may be (a) known, (b) known up to a constant factor, or (c) constant but unknown. Case (b) is no more difficult than (a), an estimate of the unknown factor can be obtained from the sum of squares of residual deviations. Further, it may be that the values X_i are (i) unknown parameters (to be estimated), or random variables whose common cumulative distribution $P(X)$ is (ii) known, (iii) of known form but with unknown parameters, or (iv) completely unknown.

Even in the linear case, various difficulties arise. Thus in case (c) the linear relationship may be *unidentifiable* (see ref. 4). Neyman and Scott⁵ have shown that when the number of parameters to be estimated increases indefinitely with n (as in case (i)), the method of maximum likelihood ($M-L$) (that is, least-squares if the residuals are assumed to be normal (Gaussian)) is not necessarily *consistent*. Cases (ii) and (iii) involve only a fixed number of parameters. Jeffreys⁶ method may be regarded as a special case of (ii) with certain conventional assumptions regarding $P(X)$, it is not consistent unless these assumptions are in fact correct. Kiefer and Wolfowitz⁷ have shown that in case (c)(iv), assuming identifiability and that the unknown variances are bounded away from zero, $M-L$ yields consistent estimates of the parameters of the line and of $P(X)$.

In general, three methods other than least-squares are already available. (I) Berkson's assumption of the 'controlled variable' (see ref. 8) which reduces case (c) to case (b), (II) the 'method of moments' in which various relations deducible from $Y = f(X)$ are summed, the sums involving X and Y being then estimated from corresponding sums involving x and y , and (III) obvious extensions of the 'method of dichotomy' due originally to Bose⁹. (I) may be inappropriate, (II) and (III) are consistent (when this is possible) but inefficient.

In cases (ii) and (iii), it is always possible in principle to find the joint distribution of x_i, y_i , and X_i , and to average over X_i , then $M-L$ can be used on the resulting distribution of x_i and y_i . This approach will usually lead to very intractable equations. Barton and David³ have proposed the following approach, which is certainly workable when $f(X)$ is a polynomial, and is nearly optimal when $f(X)$ is substantially linear.

From (1) and $P(X)$ we can find the mean and variance of y conditional on x , say

$$E(y | x) = a(x), \quad \text{Var}(y | x) = b(x) \quad (2)$$

Then we minimize

$$\phi = \sum_i \left\{ \log b(x_i) + (y_i - a(x_i))^2 / b(x_i) \right\} \quad (3)$$

with respect to all the unknown parameters. The argument proving joint asymptotic normality of the resulting estimators follows closely that for $M-L$ estimators, the analytic conditions being a straightforward modification of these. When $f(X)$ is quadratic this procedure leads to three non-linear simultaneous equations which can be solved by iteration.

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A Least-Squares Solution for a Linear Relation between Two Observed Quantities

IN a recent communication with the above title, P. A. Wayman¹ presents a solution to the problem of fitting a straight line when both co-ordinates are subject to error. He mentions some previous attempts to solve this problem, but is evidently unaware of the existence of a monograph by W. Edwards Deming².

Deming presents a completely general method for fitting experimental results by least squares and, when this general method is applied to the specific problem studied by Wayman, the same result is obtained. The statement that the solution only passes through the centre of gravity if this is found by applying a weight w_i to each point is also found explicitly made by Deming³ (Wayman's w_i is identically the same as Deming's W_i).

This republication of a result published first about twenty years ago suggests that Deming's excellent monograph is not as well known to scientists generally as it deserves to be.

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¹ Wayman, P. A., *Nature*, 184, 77 (1959).

² Deming, W. Edwards, 'Statistical Adjustment of Data', (Chapman and Hall, London, 1943).

³ Deming, W. Edwards, *loc. cit.*, p. 181.

THE DEVELOPMENT OF PUBLIC SERVICES IN A MODERN DEMOCRACY

TWO of the most valuable chapters in Dr Brian Chapman's recent book, "The Profession of Government" (London George Allen and Unwin, Ltd, 1959 28s net) are those in which he discusses the public service trade unions, and the relations between public officials and the public. The two subjects are closely connected, and in the compass of little more than a score of pages Dr Chapman focuses attention on some problems of vital importance to the functioning of a democracy, of which there is little evidence that administrators, professional associations or the public generally are aware. Nevertheless, upon the effective solution of such problems the wise use of scientific and technical resources and the very possibility of creative leadership, in the service of the State or elsewhere, may largely depend.

Dr Chapman goes unerringly to the root of the problem with public service trade unions. All the evidence points to the truth that people employed in government service tend to become not only self-governing but also self-employed. Moreover the strength of these unions is in the lower ranks and while in these grades parity with outside employment has been maintained, financially there is a genuine conflict of interest between the various grades of the public service. Unions representing the lower and middle-grade officials will not accept a policy of discriminatory rises for particular grades, and for this financial reason alone, the higher public officials insist on special representation.

Now, while the European public services have acquired most of the characteristics of a profession, even for the higher Civil Service in Britain there is no recognized professional qualification or any general acceptance that the profession should have a monopoly of government. The acquisition of a recognized public status and the growth of professional training schemes in the Civil Service only partly compensate for this lack of a professional qualification. Furthermore, the professional ways of thought of public officials, more especially the senior officials are distinctive, imposed on them by the nature of their duties, and while generally such officials are naturally affected by the way the public regard them and, in consequence, by the underlying philosophy of society and the State reflected in a country's view of public administration, Dr Chapman's comparative survey points to a surprising similarity in attitudes in senior public officials in all European public services.

Dr Chapman emphasizes the dependence of these attitudes on the nature of the officials' duties and not on his social class. In all the countries covered by him, the public official is in social terms a typical member of the middle class, but there are few reliable statistics on the social origins of public officials in Western Europe and it is not possible to

prove that public service is a factor in social mobility. It is certain, however, that social class in the public service does not work in reverse. The sons of members of the administrative class are practically never found lower down the scale, unless they can join at their father's level they enter another profession. It is also clear that the working class and the agricultural population are both under-represented at all levels of the administration in comparison with their proportion in the population.

Nevertheless, Dr Chapman's survey suggests that this question of social origin is relatively trivial, in comparison with the decisive influence of professional duties on their attitudes. Indeed, social class and their duty to society, as well as the nature of their work, alike make senior officials conservative, and their first preference is to keep the peace and maintain the *status quo*. In spite of this, they sympathize with efforts to remove the worst or most noticeable abuses in the fields of government which are their direct concern. Dr Chapman points out that they, frequently more so than politicians are aware of the black spots of society, even though their knowledge may be second hand, and that this instinct for improvement has been responsible for many minor social and industrial reforms throughout Europe, particularly in the newer fields of government. Most frequently, however the instinct to improve is confined to the official's special field.

It is inherent in this that senior officials should incline to believe that they are more disinterested, intelligent and far-sighted than other people engaged in government, and this is due not so much to authoritarianism as to the distrust of the professional for the enthusiastic amateur. Again, awareness of public responsibility and of the impossibility of full impartiality and equality of treatment can also lead to a clash between professional and amateur, and to divergence between official and public. The official is aware that he has to deal with a world that is neither efficient, rational nor equitable, and distrusts the claim that the public has an inalienable right to efficiency, impartiality and rationality. He is also better aware than the public of inconsistencies which may mar their mutual relations.

All this bears profoundly on the two questions which Sir George Schuster discusses in his review of the working of the National Hospital Service in Britain, entitled "Creative Leadership in a State Service". Can a State-directed service be an instrument of dynamic progress and provide scope for individual enterprise and initiative? Can State-directed 'welfare' measures produce true welfare—that is, welfare judged according to a standard of values appropriate to a modern society? These

* Creative Leadership in a State Service. A General Survey (Hospitals and the State Hospital Organization and Administration under the National Health Service. Sixth and final Research Paper.) Pp. III+80 (London: Acton Society Trust, 1959) 4s.

questions, however, may be considered in the light of three major points which Dr Chapman makes as the outcome of his review of Western Europe as a whole.

First, in every country the increase in public services has not been accompanied by sufficient serious thought as to the best way of absorbing them into the structure of the modern State. The haphazard creation of semi-public, public, quasi-private and partly autonomous bodies complicates law, operation and control. Secondly, clarification in this field might help to disentangle some of the more acute problems of public service law. There is no sensible reason, Dr Chapman suggests, why a postman should be a Civil servant and a gas inspector or railway driver should not. Nor is there any serious reason why the vast mass of manipulative, clerical or even executive staff employed in public administration, whose duties are exactly comparable with those in private employment, should not be engaged on private law contracts. A much more vigorous distinction in public administration between public officials and private law employees would both simplify public service law and permit an element of flexibility in personnel matters which is lacking in many countries, and also allow the general unification of the public services to be considered seriously. This is particularly important at the higher levels, where it should promote a proper balance between administrators, managers and technologists, and remove some of the anomalies which disturb the Institution of Professional Civil Servants. It might well be reconsidered whether the chemist, the physicist, the engineer, for example, engaged on professional duties in the Government service, need necessarily be a Civil servant unless those duties include public administration.

Thirdly, Dr Chapman remarks that the recent awareness of the need for better government public relations has gone no further than communicating to the public what the public service concerned is doing, rather than why it is doing it. This is an essential to informed public discussion, but in his reasoned attack on the secretiveness of British Government methods, Dr Chapman is too concerned with the negative effects of secrecy to emphasize the positive contribution of informed discussion to the functioning of democracy. In Western democratic theory, government is the task of representatives of the electorate, and no growth in the complexity of the tasks of government can make government the task of a profession; it can only emphasize the responsibility of the professional administrator for seeing that the implications and consequences of particular decisions and policies are clearly understood by the elected representatives.

The relevance of Dr Chapman's observations and suggestions to the problem of creative leadership which Sir George Schuster discusses in the context of the National Health Service in Britain is apparent from the start of Sir George's analysis. That analysis follows on a general survey of hospital organization and administration under the National Health Service made by the Acton Society Trust, which

vindicated the Government's original purpose to allow the fullest possible decentralization of the Hospital Service. While this should be maintained, the Acton Society Trust points out that the Ministry is still left with a responsibility it cannot abdicate—that of giving inspiring leadership and guidance, interpreting the lessons of decentralized experience, and involving national resources for dealing with the problems that can only be effectively handled on a national basis. In particular, the Trust's survey led to the conclusions that not enough had been done to study and interpret current experience, that a frequently changing junior political Minister is ill-placed to satisfy the need for continuous inspiring leadership in a great operating service, that the Ministry as at present organized does not provide a staff containing enough men with the right kind of knowledge based on practical experience in the field, that this staff is itself hampered by lack of an adequate statistical and intelligence service, and that the Ministry's advisory bodies cannot fill the gap.

Sir George Schuster begins with Mill's prescription—the greatest dissemination of power consistent with efficiency but the greatest possible centralization of information and diffusion of it from the centre, and with Mill's dictum that a Government cannot have too much of the kind of activity which does not impede but aids and stimulates individual execution and development. In emphasizing, however, the intensely human character of a health service and the large number of voluntary unpaid members concerned in its control, Sir George directs attention to two further questions which arise out of those to which he was asked to give special attention. First, how—by what working methods and arrangements—can the preservation of the voluntary spirit of service which is embodied in the boards and committees of management be most effectively combined with adequate power for the Minister to discharge his responsibility to Parliament for ensuring efficiency and economy in the expenditure of public money? Secondly, how can the professional freedom of medical practitioners and surgeons, on whose skill the work of the hospital service ultimately depends, be reconciled with the just claims of public authority?

Obviously, these are essentially the questions that arise in regard to public expenditure on research and on the universities, and the answers Sir George Schuster suggests are of great interest to those concerned with the functioning of the University Grants Committee, public accountability in the nationalized industries and the deployment and balance of the national effort in scientific and industrial research and the control of expenditure in that field. They are questions of far-reaching importance which should be a prime concern of the newly appointed Minister with special responsibility for scientific effort in Britain. Moreover, while Sir George Schuster does not deal to any extent with the question of professional freedom, he has raised a general issue which demands the attention of professional bodies generally, and the importance of which in its broadest context has also been admirably stated by Sir Solly

Zuckerman in his recent address (see *Nature*, July 18, p 135) delivered at the California Institute of Technology

It is no disparagement of the importance of the National Health Service to suggest that Sir George Shuster's pamphlet is of even wider public interest in the context of the problem of government generally, the place and use of the expert in public affairs, the responsibilities of professional organizations and the functions and staffing of the Civil Service. Like Dr Chapman, he displays issues where fresh thought is urgently required practices which require critical and independent examination, and preconceived ideas and even traditions which should be challenged. It is to be hoped that the place of his pamphlet in the survey of the National Health Service made by the Acton Society Trust will not lead other professional associations, or indeed the scientist and technologist generally, to miss the challenge to creative leadership which he offers to them no less than to the medical profession itself.

BRITISH INDUSTRY

The Structure of British Industry

A Symposium Edited by Duncan Burn Vol 1 Pp xvii+403 45s net Vol 2 Pp vii+499 50s net (National Institute of Economic and Social Research) (Cambridge At the University Press 1958)

FOR a long time the best general account of the main British industries in a single book has been Prof G C Allen's famous work, 'British Industries and their Organisation', first published as long ago as 1933 though modernized in successive editions since. The two volumes here under review constitute, therefore the first new major attempt for a long time to provide something which, in principle, every British student of economics (and many overseas students) would like to have.

As a new standard text book and work of reference, this book has very great strength, but also, inevitably some weaknesses. Its strength is that it calls upon an extremely able team of writers many of them fresh from, or still engaged in, the task of writing larger monographs on the industries which they here discuss the rest, who have made investigations for the sole purpose of their contributions to this symposium remarkably well selected and successful. Its weakness is that it lacks the uniformity which can be achieved by a single author, asking roughly the same questions about a number of industries. Apart from setting out the facts of size and number of firms the different contributors adopt a variety of approaches which makes the editor's gallant effort to treat some matters of general interest in his final chapter a difficult one. The student may also find the size and cost of this important work formidable.

It would be wrong, however, to judge it merely as a text-book. It is an important fact about economic studies that in the past decade or two, while at their theoretical end they have been accused of becoming more difficult for the practical man to understand, they have undeniably gained enormously in realism through economists consorting with practical men, either as Civil servants or as students of industrial problems in the field. No one man can nowadays attain to comprehensive first hand knowledge of a

wide range of industries, as Alfred Marshall was able to seventy years ago—hence the necessity for a symposium—but the intimacy of the knowledge attained by the contributors and the fundamental nature of the questions which some of them attempt to answer on such matters as pricing policy, are evidence of the increased penetration of economists generally into the realities of industrial life.

A list of the industries dealt with shows the wide scope of these volumes: agriculture, building road and rail transport, coal, oil, chemicals, steel, building materials, machine tools, motors, aircraft, shipbuilding, electronics, cotton and rayon textiles, woollen and worsted, man made fibres, pottery, pharmaceuticals, and outlery. It suggests too the variety of different atmospheres to be dealt with ranging from those dominated by State policy, as in the case of agriculture and aircraft production to the predominantly private commercial atmosphere of, for example, the pottery industry, or from ferment of technological change as in electronics or pharmaceuticals to the static environment of wool textiles. It need scarcely be said that the nature, possibility and meaning of competition vary enormously from one industry to another. The more closely one looks at most industries (even those which are in some sense the most 'competitive'), the further they appear to lie from the old model of 'perfect' competition between firms making exactly similar products. The nearest simple model of wide application, indeed, would seem to be that of oligopolistic competition, between firms which compete directly (or not quite directly) with a fairly small number of others—though with the important reservations that 'potential competition' often from users of the product who might turn to manufacturing it themselves, is frequently just round the corner, and that the weapon of competition is increasingly often an improvement in design rather than a reduction in price. Nearly everywhere there is some evidence of increasing concentration, but in very many places the small firm is remarkably viable, not by any means always for the same reason. Where concentration has gone so far as to create monopoly power it becomes very evident that this power though it may not be harmless, is subject to a variety of checks, quite apart from those imposed by legislation. The case of coal where absolute monopoly is itself the product of legislation, shows how powerful the restraint imposed by competition from quite different products can be.

The question how far the structure of British industry conduces to high and increased efficiency is one which, again, admits of no simple answer. The very general impression indeed, is that the adjustments of the past twenty years have been made with reasonable smoothness and with gains of efficiency which are often striking. This however, should not lead the reader into complacency. The contributors to this work have the relatively pleasant task of portraying British industry on the favourable wicket of expansion in the national economy and in world trade. It is a very different story from the agonizing chronicle of difficult contraction in so many of the basic industries between the Wars. It may be as well to reflect that, while we may hope never again to see general stagnation of the economy or a major depression in its total activity, we have given a number of hostages to fortune in, for example, motors and shipbuilding, which may find how much more difficult it is to be progressive in adversity than in prosperity.

A J BROWN

TURNING POINTS IN PHYSICS

Turning Points in Physics

A Series of Lectures given at Oxford University in Trinity Term 1958 By R J Blin-Stoyle, D ter Haar, K Mendelssohn, G Temple, F Waismann and D H Wilkinson (Series in Physics) Pp v+192 (Amsterdam North-Holland Publishing Company, New York Interscience Publishers, Inc, 1959) 20s

DURING Trinity Term, 1958, a series of lectures was organized by the Reader in the Philosophy of Science and the Lecturer in the History of Science in the University of Oxford. The lectures, collected in this volume, are (1) "The End of Mechanistic Philosophy and the Rise of Field Physics", by Dr R J Blin-Stoyle, (2) "The Quantum Nature of Matter and Radiation", by Dr D ter Haar, (3) "Probability enters Physics", by Dr K Mendelssohn, (4) "From the Relative to the Absolute", by Prof. G Temple; (5) "The Decline and Fall of Causality", by F Waismann, and (6) "Towards New Concepts Elementary Particles", by Prof D H Wilkinson. The audience to whom they were originally addressed was composed of philosophers and scientists who were not physicists. The publishers suggest that they can be understood by laymen. I have the word of an historian colleague, who recommended the book with great enthusiasm for the general library, that this is so. He had some reservations, it is true, about grasping all the points raised, and it is not exactly light reading, even for the scientist. As an account of the origins and development of the present state of theoretical physics it is most stimulating, and to be able to communicate so much of the physicist's outlook at a non-specialist level is a magnificent achievement.

The title "Turning Points" is itself significant. Thirty or forty years ago classical physics was spoken of in rather dismal terms of 'downfall', by inference, the supplanting modern physics was undergoing uplift—and it apparently did, quite out of this world. But the outcome of all this has not been depression or exaltation, nothing less than a complete re-orientation of all our ideas has been necessary, and this turning has not really been a sudden event. As the first lecture points out, the fulcrum was effectively set up by Faraday, and the statistical approach goes back nearly as far—but applied only to classical particles. The quotation from Niels Bohr—"My method is to try to say what I cannot say, because I do not understand it", Dr Waismann's statement that quantum physics presents a strong case against traditional logic, and Prof Wilkinson's remark that the first stumbling block for people who want to understand the elementary particles is that some of the things they learn run counter to common sense, between them emphasize the kind of turning that is demanded. In the macroscopic world of everyday life, we can 'understand', use classical ideas, relate matters as 'cause and effect', work to the rules of logic, and be guided by common sense. In the microscopic world of atomic physics, none of these things can happen. The physicist has to live a life of double-dealing between two worlds—observing with macroscopic apparatus, and interpreting in terms of microscopic concepts which have no counterparts in ordinary life, either in essence or in behaviour. Each of the lectures shows clearly the terms of reference within which modern physics operates.

Rule out causality, mechanical particles, identifiable individual particles, and the appeal to analogy taken from everyday life, and what is left of the microscopic world except concepts that can only be handled as mathematical abstractions? This question, which is the real difficulty facing the ordinary reader (and most of us older physicists as well), is squarely met in the contributions of Prof Wilkinson and Prof Temple. The answer is, general invariance or symmetry or conservation conditions, and 'properties' (if that is the term) to which such conditions can apply—such as Newton's third law of motion (Temple) or the conservation of isotopic spin (Wilkinson), which seem indeed to have much in common.

Illustrations and examples strike a fresh and original note. The derivation of the Lorentz transformation (Temple) is neater and simpler than that in the text-books. The conflict between causality and the uncertainty principle (Waismann) is illustrated by idealized experiments, and numerous examples of the application of the principle are given. The account of the elementary particles (Wilkinson) is both up to date in content and superb in its clarity, the author does not, of course, lament that physicists are large compared with m_e , and long-lived by K -meson standards—but he mentions that this immense difference in scale prevents us from even being able to describe the microscopic world in ordinary language at all. The lighter touches and personal reminiscences that drop into place here and there suggest that the authors were thoroughly enjoying their task, they must have done, to be able to accomplish it so brilliantly. G R NOAKES

CATALYTIC PROCESSES AND PETROLEUM

Catalysis

Edited by Prof Paul H Emmett Vol 6 Alkylation, Isomerization, Polymerization, Cracking and Hydroreforming Pp vi+706 (New York Reinhold Publishing Corporation, London Chapman and Hall, Ltd, 1958) 150s net

THIS volume is the penultimate one in this very comprehensive series, it deals with the catalytic processes that have now such an important place in the petroleum industry. The editor is to be congratulated on this further stage of his monumental task and in particular on achieving a very reasonable uniformity of treatment in the six 'chapters' written by eleven authors. Each chapter forms a clearly defined section dealing with an important refinery operation involving catalysis and comprising alkylation (with 59 references), isomerization (322 references), polymerization of olefins (212 references), catalytic cracking (126 references) and reforming (164 references), together with a chapter on the mechanism of polymer formation and decomposition (374 references). The large number of references makes the volume a valuable starting point for further study, particularly to chemists entering the petroleum and petrochemicals field. At the same time the authors have accepted the responsibility of surveying this mass of literature and presenting it as a coherent account and not simply as a collection of abstracts. Earlier volumes in this series dealt, of course, with the fundamentals of catalysis, so that the authors here are free to deal with the more specialized and prac-

tical aspects This still leaves a large field to be covered and in most cases the authors set clearly defined limits to the subjects they discuss.

Alkylation is dealt with in a clear and concise manner, and the comment in this chapter that "the development of a body of knowledge in alkylation embraces in chronology the development of highly precise analytical distillation methods and spectroscopic identification methods for hydrocarbons" can apply to each chapter in turn. It is interesting, though possibly fruitless, to speculate on the course of events if our modern techniques of hydrocarbon analysis had been available to the pioneers in this field.

In the chapter on isomerization, a much more complete treatment is attempted under the headings "General Aspects and Mechanisms", "Kinetics" and "Equilibria". The treatment is very systematic and will be of particular value to research workers entering this field. It is irritating, however, to find bracketed explanations such as " BF_3 (boron trifluoride)" and even " I_2 (iodine)" in a book of this type. The chapter on mechanisms of polymer formation and decomposition follows, its scope being clearly defined and topics such as polycondensation, copolymerization and hydrolytic and enzymatic cleavage reactions are included. This is an excellent survey of the specified fields. Polymerization of olefines is the subject of the next chapter, the presentation being limited to liquid polymers only, ranging up to lubricating oils and viscosity index improvers. After an excellent discussion of the thermodynamics and mechanisms, commercial processes are dealt with in moderate detail. The behavior of pure hydrocarbons is the main theme of the chapter on catalytic cracking, the commercial processes being discussed only briefly. This again is a necessary limitation in such a wide field. A list of twelve phenomena is given, which it is suggested an acceptable theory of catalytic cracking should explain. The poisoning action of nitrogen bases, a discussion of which immediately precedes the list, might well have been added to it. The final chapter, on catalytic reforming, includes a good deal on the commercial processes and is again a valuable survey.

The printing and diagrams are up to the high standard one expects, and the volume will certainly join the others of the series as an important contribution to the literature of chemical industry in the widest sense.

DAVID M. WILSON

SEX ON THE FARM

Reproduction in Domestic Animals

Vol. 1 Edited by H. H. Cole and P. T. Cupps. Pp. xv + 851. (New York: Academic Press, Inc., London: Academic Press, Inc. (London), Ltd., 1959.) 14.50 dollars.

THIS book, when the second volume is published, will have to stand comparison with such well known treatises as "Allen's Sex and Internal Secretions", a third edition of which is in preparation, "The Hormones", edited by Pincus and Thimann, and, above all, "Marshall's Physiology of Reproduction", publication of the third edition of which began in 1952 and is not yet complete.

The present volume opens with two chapters on the anatomy of the male and female reproductive organs and is thereafter almost wholly concerned with the female. There are four chapters, three of

which are of a fundamental nature, dealing with the role of various hormones and of the nervous system in reproduction. After five chapters describing the oestrous cycle of farm animals and the bitch (apparently the cat is not considered a domestic animal), fertilization, implantation, the physiology of the placenta and pregnancy, and parturition are covered in four chapters. The volume ends with a chapter on lactation.

In the space available it is impossible adequately to write a critical appreciation of so important a book, all that can be done, at the risk of appearing invidious, is to refer to those topics which particularly interest the reviewer. He well remembers the absorbing interest with which he read in 1939 C. G. Hartman's outstanding chapter in "Sex and Internal Secretions" (second edition). Does the present volume contain a chapter comparable with this? This is scarcely to be expected since the power to write so vividly is unfortunately rare. Perhaps C. W. Emmens's contribution on the role of the gonadal hormones in reproduction comes closest, for it is written in a flowing style and deals lucidly with a complicated subject. Miriam E. Simpson gives an authoritative and well written account of the pituitary and other gonadotrophins, though her treatment of the subject might appear to be orientated towards man rather than farm animals. C. W. Turner's chapter on the thyroid, adrenal cortex and posterior pituitary hormones is something of a mixed bag, heavily over-shadowed by a discussion of practical applications of thyroid physiology in the domestic fowl and farm animals, a subject which might well have been assigned a chapter on its own. The adrenal cortex and posterior lobe hormones could easily have been expanded to separate chapters. T. J. Robinson's contribution is noteworthy for an interesting and largely first-hand account of how the oestrous cycle of the ewe can be manipulated hormonally with the view of increasing fertility. It includes a short section on the 'doe' which, despite the 'Shorter Oxford English Dictionary', turns out to be the female goat. The brevity of this section reflects the paucity of experimental work on this species and it is the more surprising that a ten year old paper by the reviewer and his colleagues on out-of-season breeding was overlooked. J. Meites contributes a comprehensive review of mammary physiology with much of which the reviewer has little quarrel, though two points merit mention. Even considering that the chapter must have been written nearly two years ago, it is surprising to learn that somatotrophin has no major role in mammary growth, and also to see cogent evidence for a role of oxytocin in the release of prolactin dismissed so summarily.

A book of this nature must be considered as a whole rather than as a collection of isolated essays, and if it is to be successful the editorial guiding hand must be all pervading, if unobtrusive. One criticism of the present book is that there is too little evidence of editorial co-ordination. For example, posterior pituitary hormones, principally oxytocin, are dealt with in several chapters but with little cross referencing, the same applies to relaxin. The value of the book to the reader would have been much enhanced had adequate cross references been given in these and many other instances. A number of other blemishes could have been eliminated by sterner editorial action. There are infelicities such as the use of "beef" and "pork" to describe pituitary glands from the ox and pig (yet "mutton" is not

used for sheep pituitaries, as it should have been for consistency), and the widespread use of the inept term "let-down" which the reviewer thought he had knocked out twelve years ago, but which has persistently refused to lie down. There are some inconsistencies such as the use of "dog" rather than "bitch", while the females of the ox, horse, sheep and pig are called "cow", "mare", "ewe" and "sow". Bibliographical errors are also more frequent than they ought to be, particularly in Chapter 7. British readers are by now inured to what seems to be becoming standard American practice in the use of prepositions (two of the more startling examples being "identical to" and "different than"), but in a book of this calibre one would not expect to find a sentence like (p. 163) "A hypothyroid monkey put on a very low thyroid dosage for a period of ten days always resulted in the return of menstrual function".

The main justification for the publication of this book in face of the well-established and authoritative treatises mentioned at the beginning of this review must lie in its emphasis on farm animals and its relatively modest price, which will bring it within the reach of the private purchaser. Is this publication justified? On the showing of this first volume the reviewer thinks so, despite the criticisms mentioned above, and he is glad to recommend it.

S. J. FOLLEY

HÆMOGLOBIN AND SENSORY MECHANISMS

Progress in Biophysics and Biophysical Chemistry Vol. 9 Edited by Prof. J. A. V. Butler and Prof. B. Katz Pp. vii + 388 (London and New York: Pergamon Press, 1959) 105s net

FOLLOWING the present reviewer's criticism in *Nature* of the previous volume of this series on the grounds that few of the articles matched up to the aims stated in the preface, the editors have prudently suppressed the customary preface in this volume. Perhaps they need not have feared, their aims may well be achieved, for five out of the seven articles are written in such a way as to be intelligible and interesting to non-specialists in their subjects. Two of these articles have the special flavour that only comes when a scientist with a flair for exposition describes the development of a subject he has himself largely invented and contributed to. These are F. J. W. Roughton on the kinetics of oxygen and carbon monoxide uptake by red cells and by solutions of hæmoglobin, and W. A. H. Rushton on visual pigments and their measurement in the living human eye. The book opens with an enthusiastic and highly interesting account by Q. H. Gibson of the rapid reactions of hæmoglobin with gases. The last article which can be recommended without reservations as to style or scientific content is that in which J. A. B. Gray describes what is known of the way sensory endings, sensitive to mechanical change, convert mechanical energy into streams of nervous impulses; he illustrates the argument mainly from his own and his collaborators' pioneer work on the Pacinian corpuscle.

It would have been churlish to exclude the article by D. A. McDonald and M. G. Taylor on the hydrodynamics of the arterial circulation from the category 'intelligible and interesting', but after reading it I

found I was not convinced either that their problem was an important one, or that they had advanced much towards a solution.

The two remaining papers are by A. Peterlin on molecular dimensions and light scattering (fifteen pages of references) and by C. de Duve, J. Berthot and H. Beaufay on gradient centrifugation of cell particles. Both of these appear to be competent and clear descriptions of the theory and practice of their highly specialized techniques, which would no doubt be of great convenience to anyone directly concerned. But this volume is supposed to be about progress. Is a technical description of the methods by which progress may have been achieved in the past and by which it is hoped to achieve it in the future any substitute for a critical account of progress? It certainly makes very much duller reading than the real thing. Fortunately, there is plenty of the real thing in this mainly excellent work.

P. A. MERTON

COLOUR REPRODUCTION

The Reproduction of Colour

By Dr R. W. G. Hunt Pp. 208 + 10 plates (London: Fountain Press, 1957) 63s net

THIS book expounds the principles and the crucial technical devices of the processes used in colour reproduction in photography, printing and television. Many of these processes are now extremely intricate—for example, the action of the couplers of various kinds used in colour photography and the coding and transmitting of colour information on television wave-bands of limited width. In the difficult task of explaining essentials in an easily read text with clear and simple diagrams and a minimum of mathematics, the author has been highly successful. A course of lectures (Royal Institution, 1953) was the starting point and much of the freshness and intimacy of a good lecture style has been preserved.

A common element linking all the reproduction techniques is a dependence on the basic ideas of colorimetry and the perception of colour by the human eye, fields in which Dr Hunt's own researches are well known. The exposition here is unexceptionable and, most important, it has not been allowed to expand unduly so as to upset the balance of the work. Colour reproduction techniques, in their primitive form, are not capable—even theoretically—of giving exact reproduction, and much of what Dr Hunt has to say concerns colour correction methods. The nine-page chapter on the general masking method in photography and the discussion of developments from Neugebauer's analysis of dot image reproduction in printing are particularly informative brief-accounts. The difficulties of assessing the 'quality' of the final result in colour reproduction are well brought out, with emphasis on the inadequacy of a demand for a simple point-to-point correspondence with the original.

Although the book appears to be addressed mainly to a rather lay circle, that is to say, people having to do with colour pictures in various ways but not experts, it is certain that many readers, knowledgeable in one area of the wide field covered, will find most useful this insight into related techniques. In the quality of the coloured plate illustrations the publishers have not failed the author. W. S. STILES

Excursion Flora of the British Isles

By A. R. Clapham, T. G. Tutin and E. F. Warburg
Pp xxxiv+578 (Cambridge At the University Press, 1959) 22s 6d net

THIS volume has been developed from Clapham, Tutin and Warburg's "Flora of the British Isles", published in 1952, by curtailing descriptions to little more than is needed for identification, by omitting all information not strictly relevant to identification, by omitting most of the rarer mountain species and by simplifying the accounts of such critical genera as *Rubus* and *Hieracium*. The result is very considerably to reduce the time taken in using the keys and substantially to cut down the number of wrong turns that a beginner can take. The book also is a bare three-quarters of an inch thick as against the solid two inches of the original.

In practice, it has been found that even a beginner can identify plants satisfactorily with the aid of the excellent glossary, which has been retained from the original work, and the authors must be congratulated most warmly on having produced such a practical book with up-to-date nomenclature and equally up to date information. In these ways their work is beyond criticism. There are, however, two gaps to be filled. The first is illustrations, and this could easily be filled by a companion volume taken from the illustrations to the larger volume by Sybil Rodes Vol. 1 of which has already appeared. Her line drawings in this case with only one to the page and with only those species here included, would make an invaluable supplement. Our other need is for a student's flora in *Hooker's* sense. The present volume could easily be modified for this purpose by the addition of something comparable to *Hooker's* synopsis of natural orders and natural arrangements of families. P. FALK

Soil Chemical Analysis

By Prof. M. L. Jackson Pp xiv+498 (Englewood Cliffs, N.J. Prentice-Hall Inc. London: Constable and Co., Ltd., 1958) 57s 6d net

THE seventeen years that have elapsed since the publication of Piper's "Soil and Plant Analysis" have seen rapid advances in the subject of soil chemical analysis, notably by the widespread adoption of spectroscopic techniques, and a considerable need has been felt in recent years for an authoritative up to date treatment of methods of soil analysis. It is fortunate that Prof. Jackson has undertaken the task of meeting this need, because his diversity of interests and long experience of the complex problems of soil analysis have enabled him to write a book that is much more than a collection of recipes. Within the compass of 500 pages he deals adequately with nearly all the techniques employed in modern soil chemical analysis and also finds space for alternative methods of analysis. This coverage has been achieved by judicious selection of methods and references, concise writing and good organization of the subject material (every paragraph is numbered to permit cross reference).

It is easy to criticize a book of this type, and some analysts will undoubtedly question the omission or inclusion of certain procedures. There are a considerable number of typographical errors, the index is rather inadequate and the relevance of some of the quotations under the chapter titles is obscure. However, these are minor defects, and this work deserves praise rather than criticism. The book is

well illustrated, reasonably priced and generally well produced, although a more suitable type of paper could perhaps have been found for a book that seems destined to spend much of its life on laboratory benches.

This work is indispensable to anyone concerned with soil chemistry. It should be particularly welcome to teachers, because it includes suggestions for a laboratory course, pertinent questions at the end of each chapter, and admirably concise discussions of the principles of various methods. J. M. BRENNER

Curare and Curare-Like Agents

Edited by D. Bovet, F. Bovet-Nitti and G. B. Marin Betteolo Pp xi+478 (Amsterdam Elsevier Publishing Company, London D. Van Nostrand Company, Ltd., 1959) 85s

THIS book is the outcome of an international symposium held in Rio de Janeiro in August 1957. It is very different from previous monographs on curare and from the now familiar pattern of conferences of which the names of the participants can almost be predicted from the title. Both the wide scope of the book and the large number of contributors from South American countries are welcome innovations. The home countries of the curare alkaloids have provided specialists reporting on the botany, history and ethnology of curare, on the methods used to prepare the poisoned arrows on the survival in present days of the use of curare for hunting purposes. Other parts of the book deal with classical organic chemistry, pharmacology and clinical uses of curare and its synthetic substitutes, there are fascinating speculations on the receptor-drug interaction, which is no longer considered as a stable equilibrium but as a dynamic process in which not only the drug but also the receptor may suffer deformation and therefore changes in the course of time. The book is well produced, the autoradiographs (in P. G. Waser's article) of end plate regions of muscle poisoned with decamethonium are particularly beautiful. MARTIN VOGT

Outline of Historical Geology

By A. K. Wells Fourth edition revised with the assistance of J. F. Kirkaldy Pp xv+398 (London George Allen and Unwin, Ltd. 1959) 32s net

A. K. WELLS'S "Outline of Historical Geology" was first published in 1937 and was then intended as an introduction to the stratigraphy of Great Britain for the general reader presented in such a way as to stress the cultural or philosophical value of historical geology. Later editions, written with the assistance of J. F. Kirkaldy, enlarged the scope of the work to make it more suitable for the use of students reading for a degree in geology or geography. In the present fourth edition, further improvements and additions have been made. A new chapter has been included on the Pre Devonian rocks of Scotland, which incorporates the results of recent research on Highland stratigraphy and structure. New data on the Pre Cambrian of Shropshire, on the nature of the chalk, and on the Wealden 'delta' are also included among the revisions that have been made. Selected references now appear at the end of each chapter. Despite the pressure of new facts, the authors have contrived to maintain the emphasis on principles, in accordance with the aim with which the first edition was introduced, rather than the mass of detail into which the teaching of stratigraphy can too easily degenerate.

PREPARATION OF DIAMOND

By Drs H P BOVENKERK, F P BUNDY, H T HALL*, H M STRONG
and R H WENTORF, Jun

Chemistry Research Department, General Electric Research Laboratory,
Schenectady, New York

IT would be good to be able to write a paper entitled "The Preparation of Diamond", in which all the factors affecting diamonds were nicely accounted for and the formation of diamond was completely explained. But the work which has been carried out on this problem indicates that diamond can form in several different ways, and that stubborn mysteries still surround some of them. This article, therefore, is more of the nature of an interim report which describes the salient features of the knowledge obtained so far rather than a complete exposition of diamond formation.

All the observed cases of diamond preparation in our laboratory have occurred at pressures and temperatures appropriate for the thermodynamic stability of diamond. Fig 1 shows a diamond-graphite equilibrium curve. For temperatures up to 1,200° K the path of the curve has been estimated by Rossini and Jessup¹, Simon² and others from thermodynamic data. For temperatures between 1,500 and 2,700° K, the path of the curve has been determined experimentally by observations of the growth or disappearance of small diamond crystals immersed in suitable media³.

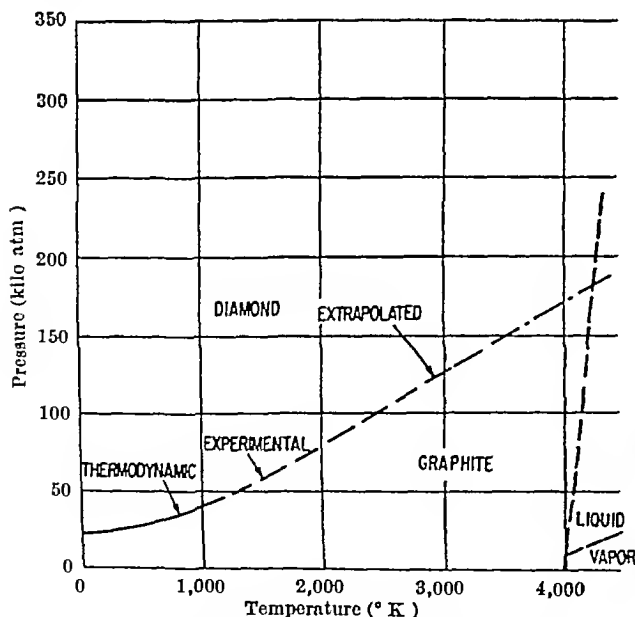


Fig 1 Carbon phase diagram

The experiments which form the basis for most of this article were usually performed in a tapered piston apparatus capable of very high pressures which enabled us to attain diamond stability at high temperature. Figs 2a and 2b illustrate the tapered piston 'belt' apparatus which will be discussed in detail by H Tracy Hall in a separate paper submitted for publication. Many of the most promising systems were examined at several pressure-levels as appropriate apparatus was developed. Diamond.

* Now at Brigham Young University, Provo, Utah

does not always form where it is thermodynamically stable, this is what makes diamond synthesis so interesting.

The chemical systems which were studied in connection with diamond synthesis can be conveniently grouped as follows: (1) direct transition, graphite to diamond, (2) systems involving carbon and oxygen, (3) systems involving carbon as salt-like carbides, (4) miscellaneous chemical reductions, and (5) systems involving carbon dissolved in molten metals.

(1) Direct Transition, Graphite to Diamond

The driving force for this reaction is the increase of density upon going from graphite to diamond. On the other hand, the high heat of vaporization of carbon (more than 100 kcal/gm. mol) implies that a high temperature will be necessary before much recrystallization of the carbon occurs. Indeed, the

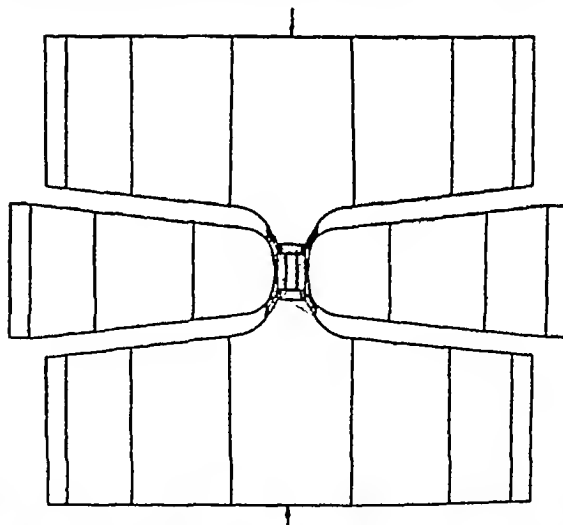


Fig 2a The 'belt', ultra-high-pressure, high-temperature assembly

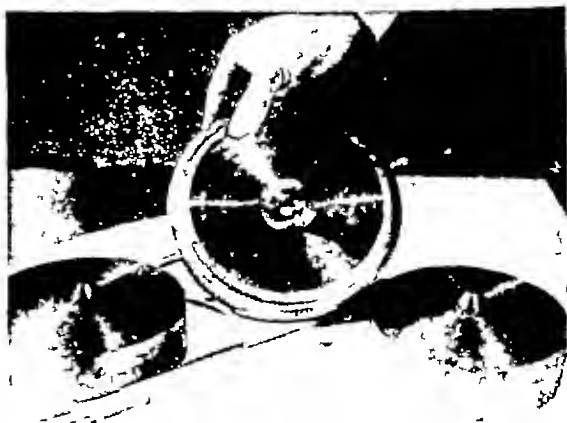


Fig 2b. Photograph of apparatus

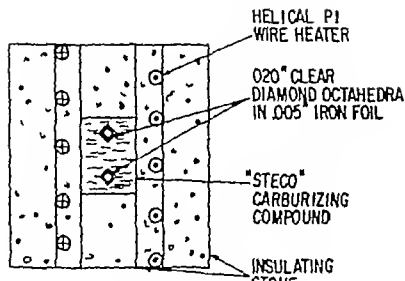


Fig. 2c. Diamond experiment

usual range of temperatures for forming graphite industrially from petroleum coke, pitch, etc. is about 1,800–2,400°C, and some carbons graphitize only slightly at temperatures higher than these.

Some studies made in this laboratory of the graphitization of diamond at 0.1 and 20,000 atm. showed that the graphitization began at 1,600–2,000°C, depending on the particular diamond, and that, in general, higher temperatures were necessary to graphitize diamond at 20,000 atm. than at 0.1 atm. From the change in rate constant with pressure, the volume of the 'activated state' was estimated at about 100 c.c./mol, and the rate of graphitization, in atoms per second, was observed to be 10^3 times the rate of evaporation for the same temperature. This indicated that the diamonds became graphitized by groups of atoms rather than atom by atom. For the reverse reactions, graphite to diamond, it would be reasonable to expect a similar reaction mechanism, because the strong intra-sheet binding forces in graphite would tend to make each sheet behave as a unit (as happens in the formation of 'graphite sulphate' or potassium graphite). Although the coherent sets of sheets of atoms ('crystallites') in graphite or various carbons contain perhaps only 10^4 or 10^5 atoms, the pressure volume energy of such a crystallite is large compared to kT at only moderate pressures (20,000 atm.). It is known that in some carbons the crystallites are rearranged only reluctantly to form commercial graphite even at 2,700°C and 1 atm. Thus the effect of increasing pressure is to slow down greatly any recrystallization of solid carbon, and thus slowing down more than offsets the thermodynamic driving force toward diamond gained by increasing the pressure. Experiments in which graphite was heated at high pressure served to squeeze the microscopic voids from the material so that its density became nearly the theoretical density of graphite, but no diamond was formed, even at 120,000 atm. Perhaps diamond could crystallize from molten carbon at a sufficiently high pressure, but supposing the melting temperature of carbon to be 4,000°C at this high pressure, one would estimate by an extrapolation that the required pressure would be in the neighbourhood of 200,000 atm. (The increasing incompressibility of graphite with pressure indicates that the required pressure might be even higher than this.) Such an experiment has evidently not yet been performed.

(2) Systems Involving Carbon and Oxygen

Such systems are attractive because they are chemically versatile and tend to favour aliphatic rather than aromatic carbon-carbon bonds. The

oxide mineral inclusions in natural diamonds⁴⁻⁶ suggest that perhaps certain oxides could play a part in diamond formation, perhaps through a shift in the carbon monoxide-dioxide equilibrium. In spite of all these attractive features, only graphite or amorphous carbon ever appeared as products from these systems, with one possible exception. This exception was the reduction of lithium carbonate by lithium metal at high pressures. The carbonaceous residue gave a feeble Debye-Scherrer pattern for diamond and scratched glass in a way characteristic of diamond (tiny helical chips were ploughed out of the scratches). A few tiny triangular faces, 1–10 μ on edge, could occasionally be seen but not identified. Further experiments did not produce more abundant or larger crystals.

Other systems which were examined included similar reductions of carbonates oxalates or formates by metals: the decomposition of iron molybdenum or chromium carbonyls either pure or in solution in stannic chloride or molten salts, the decomposition of sugars and ketones, the electrolysis of molten carbonates or finally, the attempted solution and transport of elemental carbon in various molten oxides such as borates, silicates, phosphates, blue ground⁷, etc.

(3) Systems Involving Carbon as Salt like Carbides

These systems are attractive because they are comparatively rich in carbon, contain carbon atoms as free ions which could easily be built into a diamond lattice after a simple reduction and are chemically active at low temperatures. However, only the high pressure decomposition of lithium carbide by the outward diffusion of the lithium ever yielded any potentially diamondiferous product. The material from this decomposition gave a weak Debye-Scherrer diamond pattern, corresponding to a diamond content of about 1 per cent, and also scratched glass to leave the characteristic helical chips.

Other more disappointing reactions included the decomposition $2MgC_2 \rightarrow Mg_2C + C$ the cyanamide reaction $CaC_2 + N_2 \rightarrow CaCN_2 + C$ the electrolysis of calcium or lithium carbides, and the substitution reaction $SiC + Ce \rightarrow SiCe + C$.

(4) Miscellaneous Chemical Reactions

Carbon disulphide is thermodynamically unstable at ordinary pressures and temperatures. At pressures about 45,000 atm. and 400°C it was found to change into the black solid described by Bridgman⁸. In combination with various metals used as catalysts or reducing agents, carbon disulphide changed into amorphous carbon at higher temperatures and pressures. Similar reductions of chloroform, carbon tetrachloride or cyanides formed amorphous carbon.

Hannay's method was tried in which lithium light hydrocarbons and nitrogen-containing substances were heated together at high pressure. Again only amorphous carbons appeared. The simple thermal decompositions of various hydrocarbons yielded similar products, and no diamond.

(5) Systems Involving Carbon dissolved in Molten Metals

These systems turned out to be the most fruitful and also, unexpectedly, the most complex.

In our early work, when available pressures were still less than about 50,000 atm. some experiments

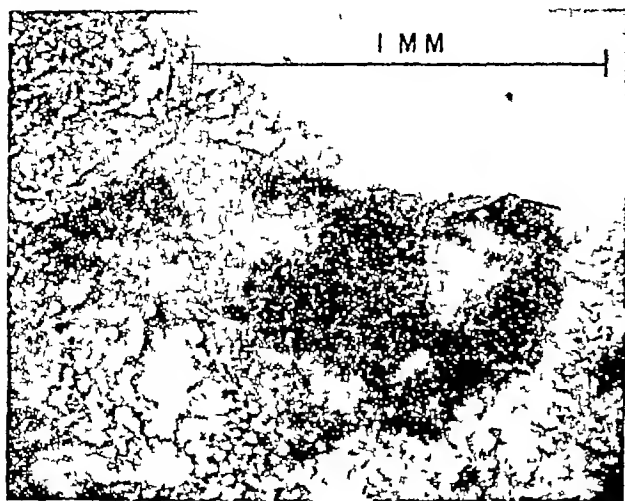


Fig 3 Diamond in metallic matrix

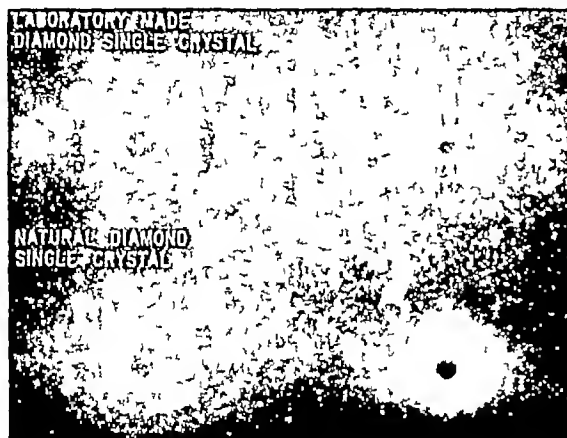


Fig 4 Debye-Scherrer patterns

were performed with molten aluminium, silver, and even iron. Of course, iron dissolved carbon in appreciable amounts, but the carbon which was precipitated from it was in the form of graphite. No matter how careful the change or how great the fluctuation of temperature, when the pressure was less than 50,000 atm, only graphite resulted. In view of this, it is difficult to see how Moissan's claim to have formed diamond from molten iron-carbon mixtures inside his quenched iron could be sustained, since he could have reached at most only 10,000 atm.^{8,9}

A number of experiments were performed using a metallic catalyst and carbonaceous material. One of the first experiments carried out involved heating some seed diamond crystals, iron and a carbonaceous steel-carburizing compound for 16 hr at about 53,000 atm and about 1,300°C (Fig 2c). Out of this there appeared two new diamond fragments with developed crystal faces, each of which was larger than any of the seed crystals. The identification was made by hardness tests and an X-ray diffraction pattern (Figs 3 and 4). Attempted repetitions of this experiment did not produce diamond. However, it now appears that the iron-carbon system is quite complex at high pressures and temperatures. Several solid phases can form, among them FeC, Fe₃C, graphite and diamond, but which one happens to form depends upon slight variations in temperature, temperature change or chemical composition. Even at 100,000 atm, certain temperature programmes

will not permit any diamond to form from iron-carbon mixtures.

Shortly afterwards, a mixture of iron-rich iron sulphide together with carbon and tantalum, as shown in Fig 5, was heated at about 1,600°C at about 95,000 atm. The heating time was short, less than 10 min. On the tantalum end disks there formed tantalum carbide, and on top of this lay a black crusty layer of small diamond crystals (Fig 6). They were identified by their hardness, combustibility and X-ray diffraction pattern. The experiment was successfully repeated many times.

Soon other substances were found to be effective as catalysts for the conversion of carbon into diamond at pressures ranging from 55,000 to 100,000 atm, and temperatures ranging from 1,200 to 2,400°C. They were chromium, manganese, cobalt, nickel, palladium, platinum, etc., or compounds which would react to give the free metals under these conditions, for example, nickel oxide, ferric chloride, etc.

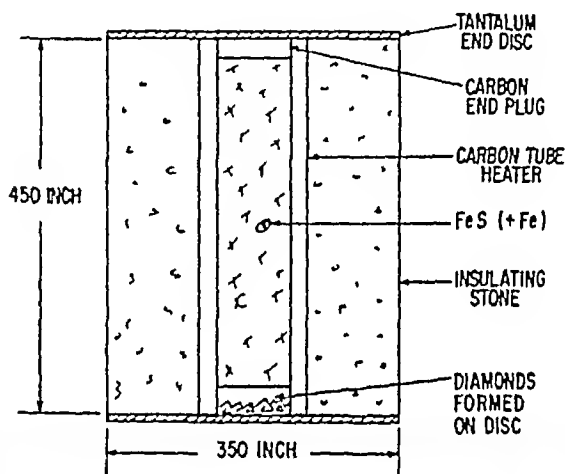


Fig 5 Diamond experiment

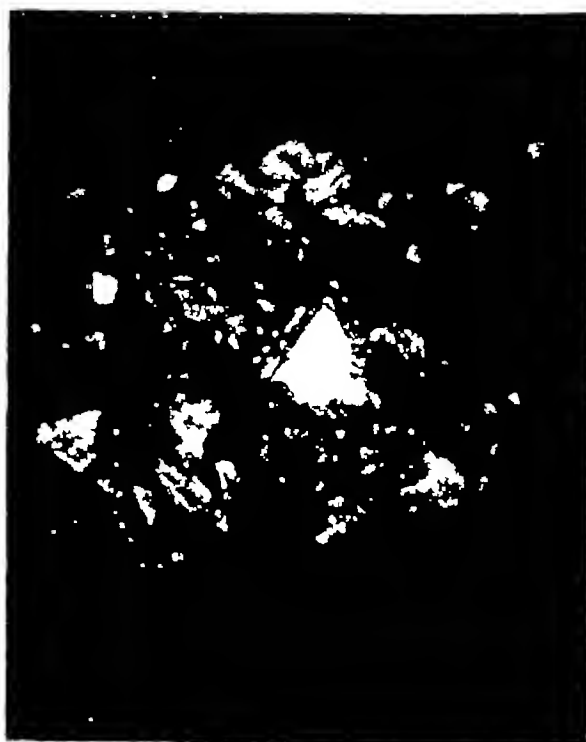


Fig 6 Cluster of synthesized diamonds

After many experiments it became possible to list some of the conditions peculiar to the formation of diamond.

(1) The pressure and temperature of the system should be those for which diamond is thermodynamically stable.

(2) The temperature must be high enough to ensure that the catalyst metal, saturated with carbon, is molten. Thus the intersection of the melting line of the metal-carbon eutectic with the graphite-diamond equilibrium line sets a lower limit on the temperature and pressure which can be used to form diamond with a particular catalyst. In Fig. 7 the diamond growing region is shown as a shaded area on the pressure-temperature diagram.

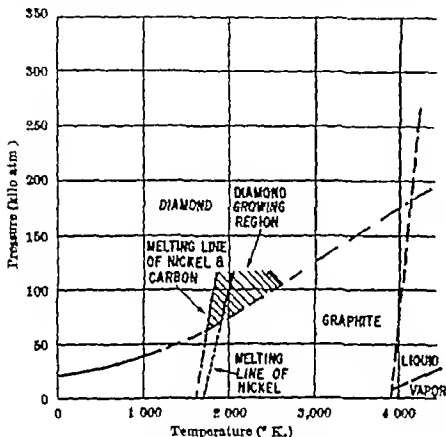


Fig. 7 Diamond-growing region

(3) The catalyst metal can be chromium, manganese, iron, cobalt, nickel, ruthenium, rhodium, palladium, osmium, iridium or platinum. Tantalum is particularly effective for inducing the growth of small diamond crystals, although in some circumstances it may not be as catalytically active as the other metallic catalysts.

(4) New diamond can form whether diamond seed crystals are present or not.

(5) As the synthesis pressure and temperature are moved further into the diamond-stable region away from the graphite-diamond equilibrium line, the rate of nucleation and growth of the diamonds increases and their average crystal size decreases.

(6) The diamond can grow at very high rates, at least 0.1 mm per min.

(7) The actual transformation from carbon to diamond occurs across a very thin film, about 0.1 mm thick, which separates the carbon from the diamond. Thus the transformation is almost 'direct', but the catalyst is essential (Fig. 8). So far it has been found to be very difficult to grow diamond buried in molten catalyst even 1 mm away from the source of carbon.

(8) Although the main driving force for the formation of diamond is the thermodynamic potential difference between graphite and diamond, temperature gradients can accelerate diamond growth due to the dependence upon temperature of the solubility of carbon in the catalyst.

(9) The kind of carbon used as a starting material has an effect on the kind and number of the diamonds

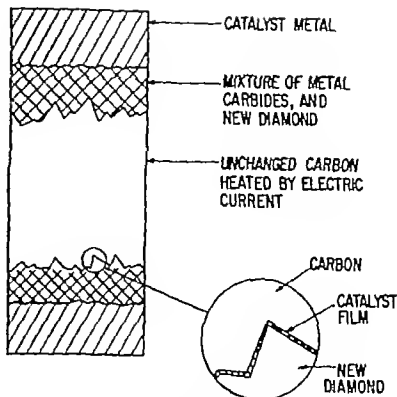


Fig. 8 Diamond growth from graphitic carbon

formed. Good results have been obtained in making diamonds employing ordinary commercial graphite as the starting material. Other carbonaceous material may be employed as the source of carbon, such as carbon black or a sugar charcoal, but graphite is preferred.

(10) Sometimes graphite forms from a carbon rich melt, particularly when the melt freezes, even though the pressure and temperature are appropriate for diamond stability. Diamond may or may not form at the same time. Apparently the formation of diamond is not a simple process.

(11) The diamonds easily include or grow around foreign particles present in the mixture, particularly at high rates of growth. Often some of the catalyst metal will be thus trapped in a diamond crystal.

(12) The diamond crystal habit varies according to the temperature of formation. Cubes predominate

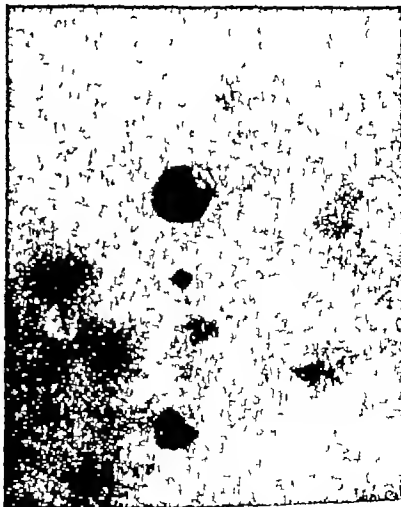


Fig. 9

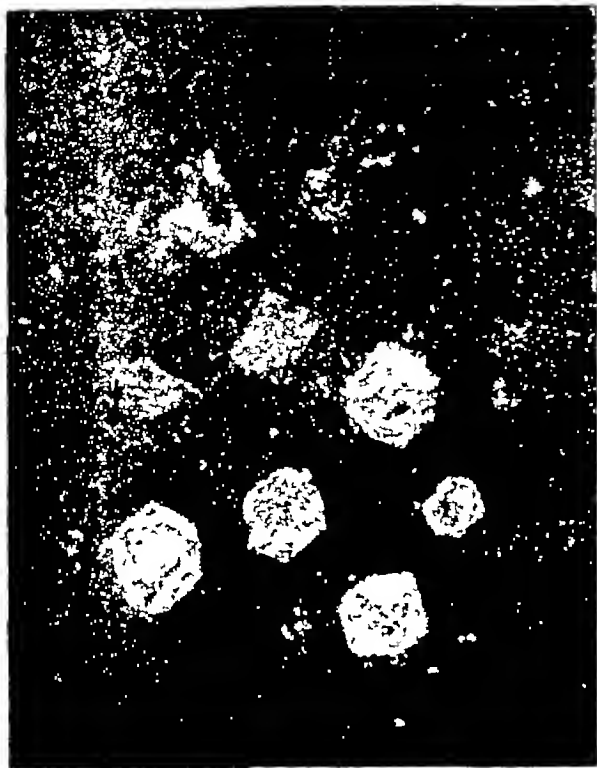


Fig 10

at the lowest temperatures, mixed cubes, cubo-octahedra and dodecahedra at intermediate temperatures, and octahedra at the highest temperatures. No tetrahedra have been found. At high growth-rates, octahedra are frequently twinned through an octahedral face as a mirror plane. Growth terraces or steps are common on the diamond crystals, but no growth spirals have been found so far. The colour varies from black at low temperatures through dark green, light green and yellow, to white at the highest temperatures. In many cases, the colour does not depend on the particular catalyst used but on the operating temperature relative to the melting point of the catalyst-carbon mixture. Green and yellow colours seem to be associated with imperfections in the diamond crystal lattice rather than with the



Fig 11

presence of a specific impurity. Many of the physical characteristics of natural diamonds have been duplicated in the laboratory.¹⁰

Some photomicrographs of various synthetic diamond crystals are shown in Figs. 9-11.

- ¹ Rossini and Jessup, *J. Res. Nat. Bur. Stand.*, 21, 401 (1938)
- ² Berman and Simon, *J. Electrochem.* 59, 333 (1955)
- ³ Bovenkerk, Bundy, DeLal and Strong (unpublished work)
- ⁴ Williams, 'The Genesis of the Diamond' (Ernest Benn, Ltd., London, 1932)
- ⁵ Gubelin, *J. Gemmology*, 3, No. 5 (Jan 1952)
- ⁶ Wentorf (unpublished work)
- ⁷ Bridgman, 'The Physics of High Pressure' 424 (G. Bell and Sons, London 1952)
- ⁸ Moissan, *C. R. Acad. Sci., Paris* 118, 320 (1894), 123, 206, 210 (1896)
- ⁹ Parsons, *Proc. Roy. Soc.* 79, 532 (1907), *J. Inst. Metals*, 20, 5 (1918), *Phil. Trans. Roy. Soc., A*, 220, 67 (1920)
- ¹⁰ Bundy, Hall, Strong and Wentorf, *Nature*, 176, 51 (1955)

FASCICULUS LIMPIDUS NOV. GEN., NOV. SPEC., A REPRESENTATIVE OF A NEW GROUP OF BACTERIA

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Pflanzenphysiologisches Institut der Universität, Göttingen

A PECULIAR organism, the nature of which puzzled me much at first, was observed in putrefaction cultures inoculated with a small quantity of soil from a dried-up pool not far from Cape Town, South Africa. It contained fragments of twigs and rock along with powdery earth. This soil sample had been very kindly sent to me by Dr. M. A. Pocock, Rhodes University College, Grahamstown, with the idea that it contained colonial Volvocaceae. This was the case. *Volvox*, a mixotrophic member of the Volvocaceae, together with species of *Chlorogonium*, *Coccomonas* (or *Dimorphococcus*), an undoc-

scribed species of *Lobomonas*, an interesting species of the Polytomaceae, and others turned up under suitable conditions.

Successful cultures were prepared in the following way: a quarter of a dry pea was put on the bottom of a test-tube, covered with clay soil and water and heated in a steam chamber for 1 hr. on two consecutive days. The following morning, or later, inoculation was done with a small amount of the original soil.

The culture was kept in the light. Other mixtures, such as grains of barley, bits of cheese, a little starch,

different kinds of soil instead of clay soil did not produce the same interesting type of biological community, but only a much more scanty growth without Volvocaceae and the new organism here described.

The original soil even in much greater quantity with water or a dilute mineral nutritive solution and trace elements, was still less productive. This is noteworthy, because it is of general application. It shows that the soil sample no longer contained enough of the substances which had originally produced the mixed population, the resting stages of which regained vitality in the tubes prepared as described. It also indicates that heating of the clay soil is necessary for these organisms to find suitable conditions for growth.

In all other instances the various organisms appearing in such putrefaction cultures could be maintained indefinitely by inoculating them into identical tubes without the original soil, in series. Not so the new organism, which also failed to multiply in a considerable number of media with various organic substances usually suitable for the nutrition of colourless flagellates, bacteria, etc. After repeated washing of the new organism before inoculation, such tubes remained clear and sterile.

In the original culture tubes the peculiar organism in question was observed in considerable quantity near the surface of the soil mud. The experiment was successfully repeated several times with the same and similar soil samples from the Cape Flats, but only when light was admitted did the new organism appear. It consisted of translucent, almost spindle-shaped structures tapering at both ends when inspected with low magnification inside the culture tubes. Later, the new organism swarmed in the higher regions too, but the water never really teemed with them, and the other organisms mentioned above were always present.

For closer investigation, specimens of the organism were picked up with the capillary pipette and inspected in hanging drops or in mounted preparations. What was mistaken for colourless, finely striated flagellates at low magnification was at high power seen to be composed of long filaments, some of them bent and twisted to form colonial bundles. These were broadly spindle-shaped, often somewhat flattened, with both poles tapering but not strictly pointed (Figs. 2-5). The individual filaments arranged more or less parallel to one another, though converging, did not all terminate at the same point. Under pressure of the cover slip they tended to spread, the filaments separating (Fig. 11). Indian ink penetrated between the units of the colony. There is, therefore, no gelatinous matter surrounding the whole or glueing the filaments together. They are united in bundles (*fasciculus*) and have a translucent limpid appearance. The organism will therefore be called *Fasciculus limpidus*.

In suitable conditions the colonies moved along their axes, rotating as flagellates generally do. They did not glide along solid surfaces but swam freely through the water, though more slowly than infusoria or even the majority of flagellates usually do.

The motile colonies may aggregate chemotactically. This became apparent when a quantity of culture fluid in a watch glass was inspected for a longer period. Various motile organisms such as *Spirilla* small infusoria and *Oocomonas*-cells, assembled around debris particles, were followed by the colonies of our organism, most of which aggregated after some

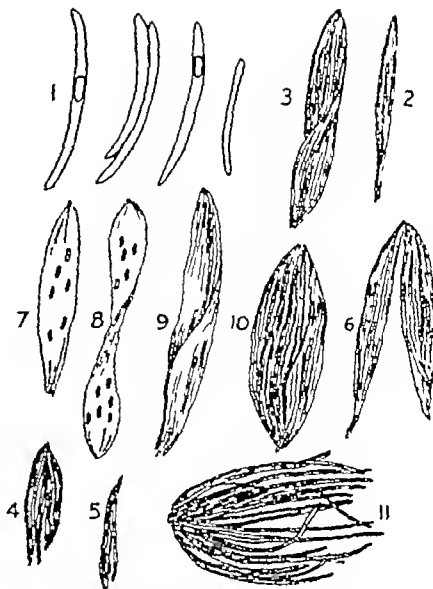


Fig. 1. Individual components of colony mechanically isolated two of them with spores. 2. Small, narrow colony. 3. Large twisted colony. 4 and 5. Small frayed colonies. 6. Rare instance of longitudinal split colony. 7-10. Colonies with spores. 7. Colony of the most frequent type—during spore formation, the outlines of the filamentous components have become invisible to a great extent. 8. Colony with narrow waist and spore formation. 9 and 10. More or less twisted colonies each with one spore. 11. Normal colony with filaments separated by pressure on cover-slip. (Fig. 1 $\times 1000$, others $\times 500$).

time at certain points. In such open watch glasses, contained in a Petri dish, *Fasciculus*, poured from a test-tube culture together with other members of the community, kept only for a few hours and could not be identified the following morning while *Volvox* and the others kept moving for a whole week. A probable inference is that *Fasciculus* is micro-aerophilic, an idea strengthened by our experience and observations with cultures.

The shape and appearance of the colonies varied (Figs. 2, 4, 5). Apart from the large closely knit spindles with only slightly frayed ends, there were smaller and narrower ones, and occasionally though rarely, slightly bent, slender rods which judging by their optical appearance, belonged to the same organism. Sometimes two narrow spindles cohering at one pole were seen (Fig. 6). Larger presumably older, colonies had a constriction in the middle, and the filaments were twisted (Figs. 3, 8). The waist is believed to indicate an imminent partition of the colony.

Cells shorter than the total length of the colonies, and others which divided like bacteria, could often be observed. There is little doubt that the units divide after reaching a certain length, and that the daughter cells glide along one another to increase the width of the colonial bundles. I did not, however, find any signs of individual filaments breaking loose from the colonies and starting

The main mode of reproduction is by binary fission. In older cultures, colonies

forma
which

were more limpid than young ones. Only their outlines were readily observable, while the inner parts of the spindle were optically almost empty except for small cylindrical bodies which by their high refractability, particularly in dark-ground illumination, revealed their nature as bacterial spores (Figs 7, 8). This was confirmed by their capacity for retaining the fuchsin stain on treatment with acid alcohol.

Later on, transition stages in spore formation were also found in colonies in which the filamentous cell-units were still readily visible. Not all of these formed spores. The spores were usually close to the middle. Their shapes varied from almost oval to, more commonly, cylindrical. Their width was about 1.5μ , their length $5-7\mu$.

These spores are no doubt the reproductive units responsible for the development of *Fasciculus* from completely dry soil. Their germination could, unfortunately, not be observed because of the failure to cultivate the organism and to separate it from other organisms. It is very peculiar that the individual cell margins vanish almost completely during spore formation, although the whole colony continues to swim about, and its outlines remain clearly visible (Figs 7, 8).

The structure or nature of the filaments composing the large spindles is also different from that of most bacteria. As already mentioned, optically the organism is fainter than other organisms. In dark-ground illumination it becomes more distinct, and the outlines of the filaments show more clearly than, for example, the outer membranes of *Myxobacteria*.

These filaments are believed to be cells. They are 2μ across and about $50-100\mu$ in length. They stain with fuchsin and methylene blue, but, in accordance with their low refractability, not strongly. They do not keep the Gram stain, contrary to most bacterial spore-formers. Only the membranes of the spores were stained, they were also more deeply coloured when treated with the Ziehl-Neelsen technique.

The mode of locomotion, rotating and swimming freely through the water, recalled that of flagellates or large bacteria. I did not succeed in demonstrating

flagella with the help of Loeffler's technique, of Deslandre's nigrosin method, or dark-ground illumination. Quick drying on fat-free cover-slips or fixing with osmium tetroxide vapour or iodine or Schaudinn's mercury chloride fixation did not make any difference. But I believe this failure was somehow due to an inadequate technique, and do not doubt that flagella do exist, since the impression of the swimming movement scarcely allows of any other interpretation.

If this were so, we would have another example of an 'organized' bacterial colony as earlier described for *Vannielia aggregata*¹. This belongs to the *Athiorhodaceae*, a family where colony formation had not been known to exist. There, also, many cells are aggregated to constitute a composite unit driven through the water and rotating by co-operation of the flagella, but here the similarity ends. While in *Fasciculus* the units of the colony are long, tube-like structures, those of *Vannielia* are rod-shaped cells radiating from the centre of the colony. Another motile bacterial colony is that of *Chlorochromatium aggregatum*, where again the arrangement of the individual components is quite different. Only one relatively large, central rod possesses a flagellum responsible for the movement of the colony, while the yellowish green small outer cells only adhere to the actively swimming central rod.

It is not possible to include *Fasciculus* in one of the taxonomic groups of the Bacteria. Very long, tubiform cells are known in *Lincola*², but this genus does not form colonies, and the production of spores and the appearance of the cells are different. In *Lincola* droplets and other contents are visible under the microscope, and the staining with various dyes is quite normal for a bacterium. *Fasciculus* is much less stainable and the inner part of the cell is almost empty optically. Moreover, the ecological conditions in which the new organism thrives seem to be peculiar. A better insight into its nature could only be obtained by cultivation. I will gladly supply portions of dry soil to bacteriologists who are interested in this creature.

¹Pringsheim, E. G., *J. Gen. Microbiol.*, 13, 285 (1955).

²Pringsheim, E. G., *J. Gen. Microbiol.*, 4, 193 (1950).

BIOLOGICAL PROBLEMS ARISING FROM THE CONTROL OF PESTS AND DISEASES

THE Institute of Biology has developed a technique for cutting through the hedges which grow up between fields of knowledge as biology undergoes speciation into ever new branches. One of the methods of doing this used by the Institute is to arrange symposia for which the subjects and speakers are chosen with considerable care. Thus, before even a word was spoken in the Royal Geographical Society's well-filled lecture hall on October 1, a look around indicated a successful meeting, for there were many well-known specialists in different fields who seldom previously have found themselves sitting in one room. The subject of this two-day symposium, namely, "Biological Problems arising from the Control of Pests and Diseases", is one of wide and topical interest. The speakers, including those who contributed to several stimulating discussions, were economic entomologists and botanists, medical men

and veterinarians, psychologists and humanitarians, in addition to academic biologists.

The symposium was arranged in four sessions, each under a different chairman. This arrangement divided the subject rather broadly into problems associated with arable agriculture, animal husbandry, human disease and health, but the matter presented tended to transcend any grouping. It became apparent that there are many connecting threads between, for example, the drug resistance developed by bacteria and the stimulation to growth of animals consequent on small additions of antibiotics to their diet, that the consequences of malaria control react quickly on the ecological problems of crop and animal pests through changes in human needs, and that too rigid a control of mental deficiency might have a retarding influence on science and art. Several facets of the discussion pointed to the human being

as the greatest pest of all. One speaker was bold enough to suggest that every pest and disease worthy of the name was, in fact, a human artefact, and given time he might convert almost every surviving wild organism into a pest. Although some would scarcely go so far, there were several expressions on the value of maintaining at least some areas of the world in a natural or semi-natural state. Thus, in the problem of controlling agricultural pests, reference was made to Elton's plea for ecological diversity if only to provide reservoirs of the predators and parasites of pests.

The stage was set by Mr F C Bawden, chairman of the first session, who directed attention to the unexpected and sometimes undesirable results which follow action against any particular pest or disease of importance in agriculture. The control of one may let in another. He was unable, however, to quote any case where the secondary trouble had resulted in greater economic loss than the primary one, and therefore concluded that on the whole there was always a net gain. This theme was taken up by Mr A. H. Strickland, of the Ministry of Agriculture and Fisheries Plant Pathology Laboratory at Harpenden. He provided a valuable assessment of recent work with insecticides, but neglected the classical work of biological control because it was well covered in a recent survey by Prof G C Varley in a paper before the Royal Society of Arts. He instanced cases where eradication of species had been attempted, such as the Colorado beetle from Europe and the Mediterranean fruit fly, which has twice been introduced into and eradicated from the United States, and he pointed out that in Britain no less than a fifth of the acreage of root and some vegetable crops is treated annually with insecticides as a routine measure. To those—including many farmers—who deplore the very widespread use of insecticides and herbicides as an excuse for sloppy husbandry, Mr Strickland had some encouraging words about recent studies of the manipulative possibilities such as physical control of the soil by rotation, and the adjustment of spacing in sowing and planting which can render crops unattractive to pests or stimulate the crop to grow away.

Dr T J Martin, of the Research Station, Long Ashton dealt with the direct risks to man arising from the fact that fifteen out of the forty two or so insecticides and fungicides in common usage are in the highly toxic category. Study of the risks to spray operators led to the Agriculture (Poisonous Substances) Regulations of 1956, and in spite of some accidents it seems that the risks to the consumers of crops which have been subjected to a variety of toxic sprays are under control at least in Great Britain. Discussion revealed that, with the exception of arsenic, for which there is a legal tolerance, the use of any spray on the land in Britain is entirely at the discretion of the manufacturer and the farmer. Neither Dr Martin nor any other speaker was in a position to deal with the influence of toxic materials on wild plants and animals or on game, although these largely unknown but important influences were doubtless in mind. It is abundantly clear that there is to-day a heavy responsibility falling on entomologists and botanists to obtain and interpret information on the selectivity and tolerance levels of these chemicals, in order to give advice to manufacturers and users on formulations, dosages and methods of application in such a way that indiscriminate slaughter can itself be brought under control.

Mr F G H Lupton, of the Plant Breeding Institute at Cambridge, set a different note by describing some striking successes in controlling diseases through genetical resistance or tolerance; but he mentioned that all too often the plant breeder is called in only when other methods have failed. Among other examples he described the ding-dong race which was started in 1912 by Sir Roland Biffen and is still in full cry between the genes of newly evolving races of the rust fungus and resistant genes of wheat sorted out by plant breeders. The series Marquis—Ceres—Thatcher—Pilot—Sellarke have so far kept alive the economy of the Great Plains, but the race is still neck and neck.

The second session introduced several problems from overseas. Thus, Mr M Crawford, of the Commonwealth Bureau of Animal Health at Weybridge, emphasized that eradication of a killing disease of livestock, such as rinderpest, could lead to harmful effects from over population, over grazing and malnutrition if achieved among peoples who regard stock as a social or religious asset without economic controls. Such experience was referred to also by Mr W H Potts, formerly of the Colonial Service with reference to the control of tsetse flies and trypanosomiasis. He was not, however, prepared to support the tendency in recent years to hail the tsetse fly as the preserver of the African soil from destruction by man. This theme, like the earlier one on controlling agricultural pests, led to discussion on the advantages or disadvantages of ecological diversity as a background for the economic use of land. There is, for example, evidence that in the African semi-arid bush the broad spectrum of wild indigenous fauna, fully adapted to living off the indigenous vegetation at all levels, could, under proper systems of management and annual cropping produce human food little if any less than is produced by the narrow spectrum of exotic domestic stock. At least there is a case for spending money to explore such possibilities in selected areas, rather than to spend all that is available on the blind eradication of wild life and tsetse flies.

The control of human diseases in tropical areas was the subject of two contributions, by Prof T Davey, of the School of Tropical Medicine at Liverpool, and Sir Gordon Covell. The latter mentioned that during the World Health Organization campaign there were two hundred teams working in India, each of which looked after one million people. Despite such campaigns, the Organization's figures show that the annual loss from malaria is still a vast one. The improvement of physique and of work undertaken by persons in malarial areas is marked, following control. There is normally some resistance to malaria, but this resistance is only local, so that an influx of persons from another district may result in severe outbreaks. Although Sir Gordon did not say so, this, of course, was known in England during past centuries, when it was noted that a wife from outside taken into such malarial areas as the Fens or Hundred of Hoo was liable to die within a short time, whereas the locals were in balance with their disease.

Prof Davey dealt more with the sociological problems expected as a result of the control of such diseases as malaria and pointed out that nowadays in India the excess of births over deaths is some 15,000 a day. In discussing birth control as the biological remedy, he mentioned that certain classes are more amenable to birth-control methods than others, and that in a low level subsistence type of

society every additional member of the family gives another worker, and so a better chance for survival. Where social conditions are better, each additional mouth is a liability rather than an asset. Thus the lower the subsistence-level the greater the birth-rate tends to be.

Dr E Slater, of the National Hospital for Nervous Diseases, raised some interesting points about the genetics of mental disease, and pointed out that the discovery of new methods of treatment enabled certain diseases which are transmitted genetically as dominants to increase their proportion in the population. This was simply done by overcoming the biological disadvantages which these dominant genes will contain, provided no treatment is given. Among the interesting points he made were that the manic-depressive type of patient is met with ten times as frequently among scientists as among the rest of the population. This may be a question of either cause or effect. Schizophrenics are found particularly among artists, and in these patients fertility is only 70 per cent that of normal. There is a possibility that this disease may be associated with some genetic advantage. The question whether certain types of mental defective should be sterilized is difficult because it is possible that workers in, for example, the artistic and scientific fields, may show improved output over the normal if they have some minor degree of mental disease.

The problems which arise from drug-resistance in bacteria were treated in a sparkling contribution by Dr Mary Barber, of the Postgraduate Medical School, London. She pointed out that not all bacteria have taken the massive attack by antibiotics in clinical medicine lying down, in the case of *Staphylococcus drogenes*, drug-resistant strains are now the major bacterial scourge in hospitals all over the world. Resistant strains of bacteria may be drug-tolerant or drug-destroying, and in certain cases may even become drug-dependant. Evidence points to the resistance being genetic rather than adaptive, and that penicillin, for example, has caused a prodigious evolution in the population structure of *Staphylococcus* by simple selection. Those strains carrying resistant genes which formerly were present in a tiny proportion have now increased to 60 or 70 per cent of the population in most hospitals. The same

principle applies in the case of insect resistance to the new synthetic insecticides, as explained by Dr J R Busvine, of the London School of Hygiene and Tropical Medicine. In more than a hundred harmful insects resistant strains have occurred, and in some cases the inheritance of the resistant trait has been shown to be of a normal Mendelian type. Whether the trait is 'physiological', which is immune to the poison, or 'behaviouristic', which manages to avoid it, its emergence seems to constitute greatly accelerated evolution on essentially Darwinian lines. Dr R Brando, from the National Institute for Research in Dairying at Shinfield, spoke on the recent experiments which show that very small amounts of antibiotics added to the diet of domestic animals increase growth-rate up to 10 per cent and the efficiency of food conversion by from 3 to 5 per cent. He explained that economic advantage of this phenomenon is being taken now on quite a large scale in the United States, although the biological reasons for it are as yet in the realm of conjecture.

The last contribution to the symposium was by Dr G C L Bertram, from St John's College, Cambridge, who spoke of 'ethical' or deliberate selection in mankind as having supplanted natural selection. He sketched the sequence of events which led to a doubling of the human population in the past eighty years or so, and the probability that it will double again during the next forty years—European dominance, followed by reduction of strife, the development of hygiene, and the control of biological competitors. Human compassion has led to death control, and now is the time for a great extension of birth control as a further expression of the freedom of choice by the individual. Having accepted Sir James Gray's concluding thought expressed in his presidential address at the York meeting of the British Association that man now has the intelligence and the knowledge to control his own destiny, the question has still to be answered what that destiny is. In a cynical moment, Dr Bertram compared modern man with a drunkard riding a runaway horse, whereas Dr A S Parkes, who guided this final session from the chair, expressed the hope that our freedom of choice would never become so wide that we would ourselves have to decide whether or not to be born.

E B WORTHINGTON

DARWIN'S ILLNESS

By PROF S ADLER, OBE, FRS

Department of Parasitology, Hebrew University, Jerusalem

DARWIN'S illness, which practically amounted to forty years of invalidism, has given rise to considerable speculation. The doctors who treated him could find no physical explanation for his distressing symptoms and apparently concluded that he was a hypochondriac.

Darwin, whose sufferings were very real, complained in a letter to Hooker "many of my friends I believe think me a hypochondriac". Commenting on this, the late Sir Arthur Keith¹, in his book "Darwin Revealed", remarks emphatically "Darwin was a hypochondriac, a very real one."

Hubble² states that "it is apparent that his illness bears the unmistakable marks of an emotional

disorder" and adds, "his psychoneurosis may be regarded as an adaptation to his environment which nourished and protected in the highest degree his uncommon genius". This author³ justifies his diagnosis on the basis of Darwin's family history. He rightly points out that Darwin's wife was an exceptionally devoted nurse and his son showed a tendency to hypochondria. It may, on the other hand, be argued that the above qualities were acquired and not inherent, chronic invalidism in the head of a family, whatever its cause, has psychological consequences and may well induce in the mother a strong tendency to nurse and protect, and in the younger members of the family an exaggerated fear of disease.

Good⁴ invokes psycho-analysis and considers the whole of Darwin's symptoms as a reaction to his father's autocratic personality. He goes so far as to say "Darwin's punishment for the unconscious patricide was a heavy one—almost forty years of severe and crippling neurotic suffering which left him at his best fit for three hours' daily work".

Keith accepts the unconscious as responsible for all Darwin's symptoms. "In Darwin's case the voluntary part of his brain seems to have too easy and too free an access to his involuntary part. Therein I believe lies the source of all his ill. Nevertheless, in referring to one episode of 1873 he writes, 'I infer this to be an attack of true angina of the heart'."

A purely psychological aetiology for Darwin's illness cannot be accepted as conclusive until all other factors have been eliminated. Gaylord Simpson⁵ has recently suggested that Darwin suffered from brucellosis. There is no direct evidence to refute or prove this theory.

It is obvious that all attempts to explain Darwin's symptoms must be based on a detailed analysis of the events recorded in the voyage of H.M.S. *Beagle*, because there is nothing of any medical significance prior to the voyage which could throw light on his subsequent illness. As Lady Barlow⁶ rightly remarks, "Charles Darwin's forty years of invalid existence moreover were an unexpected sequel to his youthful vigour, for his strength and endurance were well above the average, as Captain Fitzroy has recorded in his account of the various incidents during the *Beagle* voyage".

Darwin was a dedicated geologist and throughout his whole life maintained the keenest interest in this subject. Nevertheless, at the age of thirty three, he was compelled to abandon field work in a favourite subject because he found by experience that the physical effort it entailed exhausted him. Is it reasonable to ascribe this sacrifice to a belated reaction to a domineering father?

There is one very important point in Darwin's case history which writers on the subject have apparently overlooked.

In "The Journal of the Voyage of H.M.S. *Beagle*", Chapter 16, Darwin (March 25, 1835) writes "We slept in the village of Luan which is a small place surrounded by gardens and forms the most southern cultivated district in the province of Mendoza, it is five leagues south of the capital. At night I experienced an attack (for it deserves no less name) of the *Bonelluca* a species of *Reduvius*, the great black bug of the Pampas. It is most disgusting to feel soft wingless insects about one inch long crawling over one's body. Before sucking they are quite thin but afterwards they become round and bloated with blood, and in this state they are easily crushed." Darwin observed '*Bonellucas*' for at least four months and he fed one specimen on a ship's officer. "This one feed for which the *Bonelluca* was indebted to one of the officers kept it fat during four whole months, but after the first fortnight it was quite ready to have another meal."

The 'great black bug of the Pampas' which attacked Darwin in Luan can be no other than *Triatoma infestans*, which has become adapted to human habitations and feeds on man and domestic animals throughout extensive regions in South America. It is the most important vector of *Trypanosoma cruzi*, the causative agent of Chagas's disease in the Argentine, Chile and parts of Brazil. The pro-

vince of Mendoza has a relatively high incidence of Chagas's disease, and according to South American colleagues with whom I discussed this problem at the recent congress on Chagas's disease held in Rio de Janeiro during July 5-12 [see p. 1114 of this issue of *Nature*], as many as 60 per cent of the population in parts of Mendoza give a positive complement fixation test for *T. cruzi* and as many as 70 per cent of specimens of *Triatoma infestans* are infected with the trypanosome. Darwin was therefore definitely exposed to infection on at least one occasion. It is highly probable that he was also exposed on other occasions, but he particularly noted the incident in Luan because of the intensity of the attack of *Bonellucas*, parts of Chile through which he passed show a 10 per cent positive complement-fixation test in the population together with a considerable infestation with infected *Triatoma infestans*. We must also bear in mind that Chagas's disease has a very wide distribution in South America from Chile to Mexico (recently a few cases have been recorded in Texas) and the province of Mendoza is an area of relatively high infestation.

The incident in Luan cannot, however, explain Darwin's previous seven weeks severe illness during September and October 1834 which confined him to bed in Valparaiso and commenced during the last week of a six weeks journey. Unfortunately, no clinical details of this episode are available. Keith writes, "As to the nature of this illness I do not know of any exact information but typhoid fever is a very probable diagnosis". There is not the slightest suggestion of an emotional cause for this incident.

The complications and sequelae of Chagas's disease have been studied in detail by some of the ablest South American pathologists and clinicians particularly in Brazil, the Argentine, Chile and Uruguay, and considerable literature on this subject is now available. Particular attention has been paid to the clinical and pathological aspects of the myocarditis which appears in some victims of the disease. Darwin's exhaustion after physical effort can well be explained on the basis of an infection with *T. cruzi*.

At the above-mentioned congress a number of Brazilian pathologists and clinicians maintained that apart from, and in some cases in the absence of, cardiac complications Chagas's disease may be associated with clinical signs related to the alimentary tract, particularly the oesophagus, colon and stomach, as a result of damage to Auerbach's plexus. They based their conclusion on the high incidence of positive complement fixation tests in patients with symptoms related to these organs. There was no unanimity on this point because although many such cases have been found in Brazil few or none have as yet been recorded from the Argentine.

It is obviously impossible to prove that Darwin was a victim of Chagas's disease but two points cannot be overlooked. (1) his symptoms can be fitted into the framework of Chagas's disease at least as well as into any psychogenic theory for their origin, (2) it is possible to pin point with certainty a definite incident on March 25, 1834 during which he was exposed to optimal conditions for infection with *T. cruzi*.

¹ Keith A. "Darwin Revealed" (Watts and Co. London 1955)

² Habbis D. *Lancet* 244 129 (1913)

³ Habbis D. *Lancet* 265 1351 (1913)

⁴ Good R. *Lancet* 256 106 (1934)

⁵ Gaylord Simpson G. *Sci. Amer.* 199 No. 2 117 (August 1958)

⁶ Barlow Nora. "The Autobiography of Charles Darwin. The First Complete Version edited by his Granddaughter" (Collins London 1958)

OBITUARIES

Mr J T Davey and Mr H J Morris

In the air disaster at Bordeaux on September 24, the International African Migratory Locust Organization, which exists to prevent the escape of swarms of the Migratory locust from the recognized outbreak area in the flood plains of the Niger, south-west of Timbuktu, suffered a very severe blow. The fifty-three people killed included no less than eight associated with that Organization. Mr J T Davey, aged thirty-six, director of research, Mr H J Morris, aged thirty-six, an experienced scientist newly appointed as an assistant to Mr Davey, and his wife, Madame Duhart, wife of Monsieur A J Duhart, director of survey and control, and one of their children, and Monsieur J J Roy, one of the locust control officers, and his wife and child.

James Thomas Davey graduated from the University of Bristol and then took a diploma in agriculture at Cambridge and spent a year at the Imperial College of Tropical Agriculture in Trinidad. He first went to Africa in 1947 as an entomologist in the Department of Agriculture in Nigeria, where he investigated the habits and ecology of certain species of biting flies (tabanids and tsetse flies). At the same time, he became interested in locusts, and in 1948 he embarked on a detailed ecological study of the African Migratory locust, partly in association with H. B. Johnston. Particular attention was paid in this study to the neighbourhood of Lake Chad, which was under suspicion as a possible outbreak area, and the important conclusion was reached that while the Migratory locust does occasionally swarm there, the Chad area is not comparable as a source of swarms with the recognized outbreak area in what was then the French Sudan.

With this valuable experience behind him, he accepted in 1951 an invitation from the International African Migratory Locust Organization to visit the outbreak area on the Niger in order to extend investigations already begun by others of the ecology and seasonal movements of the locust there. His secondment to that Organization by the Government of Nigeria for this purpose was extended in 1952 for two years. An outcome of this mission was a decision by the Council of the Organization to establish a permanent Research Service. Davey became director of it, and he continued in that capacity until the time of his death. Through his own ability and personal qualities, including a very thorough practical knowledge of French acquired mainly by usage, the Research Service and its scientific work became integrated into the Organization in a highly successful manner, which could not have been achieved without the respect, affection and support which he won from all his colleagues.

His scientific work consisted mainly of studies of the seasonal movements of the locust population in and around the Niger plains in relation to the seasonal rainfall, river-level and flooding of the plains by overflow from the river. By means of an impressive programme of field-work which involved the marking of more than a million locusts individually with paints, during a period of four years, and releasing them in particular localities in and outside the plains

in the hope of recapturing some of them elsewhere, he succeeded in demonstrating a regular seasonal shift of population (already suspected by G. Romanidière, who conducted an ecological study of the locust in the flood plains during 1949-50) between the plains and the surrounding arid country. His work further indicated that certain parts of the plains are far more important than others as breeding grounds of the locust. A much better understanding of the outbreak area as such has resulted from these investigations, and this has led to important improvements and economies in the supervision and preventive control of the locust.

Davey travelled widely in Africa in the course of his duties. In 1953 he visited the outbreak areas of the Red locust in Northern Rhodesia and Tanganyika and toured parts of the vast area of eastern Africa over which the Desert Locust Survey, which has its headquarters in Nairobi, operates. Recently, he went to the Sudan Republic to see and discuss with the authorities there the circumstances in which a local increase in the population of the Migratory locust had occurred. His interests were wide and he was a good companion on journeys in remote places. His zest for life and his vigour and resourcefulness enabled him to take in his stride the many difficulties, some of them severe, which arise in 'bush travel' in Africa. The wild life of Africa appealed to him greatly. He knew the mammals of his areas well and was a keen shot, but he never shot animals solely for the sake of shooting. In connexion with his work, he made extensive collections of grasshoppers and plants, and these have added considerably to knowledge of the acridid fauna and the flora of the Niger flood plains and the surrounding country.

Fortunately, he made a point of writing accounts of his work at frequent intervals, and very little of the work that he had completed will be lost. His most important publications are two long papers on the ecology of the Migratory locust in what he called the Central Niger Delta, these form part of a planned series of three, and it is understood that the third part was virtually complete in typescript when he died. It is fitting that this valuable series of papers is being published in *Locusta*, the journal of the international organization which he served so well.

The death of 'Jimmy' Davey, while still young, removes a man who was confidently expected to play an important part in the field of locust research and control in the future. His wife survives him, with three young children.

Hilary Jolliffe Morris graduated from St John's College, Oxford, in 1948. A few years later he joined the Research Division of the Ministry of Agriculture of the Sudan, where he undertook pioneer studies of techniques of control of the Desert locust. This work, which covered a period of five years, contributed significantly to the development of aircraft-spraying and of low-volume ground-spraying against locusts, and in the course of it he became familiar with methods for the field-assessment of spray deposits and of the results of spraying operations.

In 1957 he joined the Colonial Pesticides Research Unit at Porton Down, near Salisbury, England, where

he was occupied for two years in laboratory work on the toxicity of new insecticides to mosquitoes. He was essentially a field man, however, with a strong liking for Africa and a desire to resume locust research, and when a suitable opening occurred in the Research Service of the International African Migratory Locust Organization he applied for the post and was selected.

This new appointment was for an investigation of the applicability of modern methods of locust control,

particularly spraying from aircraft, in the conditions of the outbreak area of the Migratory locust on the Niger. Morris was very well fitted by his accumulated experience and personal qualities for this important task, and he set out with high hopes and keen interest on the journey which was to have taken him to the sort of work that he liked best and considered worth while because of its benefit to Africa.

Mr and Mrs Morris had been married only six months when they died. T H C TAYLOR

NEWS and VIEWS

Scientific Adviser to the Ministry of Defence

Sir Frederick Brundrett, K.C.B., K.B.E.

It has been announced that Sir Frederick Brundrett will be retiring at the end of the year from his post of scientific adviser to the Ministry of Defence, and chairman of the Defence Research Policy Committee, shortly after his sixty fifth birthday. Sir Frederick has had a life time's association with the scientific aspects of defence, initially within the Admiralty, and for the past ten years of his career dealing with defence science in all its aspects. A member of the R.N.V.R. in the First World War, he joined the scientific staff of the Admiralty in 1919 and remained at H.M. Signal School Portsmouth, until 1937, when he moved to headquarters. His remarkable qualities as a scientific administrator and his perception of scientific ability were given full scope during the Second World War, when he made a major contribution to the selection and allotment of scientists to the several departments needing them. Since the War his talents for organization have been given full rein at the Admiralty and elsewhere but his greatest contribution has undoubtedly been in the clarification and stabilization of defence research and development policy as a whole over the past few years. His contributions to the rationalization of the research and development programme so as to harmonize the needs of the Services with the national resources have been markedly successful and a great debt is owed to him for his work in this field. What he has accomplished is due to three qualities which he has in abundance: a real understanding of Service needs and Service modes of thought, a basic understanding of scientific practices and requirements, and a capacity for hard, thorough and clear headed work equalled by few and probably excelled by none. A distinguished player of games when younger, and an extremely successful scientific agriculturist to day, it is to be hoped that his advice and his services to the Scientific Civil Service will not wholly end with his departure from the Ministry of Defence.

Sir Solly Zuckerman, C.B., F.R.S.

SIR SOLLY ZUCKERMAN, who is to succeed Sir Frederick Brundrett as scientific adviser to the Ministry of Defence, is no stranger to either defence or to Whitehall. Sir Solly was born in South Africa in 1904. He came to Britain in 1925 and rapidly became known as a distinguished research anatomist. He at present holds the Sands Cox chair of anatomy in the University of Birmingham, and he is especially well known for his work on the primates. During the Second World War his wide scientific talents were drawn on freely by many branches of the Services, but he was

perhaps most closely associated with the Royal Air Force, and he made important contributions to the operational analysis of the effects of bombardment particularly from the air. In the past decade he has combined his work at the University of Birmingham with many other activities, including his duties as honorary secretary of the Zoological Society during a rather stormy period, and with the deputy chairmanship of the Advisory Council on Scientific Policy, towards the work of which and some of its sub-committees, notably the Committee on Scientific Man Power, he has made a major contribution. He succeeds Sir Frederick Brundrett at a difficult time when it may well be that a closer integration between civil and defence science is necessary, and when indeed some re-thinking may be necessary on the balance between the two. For this task Sir Solly, by his previous experience his exceptional ability and warm personality, is excellently qualified.

Meteorological Branch of the Canadian Department of Transport Dr Andrew Thomson, O.B.E.

DR ANDREW THOMSON, who on September 25 retired from the post of director of the Meteorological Branch of the Canadian Department of Transport, a position he has held for the past thirteen years, is well known in the world of meteorology. A graduate of the University of Toronto his first studies were in geophysics, and during 1920-21 he was put in charge of investigations into atmospheric electricity during the round the world cruise of the Carnegie Institution research ship. In 1923 he became director of the Apia Observatory, Samoa, and in 1929 aerologist of the Dominion of New Zealand. He returned to Canada in 1931 as head of the research division of the Meteorological Service, and assumed charge of the whole service in 1946. Dr Thomson has done much in the international field, especially as a member of the Executive Committee of the World Meteorological Organization and as president of the Regional Association for North and Central America of the World Meteorological Organization. A great traveller who has not only done much to build up an efficient national service but also to promote international co-operation in meteorology, he was made O.B.E. in 1948, and awarded the gold medal of the Professional Institute of the Public Service of Canada in 1952 and the honorary degree of D.Sc. by McGill University in 1958. He carries into his retirement the best wishes and affection of all who know him.

Mr Patrick D. McTaggart-Cowan M.B.E.

THE appointment of Mr P. D. McTaggart-Cowan to succeed Dr Andrew Thomson as director of the

Canadian Meteorological Service comes as no surprise to the world of professional meteorology, for he has been Dr Thomson's right-hand man for many years. Mr McTaggart-Cowan, who is forty-seven, was born in Scotland but has spent most of his life in Canada. After securing first-class honours in mathematics and physics at the University of British Columbia, he won a Rhodes scholarship to Corpus Christi College, Oxford, where he graduated with honours in natural science. He joined the Canadian Meteorological Service in 1936 and quickly became known internationally, especially in relation to trans-Atlantic aviation, then in its infancy. During the Second World War he was largely responsible for the development of forecasting at the Canadian end of the ferry flights to and from Britain. When hostilities ceased he took an active part in the formation of the body which has now become the International Civil Aviation Organization. Among professional meteorologists his name stands high, not only as a forecaster, but also as an energetic and skilful administrator, with a gift of clear thinking and direct speech. The future of the Canadian Meteorological Service could not be in better hands.

Chemical Engineering at Leeds:

Prof G G Haselden

DR G G HASelden, whose appointment to the new chair of chemical engineering at the University of Leeds has been announced, was educated at Sir Walter St John's School, Battersea, and the Imperial College of Science and Technology, London. He graduated in chemical engineering with first-class honours in 1944 and afterwards undertook research under the late Sir Alfred Egerton on problems connected with the liquefaction of methane. On the results of this work he was awarded his Ph.D. In 1949 he was appointed lecturer and later senior lecturer in low-temperature technology in the Department of Chemical Engineering of the Imperial College. In addition to his teaching duties, Dr Haselden has during the past ten years built up an active school in low-temperature research. His main fields of interest have been in the liquefaction of natural gas, the development of new or more efficient gas-separating processes and refrigeration cycles, and the measurement and correlation of the thermodynamic properties of mixtures. In 1958 he was awarded the Lightfoot Medal of the Institute of Refrigeration for his work on mixed refrigerants. Dr Haselden was one of the founder members of the Low Temperature Group of the Physical Society, and he is a member of the Education and Papers Committees of the Institution of Chemical Engineers and a member of the Research Committee of the Institute of Refrigeration.

Illuminating Engineering Society Award:

Dr J. W. T. Walsh

To mark the occasion of its golden jubilee, the Illuminating Engineering Society has instituted an award to be known as the Illuminating Engineering Society Gold Medal, which will be bestowed at intervals of not less than two years for outstanding contributions to the advancement of lighting. Recipients of the medal may be of any nationality and need not be members of the Society. At the meeting of the Illuminating Engineering Society held in London on October 13, the first award of the gold medal was made to Dr J. W. T. Walsh, who is without doubt the most outstanding and highly

esteemed person in the world of lighting to-day. From Merton College, Oxford, Dr Walsh went to the Department of Photometry of the National Physical Laboratory until he retired in 1951, having been there for thirty-eight years. His first outstanding contribution was the making of a large-scale photometric survey of factory lighting for the Home Office Departmental Committee in 1913. During subsequent years, he supervised much important work relating to the principles of good lighting and to the design and performance of lighting equipment, and he published a number of papers on all aspects of photometry and illuminating engineering. Dr Walsh served for many years as chairman of the British National Illumination Committee and has participated actively in the meetings and work of international bodies concerned with lighting. He has served as honorary secretary and vice-president of the International Commission on Illumination and was president of that body from 1955 until June 1957. He has been a member of the Illuminating Engineering Society since 1923; he is the only member who has served two terms as president of the Society (1929 and 1947). He was chairman of the committee responsible for the current codes of practice for street lighting. Dr Walsh has indeed been a prodigious worker in the cause of better lighting and this together with his high principles and strict regard for scientific accuracy has endeared him to lighting people all over the world. There is no doubt that his contributions to the advancement of lighting have been truly outstanding.

Royal Australian Chemical Institute:

Mr C. E. C. Nicholls

MR C. E. C. NICHOLLS has been elected president of the Royal Australian Chemical Institute. He was born and educated in England, and gained his degree in the University of London with honours in chemistry. After spending about two years with the British-American Tobacco Co., Ltd, he joined the Distillers Co., Ltd, in October 1929, very shortly after the latter company had entered the chemical field. He spent some years at the Company's main factory in Hull, and brought into operation the first synthetic acetic acid plant in England. Early in 1942 he was sent to Australia, where he played a major part in establishing the war-time synthetic acetone production. Early in 1945 Mr. Nicholls returned to England, where he resumed duties with the Distillers Co., Ltd. He made a short visit to Australia in 1946, and again in 1947 when the Colonial Sugar Refinery and the Distillers Co., Ltd, obtained a larger interest in Robert Corbett Pty, Ltd. He is at present manager of Colonial Sugar Refinery Chemicals Pty, Ltd, and a director of Robert Corbett Pty, Ltd. He was elected a Fellow of the Royal Australian Chemical Institute in 1947, holding office as president of the New South Wales Branch for two years and during the last year of this term he was also vice-president of the Institute.

Atomic Energy Authority's Thermonuclear Programme

THE United Kingdom Atomic Energy Authority is seeking the necessary approvals to acquire and develop a site of some 175 acres within the perimeter of the Royal Naval Airfield at Culham, Oxfordshire, for development as a new research establishment. The new establishment would be for research into controlled thermonuclear reactions and plasma

physics and the study of nuclear fusion as a possible source of industrial power. Most of the thermo nuclear research now carried on at Harwell and Aldermaston will be moved to the new establishment. One of the immediate tasks at the new site, if approved, would be the construction of LOSE (Intermediate Current Stability Experiments), a large machine which (as announced at the Authority's annual press conference in July) will incorporate the results of experience with *Zeta* and of other studies in this field, both at home and abroad. It is planned that the total numbers employed at the proposed new establishment will rise to 1,000 and that this figure will be reached within four or five years.

Divorce Statistics in Britain

THE principal changes that have been introduced in the Civil Tables of the Registrar General's Statistical Review for 1957 which has been published recently relate to divorce statistics (The Registrar General's Statistical Review of England and Wales for the year 1957 Part 2 Tables, Civil Pp xii+200 London H.M. Stationery Office, 1958 11s 6d net). Figures for divorces and annulments are now given by calendar year of marriage and age of spouses at marriage so that the risk of divorce of different marriage cohorts may now be computed, and there are some other welcome new details on divorce. An appendix shows details of marriages by manner of solemnization in different countries. It is intended to publish this table at five yearly intervals, and these data give a useful indication of the distribution of different religious groups in the country. It is of some interest that the proportion of civil marriages shows a fall compared with 1952, for the first time since such marriages were instituted in 1838. In addition to these new figures more detailed fertility tabulations giving better exposed to risk are also included in this volume.

Sex Research

THE Division of Medical Sciences of the National Academy of Sciences—National Research Council is accepting applications for grants in-aid of research for consideration by the Committee for Research in Problems of Sex. The funds for support of this programme are provided by the Rockefeller Foundation and the Ford Foundation. The Committee is concerned primarily with encouraging research on the mechanisms underlying sexual behaviour, with special emphasis on the higher mammals and man. Proposals involving endocrinological, neurological, psychological, anthropological, phylogenetic and genetic studies directed toward this objective are therefore invited. Requests that deal with the physiology of reproduction or with related biological and biochemical fields should be addressed to the Committee only if they give promise of shedding light upon behavioural mechanisms. Preliminary inquiries should be addressed to Room 411 Division of Medical Sciences, National Academy of Sciences—National Research Council 2101 Constitution Avenue, N.W., Washington 25, D.C. Completed applications for the fiscal year 1960-61 should be postmarked on or before January 15, 1960.

Variation in Lizards of the *Leiocephalus cubensis* Complex in Cuba and the Isla de Pinos

Leiocephalus cubensis Gray has been regarded as one of the four species of this genus in Cuba and

the Isla de Pinos, and has been known to occur throughout both islands in suitable habitats. Albert Schwartz has collected 388 specimens and studied additional material from various museums. This has resulted in the partition of *L. cubensis* into two species, each with four subspecies. *L. cubensis* is now known from Cuba and the Isla de Pinos, the Doco Leguas keys, and the Archipiélago de los Canarreos where the new species, *L. stictigaster*, occurs in western Cuba and the Isla de Pinos. The status of Oriente lizards of this complex remains uncertain. Schwartz believes that *stictigaster* and *cubensis* arose from a common stock through isolation on western and central island masses during the Oligocene and Lower Miocene Periods. With the re-establishment of the island to approximately its present outline between the Lower and Middle Miocene these two species extended their ranges gradually from the regions of differentiation. From modern distribution it appears that the gap between western *stictigaster* and eastern *cubensis* may not yet be closed. *L. cubensis* also has spread to the east into Oriente as well as the west into Matanzas and Habana (*Bulletin of the Florida State Museum, Biological Sciences* 4, No 4, 1959).

Transparent Sintered Alumina—'Lucalox'

SINTERED or vitrified ceramic materials of poly phase composition are normally opaque owing to scattering of light by the different refractive indices of the component phases. Single-phase sintered ceramics are usually both opaque and porous owing to the difficulty of sintering refractory substances sufficiently well to produce optical contact between the grains. The General Electric Co. of America announces the experimental production of a material under the trade name 'Lucalox' which is formed by pressing from alumina powder of small grain size and fired under conditions presumably in vacuum and at a very high temperature, which permit almost complete sintering to occur. The product is non porous and sufficiently transparent for print to be read through a thickness of the material in contact with the paper. Objects viewed at greater distances are, however, blurred as though through frosted glass. It retains the refractory qualities of alumina and is said to be stable up to about 1 000° C. Possible fields of use include envelopes for high intensity light or radiant heat sources, as a superior alternative to fused silica. Light transmission in the visible spectrum through an unstated thickness is said to be 90 per cent. Since the material is in effect a polycrystalline sapphire, it may offer an alternative to synthetic mono-crystalline sapphire for instrument bearings. Its electrical properties are not stated, but would presumably resemble those of sapphire, a permittivity of about 9.5 loss angle between 10^{-4} and 10^{-3} at room temperature, and appreciable conductivity appearing around 300-500° C. depending upon purity. The problem of production as a commercially satisfactory operation is said to be still under investigation.

International Conference on Non-Destructive Testing

THE third International Conference on Non-Destructive Testing will be held in Tokyo during March 15-21. The Conference is intended to provide an opportunity for the exchange of information on

prepared, the study of emulsion paints comprising homo- and co-polymer systems has indicated a correlation between water-resistance, hardness and flexibility of latex films, and polymer composition, and the investigation of polyethers from polyols and propylene oxide has assisted the rapid growth of the polyurethane foam industry. Both the coal chemicals fellowship and the petroleum fellowship

cover a wide field and, under the power rectifier fellowship, laboratory development of the first new power rectifier was completed and the growth of highly perfect single crystals of silicon and germanium has been studied. New organosilicon compounds, monomers and polymers have been prepared under the silicones fellowship, including some hybrid organotin organosiloxane compounds.

LABOUR TURNOVER

LABOUR turnover has been a subject of inquiry and discussion since interest was first focused on the problem during the First World War. It is commonly regarded as a source of serious economic waste. The level of turnover in a firm is often regarded as an index of morale among the employees.

Research workers have attempted to analyse the causes of labour turnover by relating it to different groups of factors. The most important of the external factors are the level of employment and the availability of alternative work. The internal factors are the composition of the labour force itself, that is to say, whether men or women are employed, whether they are skilled or unskilled, the length of time workers have been employed, their age and the location of their homes. Wage rates, hours and conditions of work and the personal relationships existing within a firm may also have important effects on labour turnover.

The findings of research do not appear to have helped managements very much in their efforts to reduce labour turnover. The British Institute of Management survey of 1949 and 1950, covering approximately two hundred companies, showed annual labour turnover rates varying from 13 per cent to 59 per cent for men and from 24 per cent to 75 per cent for women per annum. These are industry rates. Individual companies fluctuated below and above this range. Labour turnover was calculated on the basis of

$$\frac{\text{Number of leavers in period under review}}{\text{Average number of persons employed during same period}} \times 100$$

Commonly agreed facts about labour turnover are that in any given period it is heavier among short-service employees than among those of longer service and that much of it does not represent true mobility but, from the social point of view, useless changes from one job to another.

What has not been established is to what extent labour turnover matters to the individual company and to society and the extent to which labour turnover can be measured in financial terms or whether its effects are largely intangible and in any event non-financial.

Excessive labour turnover is assumed to cause waste and inefficiency. Few studies have attempted to find out what exactly is the extent of this waste. One of the drawbacks is the difficulty of measurement. The effects of labour turnover are widespread and varied and attempts to assess them in financial terms can easily become either over-simplified or over-imaginative and remote from verifiable facts.

An appraisal of the importance of labour turnover to industry cannot be complete unless there is some estimate of its financial effects. Certain effects as,

for example, the impact on the morale of the working group of a continually changing labour force, cannot be assessed in financial terms. The more tangible costs are also important.

What has been needed is a series of published case-studies of the experience and of the financial cost of labour in individual concerns. The British Institute of Management has now published a series of sixteen such studies*. The studies have been of the cost of labour turnover among direct production workers. No studies have been undertaken among clerical or selling staff.

The data provided by these case studies and by supplementary information obtained from a large number of firms show that.

(1) In five out of sixteen studies, labour turnover was adding 10s or more per week to the wage cost of each individual employed.

(2) The main factors which appear to affect labour turnover cost are the impact of learners on production, the extent to which saleable production is lost through labour turnover and the methods used to make up production losses.

(3) The amount spent on training, induction and interviewing is a matter of company policy and will naturally affect the level of its labour turnover cost. Money spent in this way, however, has a constructive result and is not waste, as is the cost arising from other categories.

(4) Labour turnover has certain long-term effects which are not measurable in financial terms. Most important of these are the effect of high labour turnover on the morale of the work force, the wear and tear on supervisory staff and the loss of customers' goodwill by failure to fulfil orders and to meet delivery dates. To combat these effects by reducing labour turnover, it seems worth spending money on training, induction and interviewing.

(5) Labour turnover appears to be most costly in those firms where there is a high proportion of semi-skilled jobs peculiar to the company itself. This is because the training period is often long and it is rare to find new employees with experience of similar work. The recognized skilled occupations and the relatively unskilled ones, for example, labouring and cleaning, do not involve companies in high training costs.

(6) The results of the inquiry as a whole suggest that keeping labour turnover low may be a relatively expensive business, almost as expensive as allowing it to increase with consequent increased production costs and sales losses. The decision about how much to spend on reducing labour turnover must be based not only on the figures of tangible waste but also on management's estimate of the seriousness of the non-financial aspects.

T H HAWKINS

* "Cost of Labour Turnover", 17s. 6d.

STRONTIUM-90 IN HUMAN DIET

RESPONSIBILITY for estimating the contamination of food by radioactive fall out has now been transferred to the Agricultural Research Council. The report, "Strontium 90 in Human Diet in the United Kingdom, 1958" (London: H.M. Stationery Office, 1959 4s), thus continues the series formerly issued by the Atomic Energy Authority.

The general level of radioactivity in food in the United Kingdom for 1958 was small, comparable with that found in the United States, and well below any danger level. Most of the radioactivity in milk and dairy products, bread and flour, and in leafy and root vegetables was brought about by the deposition of radioactive debris on the leaves of herbage and crop plants during periods of rain, followed by foliar absorption of (in particular) strontium 90. Only the material deposited during the two months before herbage was eaten by cows or before crops were harvested appeared afterwards in appreciable amounts in human food. Once the debris penetrated into the soil, its 'availability' to plants was greatly reduced. Consequently the accumulation of available strontium 90 in the soil since nuclear weapon testing commenced in 1945 had been slight.

The radioactivity of milk was highest in western areas of Britain and appeared to be related to the distribution of rainfall. The level of radioactivity increased in all areas during the latter half of 1958 partly as a result of an unusually high rainfall and partly of an increase in the number of nuclear tests.

Examination of certain upland areas that are characterized by high rainfall and by slow growth of herbage had shown that milk from these areas often contained very high levels of strontium 90. This could not be accounted for entirely on the basis of high rainfall, low soil-calcium, and low production of herbage per acre. It was thought that strontium 90 must become entrapped in the mat of vegetation and roots at the base of the sward, and be held available to the plant in successive seasons, in a way not observed on lowland pastures.

The report shows that when strontium was absorbed from the diet, it tended to replace calcium in bone tissue. High levels of strontium 90 in bone could damage the bone or bone marrow, ultimately causing tumours, leukaemia, or other bone diseases.

However, it appeared that the replacement of calcium by strontium 90 in new bone tissue was governed not by the amount of strontium 90 in the diet but by its proportion relative to calcium (expressed as microcuries of strontium 90 per gm calcium). Furthermore, the human body, in absorbing mineral substances from the digestive tract, discriminated against strontium so that the ratio of strontium 90 to calcium which was found in bone was only one quarter of that in the food eaten.

The report also discusses other factors which tended to reduce the ratio of strontium to calcium in the diet. Thus, the cow discriminated against strontium when producing milk from grass, so that the proportion of strontium 90 to calcium in milk was only one seventh of that in the herbage eaten. Leafy vegetables appeared to absorb strontium less efficiently than herbage, and contained correspondingly less radioactive material. Although wheat contained a fairly high proportion of strontium 90, milling, as in the preparation of white flour, removed much of the calcium and strontium in bran and offal, while the subsequent addition of strontium free chalk as a calcium supplement further reduced the proportion of strontium to calcium in bread and flour products. The report noted that the ratio of strontium 90 to calcium in diets based on wholemeal bread was likely to be higher than average as there was no legal requirement to add chalk to wholemeal flours, while the milling process did not tend to remove any of the strontium contained in the grain.

However, even on the most unusual food and living in the wettest area, no one in the United Kingdom was likely to consume a diet containing more than 25 μCi of strontium 90 per gm calcium, about half the ratio (40 μCi) at which a Medical Research Council Committee thought that 'immediate consideration' should be given to the problem. It is emphasized that no evidence had been found of such a diet being consumed by anyone. The amount of strontium 90 per gm calcium in the average diet was about 6 μCi and, provided that the rate of deposition of the radioactive dust did not greatly increase in the future, either as a result of meteorological factors or because of further testing of nuclear devices, such a level should give no cause for anxiety.

J. M. A. TILLEY

IMMEDIATE AND LOW-LEVEL EFFECTS OF IONIZING RADIATIONS

THE biological effects of low doses of ionizing radiations, a topic of obvious interest and importance formed one of the main themes of a symposium held in Venice, June 22-26, under the joint sponsorship of Unesco, the International Atomic Energy Agency and the Comitato Nazionale per le Ricerche Nucleari di Italy. The Organizing Committee included Prof. Z. M. Baqar (Belgium), Prof. E. Boeri and A. A. Buzzati Traverso (Italy) and Dr. A. Hollander (United States). Those invited were fortunate in being able to take part in a conference of which content and programme arrangements were of a high

order and which was held in the beautiful surroundings of the Fondazione Giorgio Cini on the Isola di San Giorgio Maggiore. Each of the nine sessions was arranged to contain only a few papers, so that there was ample time for discussion and for a few short communications which were relevant to the main themes. Sixteen countries, and a wide range of scientific disciplines, were represented among the 116 research workers who took part.

The symposium opened with a review of certain aspects of quantitative radiobiology by K. G. Zimmer (Kernreaktor, Karlsruhe, Germany). After discussing

critically some of the postulated mechanisms of the biological action of ionizing radiations, he went on to describe recent results obtained by the use of microwave spectroscopy. This topic, discussed also by J S Kirby-Smith (Oak Ridge, United States), is of great interest because persistent magnetic centres can be observed in irradiated biological materials of low water content, and the signals are modified by environmental factors which are known also to modify the biological effects of radiation. However, caution is necessary in interpreting the results obtained by instruments currently in use, since the signals observed arise from about 10^{10} times as many ionizing events as those which in many cases initiate biological damage.

New techniques which have recently been developed for studying cells in mitosis have enabled investigators to undertake the difficult task of observing quantitatively the induction of chromosomal abnormalities in human cells. M A Bender (Oak Ridge, United States) had examined effects on human cells in tissue culture, and also on monkey cells *in vivo*, using bone marrow. The cells irradiated *in vivo* gave a somewhat lower yield of chromosome aberrations. Doses down to 25 r were used in these studies.

The effects of considerably lower doses on human cells were observable by M Ingram (University of Rochester, United States), who had found significant increases in the number of binucleate lymphocytes present in the blood of persons exposed to doses considered to be in the 'tolerance' range. Although ionizing radiation is not the only agent which can bring this about, it was of interest that in a field investigation of uranium miners, a higher count of binucleate lymphocytes was found in the blood of the control group of coal miners, who had been subjected to regular routine diagnostic X-ray examination. Another paper on effects of X-irradiation on the blood picture of mammals was given by S Hajdukovic (Institute for Nuclear Sciences, Yugoslavia), who used as his test effect the increase in the number of reticulocytes released into peripheral blood. He reported that increases were also obtained when serum from irradiated animals was injected into non-irradiated ones, the effect not being species specific. These changes were observed fairly early after the irradiation.

The subject of chemical protection against biological effects of ionizing radiation was reviewed by D W van Bekkum (National Defence Research Council, Holland), who discussed different groups of protective substances and critically examined possible mechanisms of action. R Brinkman (State University, Groningen, Holland) described techniques for examining the protective effect of chemicals against radiation-induced changes which could be measured very soon after low doses of irradiation. These included measurements of the viscosity of synovial fluid, and of intradermal pressure. Effects of irradiation could be observed within one second, and serotonin injected intradermally was the most effective of the protective substances used. M Ebert and A Howard (Medical Research Council and British Empire Cancer Campaign, Great Britain) described some of their latest findings with inert gases. These gases suppressed the enhancing action of oxygen when used at pressures above atmospheric, but were less effective in the cold than at room temperature. J F H Maisin (University of Louvain, Belgium) had found that small doses of radiation could themselves protect against the damaging effect of larger

doses. Yeast cells were exposed for long periods to continuous irradiation which was not itself sufficient to kill the cells, thereafter, larger doses were required to produce a given killing effect on these than on control cells. Rats which had been exposed to radiation *in utero* or as new-borns were more resistant than controls to radiation given afterwards.

Various types of immediate response to irradiation had been observed by O Hug (International Atomic Energy Agency, Austria), who showed a film which demonstrated reflex reactions of snails, sea urchins and ants. It was clear that an immediate effect of radiation could be observed with nerve tissue, long thought to be comparatively insensitive to its action. A different type of immediate response was reported by A Forssberg (Institute of Radiophysics, Sweden), who has observed reversible effects of doses as low as 10^{-2} r on the fungus *Phycomyces blakesleeanus*, the growth-rate of the sporangiotheca being immediately reduced. Depression of growth-rate was accompanied by an increase in the level of acid-labile phosphorus, and a slightly delayed increase in lactic acid. It was suggested that the use of adenosine triphosphate might be blocked by the radiation.

Radiobiologists continue to search for the biochemical links between the absorption of ionizing energy and the manifestation of the effects observed, and various approaches were reported. P. Alexander (Chester Beatty Research Institute, Great Britain) gave an account of physico-chemical studies on effects of radiation on deoxyribonucleic acid *in vitro* and in herring sperm, including a discussion of the phenomenon of cross-linking. K I Altman (University of Rochester, United States) had studied the breakdown of muscle collagen in rats previously fed with labelled amino-acids. Whole-body irradiation with lethal doses was followed by a reduction in the hydroxylation of proline and an increase in that of its precursor.

A Chevalier and S Manuel (University of Strasbourg, France) found that one result of radiation which could be measured within a short time was a drop in the ascorbic-acid content of almost all tissues, particularly the spleen. While this was true of animals irradiated as a whole, spleen slices irradiated *in vitro* did not demonstrate the phenomenon, nor was it observed when only the exteriorized spleen was irradiated. The authors concluded that the drop in ascorbic acid in the spleen depended on effects on other organs. P Mandel and P Chambon (University of Strasbourg, France) reported studies on ribonucleic acid synthesis in rat spleen after whole-body irradiation. Accumulated nucleotides were found in this organ from 12 hours after irradiation. R Goutier, M Goutier Pirote and P Ciccarone (University of Liège, Belgium) examined an effect which occurred soon after the comparatively low dose of 150 r (whole-body) to rats. Changes in the deoxyribonuclease activity of the spleen could be detected after half an hour. The activity of the extracted enzyme depended critically upon the methods used in preparing the sample. The authors considered that the effect was due to a change in the enzyme molecule, and not to the effect of the irradiation on enzyme distribution.

H I Adler (Oak Ridge, United States) reported on observations with a variant of *Escherichia coli* which did not synthesize catalase. One effect of irradiation was to sensitize the cells to the action of hydrogen peroxide. Irradiated cells exposed to its action were killed, although they would otherwise have survived.

Bacteria were used in two studies of the effects of low doses of radiation. Marcovitch (Institut du Radium, France) had examined the induction of lysogenic bacteria, and concluded that the passage of a single ionizing particle through a cell was sufficient to bring about this effect. M. Demerec (Carnegie Institute of Washington, United States) made use of three biochemical mutations which occurred spontaneously with very low frequency, so that the genetic effects of doses as low as 8.5 r could be assessed. In all three cases, the number of mutations induced was proportional to the dose at low doses, though the doses required to produce a given frequency of mutations differed for the three mutations chosen for study.

Now observations on the genetic effects of ionizing radiation on mice were reported by W. L. Russell (Oak Ridge, United States). These have confirmed his previous report that if a dose in the range 200–600 r was delivered at 80 r/min more mutations were induced in spermatogonia than if the same dose was delivered continuously as 'chronic' irradiation at 90 r/week or less. This did not apply to mutations induced in spermatozoa. The genetic effect of a single dose on oocytes was greater than on spermatogonia, whereas the reverse was true of chronic irradiation. L. B. Russell (Oak Ridge, United States) reported that chronic irradiation was less effective than an acute dose, delivered to embryos in their most

sensitive stage, in bringing about still births and neonatal deaths.

Various tests of radiation damage were used by L. J. Cole (Naval Radiobiological Defense Laboratory, United States) in comparing effects of single exposures and 'chronic' or fractionated radiation. Single doses were less effective in inducing leukaemia or shortening the life span, but the effects of chronic irradiation doses on the fertility of female mice were much lower than were single doses. The effect of as little as 25 r in a single dose could be detected in weanlings. The injection of bone marrow, which protected against the lethal effects of 800 r, did not protect against loss of fertility.

Immunological aspects of tissue transplantation after 300 r of X-rays had been studied by P. C. Koller and S. Doak (Chester Beatty Research Institute, Great Britain). After fifty days, the immune response of some 'chimaeras' had reverted to the host type, others had retained the immunity of the donor, and yet others gave a mixed response.

This very brief account of the subjects discussed at the symposium should make it evident how wide a range of materials and how many different approaches are being used in attempts to clarify some of the outstanding problems in radiation biology. The proceedings of the symposium are to be published as a supplement to the *International Journal of Radiation Biology*.
TREVAN ALLEN

NUCLEAR FORCES AND THE FEW-NUCLEON PROBLEM

MORE than 250 nuclear physicists, including about 100 delegates from fifteen countries overseas attended the international conference, which was held at the Physics Department, University College, London, during July 8–11. A conference on the behaviour of light nuclei had not taken place for several years and was initiated by physicists at Los Alamos and University College. As was stressed by Prof. H. S. W. Massey (University College), who opened the conference, although the original intention was to emphasize the few nucleon problem, discussion of nuclear forces had inevitably to be included.

The conference consisted of five main sessions, the first and longest being entirely devoted to the primary two nucleon interaction. In this session review papers were given by Prof. R. E. Marshak (Rochester), R. Wilson (Harvard), K. A. Brueckner (Pennsylvania) and G. F. Chew (Berkeley) on both the experimental and theoretical status of the problem. Interest centred on many sets of measurements, including triple scattering and correlation experiments, as well as more accurate cross section measurements at various energies and on their interpretation in terms of the S matrix. Prof. G. Breit (Yale) presented an extensive search for phase-shift fits to the scattering data up to 340 MeV., while comparison was made with phase shifts derived from various phenomenological potentials by Prof. Marshak. There was discussion on both the necessity and theoretical justification for including spin orbit and other velocity-dependent potentials in the two-body force. The experimental papers were concerned with recent triple scattering measurements in p - p scattering at Rochester and Harwell and with p - p angular distributions at Minnesota. Also n - p angular dis-

tributions and polarization measurements from 20–120 MeV were reported by Dr. J. J. Thresholt (Harwell).

Dr. J. Iwadare (Kyoto) summarized the recent work done in Japan on the meson theoretical two nucleon interaction and its comparison with experimental data. This was followed by Prof. Chew's paper which reviewed recent work on the meson field theoretical approach to the two body problem starting from the Mandelstam conjecture on the analytical form of the scattering amplitude. The inclusion of the pion-pion interaction within the context of dispersion relations seems to be the next step in the long struggle to obtain meaningful results from the meson theory of nuclear forces proposed by Yukawa in 1935.

Prof. Yukawa was chairman for the beginning of the second session, on the scattering of nucleons by light nuclei at high energy. A review paper on the impulse approximation by Dr. H. McManus (Chalk River) was followed by applications of this approach to the n - d and p - d case by Dr. L. Castillejo (Birmingham), R. Phillips (Harwell) and by Japanese workers. The problem was examined from the point of view of dispersion theory in a paper by Goldberger, Halpern and Blankenbecler (Princeton), and corrections due to multiple scattering were considered by Prof. R. J. Glander (Harvard). In this session there were reports by Drs. A. M. Cormack, T. C. Griffith and G. Huxtable on experiments done at Harwell, University College and Harwell respectively on p - d and p - α scattering at energies between 60 and 160 MeV.

The session on photoneuclear reactions with light nuclei opened with a review by Dr. D. Dixon

(Glasgow) Other papers were presented by Profs G Breit, A Klein (Pennsylvania) and Dr Iwadare. The effect on the theory of the photodisintegration of the deuteron of the spin-orbit force within the n - p system stimulated much discussion.

The fourth session of the conference was devoted to the question of binding energies and elastic scattering of light nuclei at low energies. The review papers were given by Prof H S W. Massey and Dr P G Burke (University of London) on the three-body problem and on the elastic scattering of nucleons by alpha-particles. There were also two invited papers from Los Alamos. Dr L Cranberg reported on experimental results concerning total and differential cross-sections and also polarization measurements in the scattering of low-energy neutrons from ^2D , ^3H and ^3He , while Dr L Rosen reported on charged particle scattering from ^2D and ^3H at energies up to about 20 MeV. These experiments led to several new checks on charge symmetry and time reversal invariance.

The contributed papers included one on the ground-state energy of the triton, by Prof J M Blatt (Sydney). Using the Gammel-Thaler potential, no bound state was found for reasonable trial wave functions. Among other papers from Los Alamos, Dr J L Gammel gave a preliminary account of attempts to integrate the n - d problem numerically and discussed the feasibility of spin-correlation experiments using ^4He as an analyser.

Polarization measurements in n - d and p - d scattering at low energies, reported by Dr H J Gerber (Zurich) and Dr R E Segel (North-western University), indicate that there is very little polarization at about 4 MeV. A contribution from Dr N

Vlassov (Moscow), read by Dr I A Baz, on the interaction of protons and deuterons with light nuclei ended this session.

The last session, with a title "Reactions Involving Four or More than Four Nucleons", was opened by Dr B H Bransden (Glasgow) with his paper on the collisions of neutrons and of deuterons with ^3H and ^3He . This paper was followed by a number of papers involving the application of the resonating group structure method to binding energy and scattering calculations. This method, as did the impulse approximation method at higher energies in a previous session, aroused considerable controversy during the discussion. Nevertheless, it was felt that some progress had been made, since one type of mixture of exchange forces does seem to be simulating the exact force in more than one situation involving light nuclei.

Prof G Skornyakov (Moscow) then gave his paper on n - d scattering in the zero range force approximation, this being a contribution to the previous session. The three-particle problem is solved accurately in this limit. He also read a paper by Dr T Y Barit on p - T scattering and allied reactions.

The final papers were preceded by a review given by Dr V J Emery (Harwell) of the calculations of the binding energies of nuclei using the Brueckner method. Prof Brueckner himself also presented a paper on the Hartree-Fock method for strongly interacting systems. The conference concluded with papers by Profs N Austern and S Meshkov (Pittsburgh) on preliminary calculations concerning the structure of ^4Li and ^{12}C .

T C GRIFFITH
E A POWER

CHAGAS'S DISEASE

CHAGAS'S disease or South American trypanosomiasis, occurring chiefly in Brazil and other countries of South America, is caused by *Trypanosoma cruzi* and is spread mainly by reduviid bugs. The disease was first discovered and described fully in 1909 from the State of Minas Geraes in Brazil. All the significant observations regarding the causative agent, the vector, mode of transmission and symptoms were made then, by that creative genius, Carlos Chagas. In order to commemorate the fiftieth anniversary of this discovery, an international congress on Chagas's disease was held at Rio de Janeiro during July 5-11.

Foreign delegates from European countries, Israel and the United States of America numbered more than seventy. Approximately 300 others from Brazil and the neighbouring countries of South America also attended. At a short historical session at the Ministry of Education and Culture on July 4 the life and work and significance of the discoveries made by Chagas were described by various speakers.

The inaugural meeting of the congress was held on July 5 in the National Faculty of Medicine from 9 p.m. until midnight, when addresses were delivered by Prof Alessandri (Chile), Prof Lemoigne (Pasteur Institute, Paris), Dr Candau (director general, World Health Organization), a student in the Medical Faculty, Prof Moraes, director of the Medical School and dean of the University, and replied to by Prof Carlos Chagas Filho.

The real business of the congress began on the following morning at 9 a.m. and lasted until 6 p.m. in a pavilion within the grounds of the Instituto Oswaldo Cruz. Two or three sessions took place concurrently to discuss the disease in its different aspects. In one of the lecture theatres simultaneous translations from English, French, Spanish, Portuguese and German were provided. Chagas's disease in the American continent was discussed from the pathological aspect and the different forms encountered in the various South American countries described, including the clinical findings on the two human cases thus far reported from the southern United States. Other papers on transmitting agents, animal reservoirs, including the opossum and armadillo, and their relation to the epidemiology of the disease as well as the characters of the human strains, were discussed. Public health questions were reviewed in relation to the geographical distribution of the principal transmitters of the disease which infest human dwellings. The anatomy and respiratory system of *Triatoma infestans*, the chief vector in Brazil, was described. On the following day the subject discussed in one section was the aetiological agent, with emphasis on the physiology, metabolism and nutrition of the parasite. Electron microscope studies of parasitized cells were included. In another section immunological aspects of the disease, including complement fixation reactions, precipitin and skin tests, were dealt with and the isolation of

immune polysaccharides from the organism described. The occurrence of toxins in cultures of the organism appeared to be doubtful. The epidemiology of the disease was discussed in seven papers. Polymorphism which occurs in African trypanosomes was compared with that met with in *T. cruzi*, and observations made on the nature of their evolutionary cycles. The session was concluded by the showing of a film dealing with methods of eradication of the tsetse fly, which transmits the disease in Portuguese Africa. On the same evening a meeting was held in the Brazilian Academy of Sciences from 9 p.m. until midnight, at which a paper was read on 'Chagas as Protozoologist', and others on the metabolism, phylogeny and growth of the parasite. The following day was devoted to the pathology of acute and chronic cases of the disease in different parts of the South American continent, throughout which the virulence of the causative agent varies. Discussions took place on the myocardial, nervous, cerebrovascular and blood protein changes involved, as well as on the condition of megacolon and megacosophagus now believed to be causally related to the disease. Further papers on epidemiology dealt with animal reservoirs and with the feeding habits of domestic and wild types of rediviv bugs. The danger of blood transfusion as a means of spread was also dealt with. Prophylaxis was best effected by spraying the sites where the vector was found, along with general hygienic measures. Workers from different areas of South America, where the nature of the problem varies with the transmitting agent, contributed also on the following day. The different clinical forms and diagnosis of the disease, including that met with in congenital cases, were described in seven papers. At a special session the nature of the infection caused

by *Trypanosoma rangeli* was described. This parasite was first described in 1920 by Tejera in Venezuela, where it infects *Rhodnius prolixus*, which is also the chief transmitter of *T. cruzi* there. The first forms were seen in human blood in Guatemala in 1946, and now 795 cases of infection have been described in Venezuela, chiefly in children, but the infection is not of serious character. At an evening session in the National Academy of Medicine further papers were read. On the last full working day of the congress, eighteen papers were read, chiefly on the relationship of cardiac and nervous disorders, including megacolon and megacosophagus, to Chagas's disease. Discussions also took place on chemotherapeutic agents, but the sad fact remains that no curative agent is known for this disease. A short ceremony took place during the morning at which a plaque, presented by the Argentinian delegation, to the memory of Carlos Chagas was unveiled.

On the same day a paper was read by Prof. Jean Coudert on the action of *T. cruzi* extracts on cancer cells, another by William Frye on antibiotics in tropical disease, and René Dubos gave a talk on general aspects of infection.

The final meeting on July 11 was devoted to round table discussion of the subjects dealt with earlier in the week. Resolutions were also submitted regarding the holding of another international congress within the next few years, but no definite decisions were arrived at. During the week more than 150 papers were read. Two medals were struck to commemorate the congress, each with the head of Carlos Chagas on one side but differing on the obverse side. The proceedings of this inspiring congress will be published in due course.

J. D. FUZZON

SPECIAL CERAMICS

THE challenge of temperature, which has inspired the metallurgist to some of his more notable developments, has in recent years been renewed and has been taken up by the ceramist, who is seeking materials of low creep resistance, high thermal shock resistance and high hot-strength to meet the demands of propulsion engineering, high speed vehicles and nuclear engineering. The ceramist has for many years made his own special contribution to communications engineering, chiefly in the exploration of oxide type materials, the field of non-oxide materials remained largely unexplored, but it is now being opened up by the drive for new materials in other engineering applications. The British Ceramic Research Association has for the past five years had a small group devoted to these studies and has been working in close co-operation with various Service departments and industrial concerns. It was felt that some attempt to set up a forum for the exchange of ideas would be timely, and the outcome was a Symposium on Special Ceramics held at the Laboratories of the British Ceramic Research Association in Stoke on Trent during July 13-15. About 150 delegates attended the symposium and seven countries were represented. The subject-matter of the symposium was divided into four sessions dealing with: (1) properties and structure, measurements, (2) preparation and properties of nitrides, (3) preparation and properties of other non oxides, and (4) furnaces techniques, analysis, applications, etc.

After a welcome to the delegates by the chairman of the Association, Mr. E. James Johnson, and the director, Dr. A. T. Green, the deputy director Dr. N. F. Astbury, gave an introductory lecture on the fields of application for new ceramic materials, and spoke of the special ceramics research programme of the British Ceramic Research Association, in which particular reference was made to boron nitride, a machinable dielectric capable of withstanding high temperatures, and to a new form of self bonded silicon carbide and to silicon nitride. Both the latter materials are being actively studied in connection with rocket engineering. The dependence of macroscopic properties on crystal structure and the trends observed in groups of materials of the same structure were discussed in a paper by Dr. S. N. Ruddlesden (British Ceramic Research Association), who illustrated her arguments by non-oxides such as silicon nitride and boron phosphide, the latter being a new compound of the III-V series of zinc blende structures. Like silicon carbide, boron phosphide is very hard and it is a semiconductor with an energy gap of the order of 5 eV.

The greatest challenge that ceramics must face in meeting metals in their chosen field is the absence of ductility and their comparatively low breaking strain. The reply to this is being sought by a study of the properties of certain oxide crystals, and it was of special interest, therefore, that Dr. F. J. P. Clarke (UK Atomic Energy Authority Harwell) was able

to give an account of his experiments on the room-temperature ductility of single crystals of magnesium oxide, together with his observation of slip bands and fracture starting at the intersection of these slip bands near a crystal face. Dr Clarke discussed possible applications of his results to polycrystalline materials.

Methods of measuring thermal conductivity requiring much less time than traditional methods were described by Mr T W Lindop (Morgan Crucible Co.), and Mr R P Tye (National Physical Laboratory) contributed to the discussion with an account of an even more rapid (< 1 min) comparator method. A simple apparatus for the measurement of creep at high temperature ($1,200^{\circ}\text{C}$) was described in a paper by Messrs N L Parr and G F Martin, read by Mr D M Rae (Admiralty Materials Laboratory). Dr Clarke ended the first session with a description of the effect of reactor irradiation on ceramic materials, which aroused some lively discussion on the damage mechanism and the neutron energies causing most damage.

Silicon nitride is a hard, very strong material (the modulus of rupture at $1,200^{\circ}\text{C}$ is of the order of $18,000$ lb/sq in) which can be made into shapes of accurate dimensions by nitriding pressed silicon-powder, since no contraction occurs during the firing. Its preparation, its properties as an engineering material (it possesses very good thermal shock resistance and satisfactory resistance to creep) and its microstructure were described by Messrs N L Parr, G F Martin and E R W May (Admiralty Materials Laboratory). In the subsequent discussion, Mr P Popper (British Ceramic Research Association) showed photographs of some intriguing spiral 'whiskers' of silicon nitride. A new hexagonal form of Be_3N_2 was described by Drs A Rabenau and P Eckerlin (Philips, Aachen), who had studied the system Be_3N_2 — Si_3N_4 and found two other compounds, Be_2SiN_4 and a wurtzite-type compound, BeSiN_2 .

There is a wide gap between organic plastic insulators, which can be easily shaped by moulding or machining but which cannot withstand high temperatures, and refractory insulators, which can withstand very high temperatures but are difficult to make to accurate dimensional tolerances. One material which helps to bridge this gap is boron nitride, a refractory insulator which can be easily machined, a property which is attributed to its layer lattice crystal structure, which resembles that of graphite, with which it is isosteric. It is not wetted by many molten metals and has a high electrical resistivity (10^6 ohm cm at $1,300^{\circ}\text{C}$) and high resistance to chemical attack. The preparation of boron nitride, its possible uses, the control of hot-pressing and stability by additions of 'impurities' were described by Dr T A. Ingles and Mr Popper (British Ceramic Research Association). Other possible materials to bridge the gap are being sought in polymers which contain boron and nitrogen or phosphorus and nitrogen. The paper by Messrs F W. Anger and I. M. Herbert (Plessey Research Laboratories) on the preparation of phosphorus-nitrogen compounds as non-porous solids was remarkable for the presentation of so much inorganic chemistry in the language of the organic chemist.

Knowledge of dissociation pressures is important in considering materials for high-temperature applications, and measurements of the dissociation pressures of metallic silicides and of silicon carbide were

reported by Mr P Grievson and Dr C B Alcock (Imperial College of Science and Technology), who interpreted their results on a thermodynamic basis. A novel way of preparing an extremely strong, dense silicon carbide, without the need for hot-pressing, was described by Mr P Popper. The method involves heating a cold-pressed mixture of carbon and silicon carbide powder in an atmosphere of silicon vapour when, under appropriate conditions, a material is obtained with a density of 3.05 gm/cm³ (corresponding to 95 per cent crystallographic density) and a modulus of rupture at room temperature of the order of $30,000$ lb/sq in. Another silicide, MoSi_2 , described by Mr J B Huffadine (Plessey Research Laboratories), has a very low electrical resistivity and is used in heating elements. It has a remarkably high oxidation resistance and an expansion coefficient substantially the same as alumina, from 0° to $1,000^{\circ}\text{C}$. It also adheres strongly to alumina if hot-pressed with this oxide, and it was suggested that composite MoSi_2 — Al_2O_3 pressings could provide useful electrical components.

The preparation and properties of calcium fluoride ware were described by Mr P Rado (Worcester Royal Porcelain Co.). Although this material has a very poor thermal shock resistance, it has found application as a crucible material for the reduction of metallic fluorides, particularly uranium fluoride.

Photoconductive materials have normally been used in the form of single crystals, but Drs W van Gool and J G van Santen (Philips, Eindhoven) showed that a polycrystalline aggregate of cadmium sulphide could be used as an element in photosensitive devices.

Throughout the symposium attention was repeatedly directed to the high-temperature techniques required in the preparation of special ceramics, and some of these were discussed in detail in the final session, which included three papers on furnace design. Dr A Z Borucka (Metals Research, Ltd) described the construction of a furnace to give a hot zone ($1,200^{\circ}\text{C}$) of very uniform temperature by having the furnace windings split into several sections with the spacing of the windings graduated in each section. Dr M Cole and Dr Borucka (Metals Research, Ltd) described a novel replaceable heating element, consisting of a molybdenum heater encased in an alumina sheath through which hydrogen or another protective gas is passed. These elements can heat a furnace with a capacity of several cubic feet to $1,800^{\circ}\text{C}$ in either oxidizing or reducing atmospheres, giving a uniform temperature distribution with no contamination of the furnace atmosphere. The construction and advantage of various types of carbon-tube furnace, that is to say, the simple tube, the single-ended, hairpin-cut tube and the spiral-cut tube, capable of operating at temperatures above $2,000^{\circ}\text{C}$ *in vacuo* or in controlled atmospheres, were described by Mr C J W Baker (British Ceramic Research Association).

Many of the special ceramic materials cannot be melted under normal conditions, and so sintering cannot be used as a means of densification. The alternative technique is hot-pressing, but this has the disadvantage in general that only simple shapes can be produced without further machining. Dr J S Jackson and Mr P F Palmer (British Thomson Houston Research Laboratories) described an apparatus designed for hot-pressing small specimens of refractory hard materials to high density in graphite

dies heated by passing a high current through the walls. They reported the contraction of various carbides, borides and oxides as a function of temperature, and showed that reduction of particle size reduced the temperature needed for densification.

One of the difficulties of powder aggregation is the variation in density which may occur through the compact. This difficulty can be circumvented by isostatic pressing and the use of a reversible gel, such as a polyvinyl polymer, as a mould material giving substantially true hydrostatic pressures up to 50 tons/in.² was described by Mr. T. W. Penrice (Production Tool Alloy Co). The technique is evidently applicable to quite complicated shapes.

The analyst's outlook on the new materials was touched upon in a paper by Mr. H. Bennett (British Ceramic Research Association) on the chemical determination of nitrogen in refractory nitrides, which posed many new problems. The final paper was a description by J. Peyssou (C.S.F., France) of the possible variations of properties of ceramic articles caused by variations in firing conditions and methods of manufacture.

The symposium concluded with a tour of the laboratories of the British Ceramic Research Association. The proceedings of the symposium are to be published by Heywood and Co. as a book, 'Special Ceramics', which is being edited by Mr. P. Popper.

N. F. ASHBURY

SOLID STATE PHYSICS

A CONFERENCE was held at Melbourne on "Solid State Physics" during August 17-21 under the auspices of the Australian Branch of the Institute of Physics. Grants from Australian industry, learned societies, government organizations and universities and support by the United States Government research authorities, the United Kingdom Atomic Energy Authority and the Canadian Government enabled several Americans, a Canadian and three Englishmen to attend. Other States of the Commonwealth of Australia and New Zealand were well represented.

The matter was drawn from across almost the whole range of this enormous subject, and one could hope that it might set a style of conference where the programme would be not so specialized that only a few experts could really benefit.

The programme opened with a day devoted to low temperature properties of metals and alloys. Precision lattice parameters, superconductivity and superfluidity, dislocation phonon scattering and electron phonon drag effects were discussed. The changes of lattice parameter in bismuth on alloying set a challenge to the theorists, and the dislocation scattering of phonons seems still to be in error by a factor assessed as between three and seventy by one speaker.

Electron field emission, low-energy spattering, epitaxial growth and dislocation barriers at surfaces served during the next day to remind those present just how little of the surfaces of solids is understood. The afternoon and following day were devoted to plasticity studies, when softening by adiabatic heating was used to explain the serrated load extension curves of iron at temperatures immediately above the brittle fracture region as well as for aluminium at very low temperature. The dependence on orientation of work hardening and of slip system geography in face-centred cubic metals were presented, and it was clearly the opinion of the majority that current theories are far too simple in their outlook. The Peierls-Nabarro force, its connexion with lattice friction, and the significance of the friction term in the hardening curves formed a recurrent theme in and out of the lecture room. Preliminary results indicate that reliable twin fault densities may be obtained from the asymmetry of Bragg peaks and this may inject a little more knowledge of the deformed state. Measurements of the mechanical properties of the

alkali metals at very low temperatures, along with optical microscope studies, have confirmed the X-ray evidence of shear transformations in sodium and lithium, and have brought to light a great sensitivity to structural details in the transformation of the crystalline aggregate.

On the third day attention was swung to optical properties of solids, with papers on soft X-ray studies of the light metals, infra-red and optical absorption in ionic crystals. Dielectric properties of doped alkali halides, evidence for aggregation of F centres and new techniques and facts in luminescence studies were the subjects for the remainder of the day. The analysis of rare-earth spectra in crystals is getting steadily more detailed and very large-scale calculations are rapidly elucidating the details of interactions within the f electron shell.

The last day saw an interesting mixture of papers: the dreadful maze into which theoretical physicists lead each other when the anharmonic terms leading to thermal expansion are studied was on show as was the theory of zone structure in liquids. Here some progress seemed to be made for the one-dimensional model. The magnetic structure of metallic chromium and its alloys was discussed in terms of magnetic properties and neutron diffraction evidence. Then came the grand finale with one situation well on the way to elucidation and three well on the way to confusion. The ordering of α brass at temperatures of about 135° C has been most convincingly shown and will probably remove the few remaining anomalies in the properties of the α Cu-Zn phase in this temperature region. But in copper the first annealing observed after very low temperature bombardment now occurs at only 7° K., and the atomic processes involved got steadily more mysterious. Polycrystalline calcite or 'marble' plastically uniaxially compressed at high hydrostatic pressure, largely recovers its axial dimensions on release of the hydrostatic pressure. In lithium fluoride as well as silicon iron, plastic hardening seems to denote a drop in dislocation speed under a given stress, indicating an increase in dislocation viscosity—or is it a drop in effective stress?

It was a stimulating conference, and those from overseas were impressed to find such a wealth of first-class work, enthusiasm and hospitality in this rapidly growing and developing continent of Australia.

W. M. LOMER

UNIVERSITY GRANTS IN GREAT BRITAIN

THE annual returns from universities and colleges in receipt of Treasury grants from the academic year 1957-58, now covering twenty-one universities and three colleges, issued by the University Grants Committee, records a further increase in the number of full-time students to 95,442, compared with 89,866 in 1956-57 (Pp 54 Cmnd 832 London H.M. Stationery Office, 1959 5s not) Statistics collected in October 1958 showed a university population of about 100,000, and this number is expected to reach at least 110,000 by 1961-62. There were 6,180 full-time and 2,208 part-time students from overseas within the British Commonwealth and 3,982 full-time and 1,904 part-time students from foreign countries, for 1956-57 the corresponding figures were 6,115 and 2,016 for the Commonwealth and 3,792 and 1,756 for foreign countries. Of full-time new students 36.4 per cent were in arts, 23.7 per cent in pure science, 19.0 per cent in technology and 13.7 per cent in medicine these figures compare with 38.7, 15.2, 13.5 and 26.1, respectively, in 1938-39. For full-time women students the corresponding figures for 1957-58 are 63.5, 20.0, 0.8 and 12.1, respectively, and for 1938-39, 64.7, 15.9, 0.8 and 16.2. Full-time advanced students of pure science numbered 3,853 (34.8 per cent), of technology, 1,916 (17.3 per cent), and of medicine, 968 (8.8 per cent), 3,007 students were taking postgraduate courses in teacher training.

Of the full-time students 76,687 were reading for a first degree, 3,937 for a first diploma and 14,069 engaged in research or other advanced work, the corresponding figures for 1956-57 being 71,713, 3,969 and 13,379, respectively. Of the new full-time students, 24.0 per cent were in pure science, 15.4 per cent in technology and 9.3 per cent in medicine,

for 1956-57 the corresponding figures were 23.8, 15.0 and 9.6 per cent, respectively.

The proportion of assisted students was 79.2 per cent compared with 75.7 per cent in 1956-57 and 71.9 per cent in 1953-54, ranging from 92.2 per cent in Wales, 86.7 per cent in English universities, excluding Oxford, Cambridge and London, to 67.2 per cent for Scotland. Full-time teaching and research staff increased to 10,542, compared with 10,485 in 1956-57. The proportion of full-time students residing in colleges or halls of residence was 26.4 per cent compared with 27.4 per cent in 1956-57 although the total, 25,174, was higher. The proportion of men in residence, excluding Oxford, Cambridge and London, was 22.4 per cent and of women, 38.6 per cent, whereas 46,237 (48.4 per cent) were in lodgings and 24,031 (25.2 per cent) at home, compared with 46 per cent and 26.6 per cent, respectively, the previous year.

Of the recurrent income of £49,418,302 (an increase of £7,762,693 on 1956-57) £34,953,406 was from Parliamentary grants (70.7 per cent). Income from fees increased from 11.2 per cent to 11.5 per cent, local authority grants decreased from 3.1 to 2.8 per cent, endowments from 4.0 per cent to 3.6 per cent, donations and subscriptions from 1.2 to 1.1 per cent, and payments for research (£3,008,898) from 6.5 per cent to 6.1 per cent. Non-recurrent grants in respect of capital expenditure amounted to £11,816,479 compared with £9,134,185 in 1956-57 and of the recurrent expenditure of £48,335,053—an increase of £6,825,350 on 1956-57—7.1 per cent was spent on administration 68.6 per cent on departmental maintenance and 12.5 per cent on maintenance of premises. Expenditure on libraries increased from £1,620,958 to £1,821,943 but decreased to 3.8 per cent of the total.

NUCLEAR RESEARCH IN AUSTRALIA

IN the sixth annual report of the Australian Atomic Energy Commission (Commonwealth of Australia, 1958 Pp 62 Sydney Australian Atomic Energy Commission, 1959), covering the year ended June 30, 1958, considerable space is devoted to the Commission's Research Establishment at Lucas Heights, which was officially opened by the Prime Minister of Australia, the Rt Hon R. G. Menzies, on April 18, 1958. During the period up to the beginning of May approximately 4,500 visitors went to the Establishment. Many of the major buildings have been completed and this has enabled the research staff to return from Harwell and to begin to design and assemble equipment for their research projects. The Commonwealth Government has approved a further building programme involving an expenditure of £1.6 million during 1958-59 and 1959-60 on new laboratories and services, including engineering research laboratories, a building in which the fabrication and chemistry of beryllium fuels can be studied, and post-irradiation handling equipment.

The report details the work of the principal sections of the Establishment and the various research projects to be undertaken. The main function of the

Isotopes Section is the advisory service to industry and research, and 310 requests for advice on various aspects of isotope production were dealt with during the year. Australian industry and research in comparison with the United States of America or the United Kingdom has, however, been slow to accept the use of radioisotopes. The Section assisted in a large-scale field test, in which a radioisotope technique was used to measure the efficiency of mixing in a cooling pond in an electrical power station. Other investigations included the development of a method for the continuous investigation of moisture content of brown coal, a technique for tracing sewage sludge in sea disposal, siltation in the Hunter River, and the use of radioisotope tracers in cloud physics.

A large proportion of the work of the Technical Physics Section has been concerned with the installation and commissioning of the control gear and instrumentation of the High-Flux Australian Reactor, at the Establishment. Other equipment constructed and tested include a fast scaler, using transistors, with 'plug-in' scales of ten, and a discriminator with resolving time of 1 μ sec, a beta-gamma coinci-

dence unit, and linear amplifiers and scintillation counters for the Health Physics Section.

One of the aims of the fuel element research conducted at the Establishment is to develop a 'self breeding' fuel in which thorium is present in such quantities that fissioned uranium is continuously replaced by uranium 235. Beryllium and beryllium oxide are also being studied as moderator materials and fuel carriers. Another problem under study is the production of graphite which is impermeable to fission product gases and several methods of sealing inherent porosity are being investigated. Research on a sodium based liquid metal fuel reactor was begun at Harwell and is being continued at Lucas Heights. The experimental assemblies built by the Australian staff while at Harwell have been purchased and shipped to Australia. The sodium plant built by the Australian Atomic Energy Commission at the Research Establishment is a research tool designed to pump molten sodium at 500°C at 10 gall per min and it will provide facilities for carrying out research on compatibility problems, sodium component testing, heat-transfer investigations and the training of staff in the handling of liquid metals.

In the sections of the report dealing with the search for, and mining of uranium details are given of the airborne radiometric and geological surveys carried out by the Bureau of Mineral Resources. There was a marked decline in interest in the search for uranium both by companies and individual prospectors. This is attributed to the uncertainty regarding the future of the world uranium market. The picture presented in the report is that of a rather difficult period in the years immediately ahead, but that the present rate of production could well

prove insufficient within the next decade. The production of uranium oxide at Rum Jungle was lower than in the preceding year. Full-scale open-cut mining has been in progress at Mary Kathleen during the year and a large stock pile of ore for treatment has been built up. A recalculation of the ore reserves of the Mary Kathleen deposit has shown that the total reserves of recoverable uranium oxide are greater than was originally thought and more than enough to complete the contract with the United Kingdom Atomic Energy Authority.

A symposium on the 'Peaceful Uses of Atomic Energy in Australia' was held in Sydney during June at which 114 papers were presented. Brief details of the proceedings are given in the annual report and a record of the papers and discussions is to be published. The publication of a new quarterly, *Atomic Energy*, giving information on developments in and applications of nuclear science and technology was commenced during the year and the booklet entitled 'Prospecting and Mining for Uranium in Australia' was reprinted. Six atomic energy exhibitions in various towns in the Commonwealth were presented by the Commission in addition to several television programmes at national and commercial stations in Sydney. The annual report concludes with a statement of the net expenditure of the Commission for the year ended June 30 1958, details of the extra mural research projects at various Australian universities, the names of the senior research staff and holders of the postgraduate research studentships and undergraduate scholarships and a bibliography of the principal publications of members of the Commission, its staff and advisory committees.

CONSERVATION OF ENGLISH WALLPAINTINGS

IN recent years those interested in early wall paintings have been greatly perturbed by their condition and the rather haphazard methods sometimes employed for their preservation. It was therefore more than timely in 1953 for the Central Council for the Care of Churches and the Society for the Protection of Ancient Buildings to appoint a committee to report on the nature and causes of the troubles which have been observed in such paintings, the remedies which could be applied and the methods which would give the best hope of successful preservative treatment in the future. The report* was compiled under the able chairmanship of Mr W I Croome. The committee included well known archaeologists and scientists who had made a special study of this problem.

At the outset the committee was seriously perturbed by the use of varnish and wax as a preservative, for these act as relatively impervious skins and impede the rate of evaporation of moisture and cause disintegration of the surface. As a preliminary measure it advised that these two methods should cease immediately.

The report continues with an instructive and necessary explanation of the technical terms and

materials used in wallpainting. Then follows a useful summary of English and foreign practice in relation to wallpaintings with some pregnant notes on the effect of time. These clearly show that the conservation methods used were not satisfactory.

It was therefore abundantly clear that much fundamental work was necessary and the constructive recommendations of the committee are based on the practical applications of its conclusions.

The main recommendations deprecate the use of wax varnish, sodium silicate, or ethyl silicate for any preservative treatment. The use of caesin in a maximum 2 per cent solution in appropriate cases should be confined to the binding of loose pigment. Lime water should be used for the consolidation of the plaster foundation and in the case of disintegration of the paint it may be mixed with skim milk. The committee stresses that since wallpaintings are liable to deteriorate under conditions of damp every care should be taken to make the church structurally sound and thus exclude any excessive moisture.

The committee feels that much further research should be undertaken on this problem and suggests a course of training which will eventually provide a succession of practitioners for this important work.

The report concludes with some practical notes for the removal of wax preparations, retouching and overpainting, recording and some excellent illustrations of work that has already been undertaken.

* The Conservation of English Wallpaintings, being a Report of a Committee set up by the Central Council for the Care of Churches and the Society for the Protection of Ancient Buildings. Pp 20+18 plates. (London: Central Council for the Care of Churches, Fulham Palace 1959) 7s 6d.

subject of recent investigations. Briefly, the results are that close to the Sun the colour is not significantly different from that of the average solar disk⁹, but in the outer parts the infra-red excess becomes appreciable, at a distance of $2.5R_{\odot}$ and at a wave-length of 1.9μ it has been measured to be 2.17. Such an excess is naturally explained by the diffraction theory of the F corona¹⁰. That there is dust in the solar system is shown by the existence of the zodiacal light, and both van de Hulst¹¹ and Allen¹² have shown independently that both the F corona and the zodiacal light can be explained by a single model for the interplanetary dust. The variation in infra-red excess mentioned by Kellogg and Ney is again accounted for by a varying ratio of electron component (with colour identical with that of the Sun) and dust component (which shows an infra-red excess).

We may remark here that after allowing for the dust corona in the conventional model the true electron densities in the outer solar atmosphere are considerably lower than indicated by the Baumbach curve in our Fig. 1, and in fact are in rather better agreement with Kellogg and Ney's curve—but not for the reason these authors suggest. However, at $10R_{\odot}$ there still remains a discrepancy of about $\times 40$ between the true electron density and the lower value given by Kellogg and Ney.

There is a contradiction here that is not satisfactorily explained by these authors in their article. If the conventional electron densities, or particularly Kellogg and Ney's densities, are accepted, the computed brightness at large distances from the Sun is much smaller than the observed brightness. In conventional theory the extra light arises from dust scattering, but Kellogg and Ney attribute it to synchrotron radiation. If this attribution is correct, synchrotron radiation must increase in importance with increasing distance from the Sun—and indeed we have shown that the infra-red excess increases in the outer corona. But synchrotron radiation does not explain the existence of unbroddened Fraunhofer lines in these parts of the corona, although these lines are satisfactorily explained in terms of scattering by interplanetary dust particles far from the Sun.

We shall not detail other criticisms which we feel could be made, but mention one last observational point. Kellogg and Ney propose that if the solar corona is really analogous to the Van Allen particle belt, one might expect a maximum in the coronal intensity close to the Sun. They believe that such a maximum might exist, supposing that "the problem of reversal in photographic emulsions has previously masked the possible presence of a maximum." So gross an effect as photographic reversal has not complicated the interpretation of eclipse photographs in any competent observations made since the 1890's. There are in fact other much more subtle sources of error in the photometry of such a difficult object as the solar corona, and these errors may more readily be overlooked in photoelectric than in photographic photometry. The most careful work in this region has never shown a maximum of the kind suggested by Kellogg and Ney, and its existence is very doubtful.

We agree with Kellogg and Ney that further observations of the polarization over a greater range of wave-lengths are required and should be made at future eclipses. Also, it is unfortunate that the most reliable measurements of polarization, and to some extent of infra-red excess, have been made near

sunspot minimum, repetitions near maximum would be of value.

However, we are of the opinion that the authors have not substantiated their claim that this interesting new theory accounts better for the observed properties of the corona. While it may be that synchrotron radiation is a third contributor to the coronal light, we do not think the present observations support the postulate that sufficient synchrotron radiation exists to justify a major modification to the present two component model of the corona.

D. E. BLACKWELL

D. W. DEWHIRST

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⁴ von Klöber, H., *Mon. Not. Roy. Astro. Soc.*, **118**, 201 (1958).

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⁶ Zakharin, K. G., 'Total Solar Eclipse of June 10, 1930, Report of Soviet Expeditions' (Leningrad, Acad. Sci. U.S.S.R., **1**, 56 (1939)).

⁷ Schmidt, W., *Bull. Astro. Inst. Neth.*, **12**, No. 447, 61 (1953).

⁸ Salto, K., *Tokyo Astro. Bull.*, series 2, No. 8, 63 (1948).

⁹ Grotian, W., *Z. Astrophys.*, **3**, 109 (1931).

¹⁰ Blackwell, D. E., *Mon. Not. Roy. Astro. Soc.*, **112**, 652 (1952).

¹¹ van de Hulst, H. C., *Astrophys. J.*, **105**, 471 (1947).

¹² Allen, C. W., *Mon. Not. Roy. Astro. Soc.*, **108**, 137 (1940).

We wish to express our appreciation for the critical comments made by Drs Blackwell and Dewhirst concerning our suggestions about the nature of the solar corona. We are not professional astronomers and for this reason we may have placed undue emphasis on certain published literature, with perhaps too little emphasis on other literature more generally accepted by astronomers. We do feel, in spite of the remarks of Drs Blackwell and Dewhirst, that under each of the topics which were discussed in our original article, experimental evidence exists which makes the possibility of synchrotron radiation from a magnetically contained corona at least a very plausible hypothesis.

The principal objection of Drs Blackwell and Dewhirst seems to rest on a question of terminology. To us, the F corona is not a real part of the corona, but represents a spurious effect which must be removed. In the interests of brevity, we omitted any mention of the experimental difficulty of separating the F -coronal light from that of the electron corona, except for one or two comments, but we are aware of at least part of the evidence for the existence of the F corona. Thus the curve which we marked curve 1 in our Fig. 1 is supposed to represent the electron density and not the total coronal light. It was plotted as $1/R^6$ not by mistake, as Blackwell and Dewhirst imply, but to represent the currently accepted electron densities. Eclipses subsequent to the one observed by Turner have led to electron densities falling off as $1/R^6$ instead of $1/R^5$, as would have been obtained from the 1898 eclipse alone. In order to obtain electron densities at large distances, the F corona must of course be removed. Considering the rough nature of the ideas involved and the difficulties of measurement, we consider that the result is in reasonable agreement with our curve. We pointed out the similarity of the solar corona and the radiation belt to indicate the attractiveness of confining charged particles by a magnetic field, in contrast to a gravitationally confined atmosphere. The comparison with the Van Allen radiation is intended only to be suggestive, and obviously no

very close agreement is to be expected. However the most recent observation of the radiation belt by the Iowa group shows even better agreement with the coronal curve 1 than the results shown in curve 3 of our original article.

It is unfortunately true that the measurements of Zakharin were made with some instrumental difficulties and the resulting plates were not of the highest quality. Nevertheless, these and the other measurements quoted by us remain the only measurements of the direction of polarization of the coronal light which were made near sunspot maximum. It seems very likely that synchrotron radiation will be observed only near solar maximum. Again, Nikonov's measurements of the infra red excess were probably not as well done as the measurements by Blackwell in the 1952 eclipse. Nevertheless as they stand, they do not agree with the idea that the infra red excess is due to the scattering by dust, since Nikonov observed that the infra red excess was greatest at sunspot maximum when the electron density in the corona is greatest, and therefore the relative contribution of the F corona should be least. So long as there are no more modern experiments to replace this Russian work, the answer to the questions which we are discussing must remain in doubt.

In defence of our basic idea, we believe that Drs Blackwell and Dewhurst have taken too seriously the details of our suggestion but have tended to overlook or misunderstand the main features of a trapped corona. Our concept is that magnetic fields anchored at the surface can act as guiding centres for particles which may then be confined between mirror points as they are in fact in the Earth's magnetic field. We accept as a working hypothesis that magnetic fields exist in the region of the solar corona. We also believe, because of cosmic ray evidence, that the Sun is able to inject high energy particles into these magnetic fields. If high energy electrons are injected into magnetic fields, then synchrotron radiation will automatically occur. In fact, if the corona were examined in light of long enough wave length, the synchrotron radiation would necessarily be observable. We wish to emphasize the point, which was made in our article, that the extent of the trapping of particles in the corona may depend strongly on solar activity, and therefore polarization and infra red excess measurements made at sunspot minimum are definitely not evidence against our suggestions.

Perhaps the title of our paper, "A New Theory of the Solar Corona", was too ambitious, since our model requires so many of the constituents of the description of the corona currently accepted. The comments made by Drs Blackwell and Dewhurst

seem to indicate that they believe we would reject the description of the corona in terms of K and F corona. This is not correct, we certainly believe that the majority of the visible light from the inner corona is produced by Thomson scattering by slowly moving electrons, and it is almost impossible to escape the conclusion that the outer corona must be largely composed of dust grains, as has been very effectively discussed previously by Dr Blackwell. We feel however, that ultimately some experiment will reveal the existence of trapped particles, and that it is possible that this experiment may consist of measuring in redder and redder light the polarization of the corona at times of high solar activity. Should the experiments in the visible or near infra red reveal synchrotron radiation, our postulate of the magnetically trapped corona would be confirmed. However, we do not believe that the absence of synchrotron radiation at visible wave lengths would disprove our hypothesis. Our calculations show that in order to see synchrotron radiation in the visible region of the spectrum, an integral energy spectrum for trapped particles would be required that goes at least as slowly with energy as $1/E$. An energy spectrum which falls as steeply as $1/E^2$ would not produce synchrotron radiation in the visible region in great enough intensity to be seen against the background of the Thomson scattered light.

The reason for presenting our article in *Nature* was that a study of the literature to which we referred had in fact convinced us that enough doubt existed as to the coronal polarization to justify an intensive experimental study of the problem at sunspot maximum. In the months that have followed since its submission, we have designed and constructed electronic telescopes which use photomultiplier detectors and television raster scanning to measure the polarization out to three solar radii in a pattern consisting of approximately 800 individual points. The polarization will be measured in fixed positions in the corona and the scan will proceed from one position to the next until the entire area is covered. This method eliminates many of the inherent difficulties involved in photometric measurements of coronal polarization. The equipment which we have designed is to carry out the programme just described six times during the total eclipse of October 2, 1959, and we therefore hope that, cloud-cover permitting, we will be able to contribute some useful results on this rather important problem.

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PROTON RESONANCE RELAXATION TIMES IN MOBILE LIQUIDS

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WE have measured the proton magnetic resonance relaxation times, T_1 , at 250 ± 25 gauss and at 5 000 gauss and T_2 at 0.75 gauss, for a number of organic liquids and solutions at 25°C . The results are summarized in Table 1.

Although T_1 and T_2 have not been measured at the same field and so are not strictly comparable, the results suggest that T_1 may be appreciably

shorter than T_2 . The difference is most striking for the benzene solutions. Some examples in which $T_1 = T_2$ have been observed, and also cases where more than one chemical type of proton is present have been studied.¹

Both T_1 and T_2 are strikingly shorter in fluorobenzene than in any of the other substituted benzenes. The short T_1 is implicit in the results of Elliott and

Table 1 VALUES OF T_1 AND T_2 IN SEC FOR VARIOUS ORGANIC LIQUIDS AND SOLUTIONS AT VARIOUS FIELDS AND AT 25° C

| Liquid | $T_2 \pm 10$ per cent at 0.75 gauss | $T_1 \pm 10$ per cent at 250 \pm 25 gauss | $T_1 \pm 5$ per cent at 5,000 gauss | Literature values of T_1 † (in sec) | Literature values of T_1 † at field (in gauss) | Literature values of T_2 † (in sec) | Literature values of T_2 † at field (in gauss) |
|--|-------------------------------------|---|-------------------------------------|---------------------------------------|--|---------------------------------------|--|
| Water (H ₂ O) | 2.7 | 3.6 | 3.6 | 3.4 (a) | 2,000 and 7,000 | 2.7 (d) | 7,000 (temperature not stated) |
| | | | | 3.5 (b) | 1,650 | | |
| | | | | 3.4 (g) | 7,000 | 3.0 (e) | 0.5 |
| Cyclohexane (C ₆ H ₁₂) | 3.5 | 5.5 | 7.1 | 6.5 (b) | 1,650 | — | — |
| Benzene (C ₆ H ₆) | 11 | 18 | — | 10.3 (c) | 0,500 | 17 (e) | 0.5 |
| | | | | 19.0 (b) | 1,650 | 10 (d) | 7,000 |
| Nitrobenzene (C ₆ H ₅ NO ₂) | 3.3 | 6.7 | 7.0 | 6.5 (b) | 1,650 | — | — |
| Chlorobenzene (C ₆ H ₅ Cl) | 7.0 | 12.5 | — | 15 (b) | 1,650 | — | — |
| Bromobenzene (C ₆ H ₅ Br) | 4.0 | 7.0 | 14.0 | — | — | — | — |
| Fluorobenzene (C ₆ H ₅ F) | 0.7 \pm 0.2 | 0.7 \pm 0.2 | — | — | — | 0.4 (f) | 0.5 |
| 73.1 per cent C ₆ H ₆ * in CS ₂ | 3.0 | 17.5 | — | — | — | — | — |
| 40.5 per cent C ₆ H ₆ in CS ₂ | 5.5 | 24 | — | — | — | — | — |
| 71.7 per cent C ₆ H ₆ in CCl ₄ | 6.0 | 16 | — | — | — | — | — |
| 42.0 per cent C ₆ H ₆ in CCl ₄ | 8.0 | 28 | — | — | — | — | — |

* Molecular

† Corrected to 25° C using viscosity if at slightly different temperature

References for literature values in Table 1 (a) = 17, (b) = 18, (c) = 4, (d) = 8, (e) = 7, (f) = 3, (g) = 10

Shumacher³ at 0.55 gauss, although they do not claim to have measured a value of T_2 .

T_1 for the benzene solutions rises with dilution and would probably reach the value of $T_1 = 60$ sec observed by Nederbragt and Reilly⁴ at 9,500 gauss for 8 per cent benzene in carbon disulphide measured by the recovery from saturation. This emphasizes the anomalous nature of the T_2 values.

The measurement of T_1 at any field-strength is straightforward. Measurement of T_2 is much more difficult and values of T_2 in excess of about 1 sec require special care. We have taken considerable pains to ensure a true measure of T_2 , as has been briefly described⁵, and which will be discussed in detail elsewhere⁶.

For water a difference between T_1 and T_2 at 7,400 gauss has been reported⁶ but the sample evidently contained dissolved oxygen and so the values are not strictly relevant. The value of T_1 is well established and appears to be independent of the field. A value of T_2 of 3.0 sec has been reported⁷ and a value of 2.7 sec is implicit in the measurement of Meiboom and Gill⁸ at 7,000 gauss. Another result⁹ appears to be T_2 in presence of a radio-frequency field.

For benzene the value of T_1 of about 18 sec is well supported and is independent of the field. A T_2 value of 16 ± 3 sec at 20° C and 0.5 gauss is reported from direct measurement of line-width⁷. A reported value¹⁰ of T_2 of 18.5 sec, at 2,000 gauss, was measured in the presence of the radio-frequency field, and theory^{11,12} indicates that this T_2 should have the same numerical value as T_1 , as observed. We note an apparent dependence of the field of T_1 in bromobenzene and possibly in cyclohexane.

Although the difference of T_1 and T_2 is most striking for the longer relaxation times, it is more realistic to consider the quantity $(1/T_2) - (1/T_1)$. This is of order of magnitude 0.1 sec⁻¹. If the relaxation times are shorter than about 1 sec, such a difference is difficult to observe¹.

Current theories of nuclear resonance relaxation^{13,14,20} indicate $T_1 = T_2$ for these materials, since the molecular correlation time, τ_c , is of order 10⁻¹¹ sec and the highest resonance frequency, ω_r , is of order 10⁸ r/s so that $\omega_r \tau_c \ll 1$. A difference only arises for slow interactions, that is, $\omega_r \tau_c > 1$, and then it is usually very dependent on the field.

The magnitude of the difference could be explained by the static interaction of any given proton with

one other proton at about 300 Å (about 50 molecular diameters), but since we have observed exponential decays, a substantial static interaction contribution is excluded. This led us to consider the possibility that the difference could arise from interactions with distant protons which although weak, because of the factor r^{-3} , are numerous. However, calculations in which the motional effects were allowed for, using the self-diffusion equation, showed that the effect is too small. (We are grateful to Mr. D. P. Rooke for assistance with these calculations.) Most other known interactions make equal contributions to T_1 and T_2 ; for example, direct dipolar, anisotropic chemical shift, anisotropic indirect interaction and paramagnetic ions in low enough concentration. The difference of T_1 and T_2 for water has been explained⁶ in terms of the slow fluctuating field produced as a result of proton-exchange processes. However, this effect should be proportional to the square of the field and it can scarcely explain benzene, cyclohexane, etc. The only moderately plausible general explanation we have found is that of a fluctuating isotropic indirect spin-spin (J type) interaction. A constant J interaction does not cause line-splitting (except in fluorobenzene) because the protons are equivalent¹⁵. However, if this coupling is explicitly dependent upon time, it becomes observable because the Gutowsky, McCall, Slichter¹⁶ theorem is no longer valid. It contributes to T_2 but not to T_1 . A similar but not identical effect is found in liquid hydrogen fluoride¹⁶. However, in order to produce $(1/T_2) - (1/T_1) \approx 0.1$ sec⁻¹ with $J \approx 10$ c/s, the coupling must be interrupted at about 10⁵ times per sec. This might be brought about by relatively infrequent 'violent' collisions between molecules. Proton exchange is in this sense a violent collision. The large effect in the benzene solutions would then be occasioned by the large electric fields produced by the polar solvent molecules. However, interruption of J at this rate is unlikely, except in dissociating molecules, because J -type splitting of tens of cycles per second between inequivalent nuclei is observed in molecules in similar circumstances.

Other experimental results on molecules containing more than one chemical type of proton will be discussed elsewhere⁶.

The measurements of T_1 at 5,000 gauss were made by Mr. A. Hartland.

Note added in proof. A recent report²¹ of measurements at 6,500 gauss shows precise agreement

with our measurements for water but $T_1 \approx T_2$ for benzene. The explanation of the difference between T_1 and T_2 for water in terms of surface effects in the small sample seems scarcely applicable to our sample of 200 ml

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POSSIBLE MECHANISM OF CYSTEINE PROTECTION AGAINST RADIATION CATARACT

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EXPERIMENTS have shown that cysteine injected into an animal shortly before the eye is irradiated will largely prevent development of radiation cataract. von Sallmann, Munoz and Barr¹ compared the histology of the lens epithelium in rabbits irradiated with or without a previous injection of cysteine and tentatively concluded that initial inhibition of mitosis by X ray was unaffected but that the number of nuclear fragments that developed after irradiation was smaller in the cysteine-treated lens. von Sallmann *et al.* used a dose of 1,500 r and it seemed possible that it might be easier to show histologically that cysteine affected radiation damage if the dose were nearer the threshold for mitotic inhibition. We have therefore examined the effect of a pre-irradiation injection of cysteine on the mitotic inhibition, the subsequent mitotic overshoot and on the production of fragmented nuclei in the lens epithelium of rabbits using a dose of 500 r to the right eye. The methods described by Pirie and Drance² were used. Comparisons were made between litter mates and between right (irradiated) and left (not irradiated) lenses of the same rabbit. These experiments have confirmed von Sallmann's earlier results. The inhibition of mitosis is as great and even more prolonged after cysteine injection followed by X irradiation than after X irradiation alone. The lens epithelium of the cysteine-treated rabbit shows no excess mitosis after inhibition has worn off. In two experiments a dose of 300 r was given and again cysteine treatment did not prevent complete mitotic arrest at 24 hr. Fig. 1 shows that at all stages examined (2–28 days after X ray) fewer fragmented nuclei were present in the lens epithelium of the cysteine-injected rabbit than in that of the animal irradiated without cysteine treatment.

But we noticed that in the cysteine-injected rabbits the epithelium of the lens of the left, non irradiated eye also showed an inhibition of mitosis. This inhibition could be estimated through a com-

parison with the non irradiated left eye of a litter mate not injected with cysteine. In order to determine the degree and duration of this inhibition of cell division by cysteine a series of experiments was done in which one rabbit received an injection of cysteine and a litter mate was used as a control, no radiation being given to either. Such pairs of rabbits were killed at intervals after the cysteine injection to one of the rabbits and comparisons made of epithelial

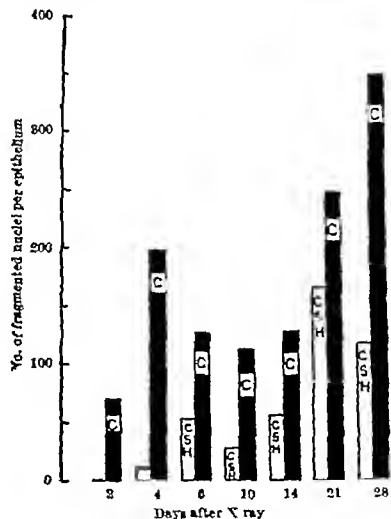


Fig. 1. Effect of cysteine injection on the development of fragmented nuclei in the lens epithelium after X-irradiation.

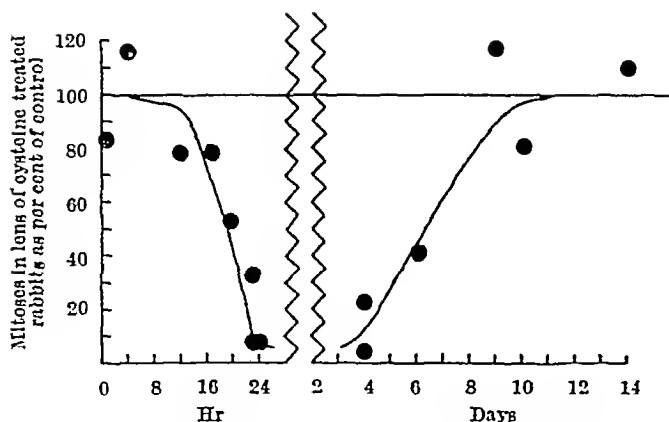


Fig 2 Effect of cysteine injection on mitosis in the lens epithelium

histology Fig 2 shows that cysteine injection arrests mitosis in the lens epithelium from 24 hr to 4 days. This inhibition of cell division then gradually wears off without any subsequent excess of dividing cells or formation of fragmented nuclei or abnormal forms up to 28 days after cysteine injection.

von Sallmann *et al*¹ had previously found in two rabbits that mitosis was normal 2 hr and 8 hr after injection of cysteine. We examined lenses, 30 min, 4, 12 and 16 hr after cysteine and found mitosis only slightly if at all depressed at these times. The total number of dividing cells and the proportion in prophase and succeeding phases of mitosis were unchanged compared with the control lenses. But at 20 hr mitosis was only 53 per cent of the control and at 23 hr it had fallen in one rabbit to 32 and in another to 8 per cent.

1 gm./kgm is a very large dose of cysteine and was used only because this dose has been shown to prevent irradiation cataract. For injection, cysteine hydrochloride was, in most experiments, neutralized with sodium hydroxide and injected, in a total volume of 5-8 ml, into the ear vein of the unanæsthetized rabbit. It was noticed that the animals became almost immediately quiet, and in some cases their hind legs became inco-ordinated and they did not feed for some hours. Controls injected with an equivalent amount of sodium chloride or 1 gm. glycine per kgm did not show these signs, nor was there a fall in the mitoses of the lens epithelium. In one experiment the cysteine hydrochloride was neutralized by shaking with 'Dowex-1'-bicarbonate resin, and the carbon dioxide blown off by passing nitrogen through the solution, thus avoiding the presence of sodium chloride in the solution to be injected. The rabbits injected with this solution of cysteine showed the same signs of inco-ordination as those injected with cysteine neutralized with sodium hydroxide and the fall in mitosis in the lens epithelium was also apparent.

The question arises whether mitotic arrest by cysteine is related to its protective effect against X-ray damage to the lens. von Sallmann, Dische, Ehrlich and Munoz³ found that cysteine and cystine reached a maximum in the aqueous humour about 1 hr. after intravenous injection. After a dose of 2 gm cysteine to an adult rabbit a concentration of 40 mgm cysteine/100 ml aqueous humour (3 mM) was reached. The concentration of cystine was about the same, both gradually declined over the next few hours. Protection of the lens against radiation is effective 30 min after cysteine injection and, in spite of the fact that mitotic arrest cannot be

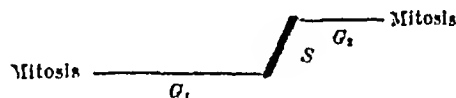
demonstrated for at least 19 hr after cysteine injection, it seems reasonable to consider that the reaction(s) between cysteine or cystine and cell constituent(s) which leads to mitotic arrest must take place shortly after injection when cysteine and cystine are present in the aqueous humour. von Sallmann *et al*¹ consider that mitosis in the lens epithelium may take only 30 min, but interphase must be prolonged, probably taking several days as in corneal epithelium (Friedenwald and Sigelman⁴). If cysteine interrupted some process early in interphase, all cells already past that point in the mitotic cycle could divide normally before any mitotic arrest became apparent. This could explain the slow development of mitotic inhibition by cysteine.

The effect of cysteine on synthesis of deoxyribonucleic acid was investigated in human bone marrow cells *in vitro* by measuring the incorporation of formate labelled with carbon-14 or thymidine labelled with tritium into deoxyribonucleic acid⁵.

Cysteine, in a concentration of 1 mM, produced a 60-80 per cent depression of synthesis of deoxyribonucleic acid as indicated by grain counting on autoradiographs, a concentration of 0.1 mM also produced a significant depression, ranging from 30 to 50 per cent.

The concentration used in the rabbits was 1 gm/kgm, which corresponds to a concentration of about 10 mM in the whole animal, the concentration in the aqueous humour being of the order of 1 mM (von Sallmann *et al*³).

The following is a scheme of the intermitotic cycle where S is the period of synthesis of deoxyribonucleic acid, G_1 and G_2 are pre- and post-synthetic gaps respectively.

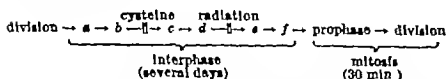


If synthesis of deoxyribonucleic acid is reversibly depressed in a cell, the onset of mitosis will be delayed. If the G_2 period is not affected then the delay in mitosis will appear only after a certain period, that is, cells already in G_2 period can proceed normally and enter mitosis, but the 'feed' of cells into the G_2 period will be depressed if the S period is elongated. The findings on mitotic counts in lens epithelium indicate that this, in fact, may be the case: the depression in mitosis by cysteine is observed only after a certain period (presumably corresponding to the length of G_2 period in these cells).

It is not known at this stage whether processes in the G_1 period are affected by cysteine or not. It is unlikely, however, that such concentrations of cysteine would affect synthesis of deoxyribonucleic acid only—nuclear phosphorylation is known to be affected by large doses of cysteine (Stocken and Creasey, personal communication), and Mazia⁷ has shown that mercaptoethanol will inhibit division of the fertilized egg of the sand dollar, he suggests this is due to a reaction between mercaptoethanol and the protein which forms the mitotic spindle. He considers that formation of the fibrous spindle requires S-S links between protein molecules and that mercaptoethanol prevents their formation by competing with the available SS or SH groups.

If the process in interphase which is interrupted by cysteine lies earlier than the process which is radio-sensitive, then so long as arrest by cysteine is reversible, one can postulate that cysteine protection is

related to its ability to arrest mitosis. Such protection can never be complete, as some cells will be in a stage of the mitotic cycle that is insensitive to cysteine but is radiosensitive. Cysteine protection against radiation cataract in fact never been found to be complete.



The above scheme suggests a possible mechanism but there is no evidence that this is a correct hypothesis, and the possibility of enhanced recovery phenomena in cysteine-treated cells should also be borne in mind. At present there is only the observation that cysteine arrests cell division in the lens

epithelium of the rabbit and that if given before irradiation the number of fragmented nuclei that develop afterwards is reduced. Previous work has shown that cysteine largely protects from X-ray cataract.

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RELEASE OF ADENOSINE TRIPHOSPHATE AND SEROTONIN FROM INJURED CELLULAR BLOOD ELEMENTS IN EXTRACORPOREAL CIRCUITS

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CORPUSCULAR blood trauma, especially red cell and platelet damage, is still a problem inherent to extracorporeal circulatory systems, including the heart-lung machines.^{1,2} Hemolyzed blood has been reported to possess vasodilator properties attributed to the release of adenosine triphosphate and/or closely related compounds from injured red cells.³ Platelets, in turn, are known to contain large amounts of 5-hydroxytryptamine (serotonin),⁴ a biogenic amine with powerful vasoactive, bronchomotor and other effects.⁵ In consequence, the question arose whether these humorally acting agents would be released into plasma in extracorporeal blood circuits and whether the resultant humoral pathological blood changes would serve as a guide for disentangling the mechanisms of some complications associated with the use of heart-lung machines for open cardiac surgery.

As a tentative approach to the problem an arterio-venous (femoral artery-superficial jugular vein) shunt, consisting of a polythene tube 1 m. long, was created in four dogs and five rabbits pretreated with subcutaneous pentidine hydrochloride (2 mgm./kgm.) and anesthetized with intravenous sodium pentobarbitone (30 mgm./kgm.). To mimic the blood trauma in the current heart-lung machines with greater surface area, pumps and filters, the inner surface of the shunts was intentionally 'cleaned' with steel wool. Just prior to opening of the shunt the animals were heparinized (5 mgm./kgm.). In the period of extracorporeal circulation via the shunt the corpuscular blood changes and the whole blood and plasma levels of adenosine triphosphate and 5-hydroxytryptamine were observed. For that purpose three blood samples of about 4 ml. were taken with a siliconized syringe needle from a rubber tube incorporated to the shunts. The first blood sample

was taken immediately after opening of the shunt and the subsequent samples 30 and 90 min. later. The corpuscular blood changes were determined by using routine techniques. The whole blood and plasma levels of adenosine triphosphate were determined by the colorimetric micromethod of Rebell et al.⁶ The 5-hydroxytryptamine content of whole blood and plasma was after overnight extraction in cold acetone (4°C) assayed by the method of Erspamer⁷ based on the contraction of castrated virgin rat uterus. The urinary excretion of this substance and 5-hydroxyindoleacetic acid (the main excretory product of 5-hydroxytryptamine) was studied in dogs only. The urinary bladder was catheterized immediately after induction of anesthesia. Then the urine excreted before (45 or 90 min.) and during (90 min.) extracorporeal circulation was collected, measured for volume and analyzed for 5-hydroxytryptamine and 5-hydroxyindoleacetic acid. The former was assayed by the same technique as that in blood and plasma, the latter according to the spectrophotometric method described by Udenfriend and associates.⁸

No major alterations were found in the whole-blood adenosine triphosphate during extracorporeal circulation. This was particularly true for dogs, while in rabbits some decrease in the whole blood adenosine triphosphate became evident. The erythrocyte count and the hematocrit values, correspondingly, remained substantially unaltered in dogs while in rabbits there was some decrease in the erythrocyte count and hematocrit values. At the start of extracorporeal circulation no adenosine triphosphate was detected in the plasma of either rabbits or dogs. In both rabbits and dogs however increasing amounts of adenosine triphosphate appeared in the plasma during extracorporeal circulation.

tion, the rising trend being more pronounced in rabbits than in dogs (as terminal phosphate-P, from zero to an average of 0.9 mgm/100 ml and from zero to an average of 0.35 mgm/100 ml, respectively). We had the impression that the degree of hemolysis, estimated visually from the colour of the plasma in the successive samples, paralleled the changes in the adenosine triphosphate of the plasma, with increasing hemolysis more adenosine triphosphate was detected in the plasma. The whole blood 5-hydroxytryptamine generally showed a clear-cut trend to decrease during extracorporeal circulation in both rabbits and dogs. Concomitantly the platelet counts fell, while the plasma 5-hydroxytryptamine levels were increased. Again, the drop in the platelet count was more pronounced in rabbits than in dogs (on the average from 318,000 to 71,000/cu mm and from 329,000 to 249,000/cu mm, respectively). The same held for the fall in the total white cell count observed in both rabbits and dogs. In contrast to the plasma adenosine triphosphate, considerable activity of 5-hydroxytryptamine was found in the plasma at the start of extracorporeal circulation (average 0.2 μ gm/ml in rabbits and 0.025 μ gm/ml in dogs). In rabbits the levels of plasma then steadily increased during extracorporeal circulation (up to an average of 0.38 μ gm/ml). In dogs the plasma 5-hydroxytryptamine increased in the early period of extracorporeal circulation (on the average from 0.025 μ gm/ml to 0.045 μ gm/ml), but towards the end of extracorporeal circulation 5-hydroxytryptamine of the plasma showed some tendency to fall. The urinary excretion of 5-hydroxytryptamine in dogs prior to extracorporeal circulation averaged 0.002 μ gm/min. In two of the four dogs there was actually no activity of 5-hydroxytryptamine in the urine before extracorporeal circulation. In the urine collected during the period of this circulation the activity of 5-hydroxytryptamine was consistently increased, the urinary excretion of 5-hydroxytryptamine attained an average level of 0.005 μ gm/min. Reverse changes were noted in the urinary excretion of 5-hydroxyindoleacetic acid, this fell from an average of 0.78 μ gm/min before extracorporeal circulation to an average of 0.38 μ gm/min during this circulation.

Adenosine compounds are presumably liberated from all injured tissues. Platelets, for example, are rich not only in 5-hydroxytryptamine but also contain appreciable amounts of adenosine triphosphate.⁹ However, proceeding from the knowledge that red cells are particularly rich in adenosine compounds, including the phosphate¹⁰, that they are susceptible to mechanical trauma⁸ and that their total mass in the circulatory system is enormously greater than that of the other cellular blood constituents, it is obvious that the red cells were the main source of the adenosine triphosphate released into the plasma in the present experiments. According to Udenfriend and Weissbach⁴, platelets contain all the 5-hydroxytryptamine present in the whole blood, while none is found in the plasma. Yet we found considerable activity of 5-hydroxytryptamine in the plasma already at the start of extracorporeal circulation. This may be explained by the fact that after short centrifugation at low running rates, as used to avoid hemolysis in the present experiments (for 10 min at 2,000 r.p.m.), the plasma still contains platelets.¹⁰ Nevertheless, the gradually increasing levels of plasma 5-hydroxytryptamine during extracorporeal circulation, with an associated fall in the platelet counts,

indicate that 5-hydroxytryptamine was steadily liberated from disintegrated platelets. The consistently increased urinary excretion of 5-hydroxytryptamine during extracorporeal circulation further indicates that 5-hydroxytryptamine was actually released into the plasma in the period of this circulation, for increased urinary excretion of 5-hydroxytryptamine has been observed after administration of exogenous 5-hydroxytryptamine.¹¹ Finally, the definitely higher levels of whole blood (and plasma) 5-hydroxytryptamine in our rabbits as compared with those in dogs, the platelet counts being equal, are in agreement with the figures for 5-hydroxytryptamine content of platelets in these species.⁴

The blood trauma in the present experiments was of the same general degree as that in the current heart-lung machines. On the other hand, exogenous adenosine triphosphate and 5-hydroxytryptamine at minute dose-levels have been reported to elicit vaso-dilatation and systemic hypotension^{3, 5, 12}. Intense bronchoconstriction⁵, pulmonary vasoconstriction⁴ and potentiation of the action of hypnotics (barbiturates)¹³ are further reactions to exogenous 5-hydroxytryptamine. With these facts in mind it seems possible that the complications associated with the use of heart-lung machines for open cardiac surgery, such as hypotension, cyanosis and a delay in the recovery from anaesthesia with eventual death², might be largely effected by such physiologically highly active agents as adenosine triphosphate and 5-hydroxytryptamine liberated into plasma from injured cellular blood constituents. Significantly enough, even in the present experiments deepening of the anaesthetic level during extracorporeal circulation, as well as a delay in the recovery from anaesthesia, were repeatedly observed. In addition, 5-hydroxytryptamine has been found to be about one hundred times as effective as histamine in raising capillary permeability and in producing oedema.¹⁴ Taken together with the above results, it also seems possible that such unexplained features as the oedematous changes in perfusion preparations of different types and more particularly the myocardial oedema, continuously increasing coronary flow and "Spontaninsuffizienz" known to occur in the heart-lung preparations¹⁵ would be causally related to the humoral pathological blood changes under consideration. The present results are being described and discussed in detail elsewhere.¹⁶

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AMPLITUDE-MODULATION RADIO-TELEMETRY OF NERVE ACTION POTENTIALS

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INFORMATION concerning the functioning of intact animals has been successfully telemetered to remote points from satellites, missiles, large centrifuges and other situations¹. The present report describes experiments in which the response of a single type of excitable tissue (nerve trunk or fibre) was relayed to and recorded at a distant point by telemetry. The basic problem is one of transmitting a pulse to the preparation at a distant point, and receiving the response to this stimulus at the point of transmission.

Thus series of experiments passed through several phases which will be described in another communication². The system made use of two radio links one for each direction in which information was to flow, and was set up in one building. The required stimulating pulse was produced by a Grass S4C stimulator and used to amplitude-modulate a Hallcrafters S27RS radio transmitter by means of the Model 115 amplitude modulator of Measurements Laboratory (Boonton, New Jersey). The modulator operated at a minimum external modulating frequency of 30 cycles, provided up to 100 per cent modulation with low envelope distortion, allowed accurate metered per cent modulation calibration, and produced amplitude modulation of the stimulus intelligence with negligible accompanying incidental frequency modulation, thus allowing narrow band receiver operation. In accordance with amplitude modulation theory, the stimulus, or modulating voltage, was introduced in the plate voltage supply line and added to the plate supply voltage at a rate

and magnitude determined by the modulating signal and the modulator output. In this type of system, developed by Hartley, the carrier signal originates in a crystal controlled oscillator, is raised to full power by amplifiers and is modulated in the final stage of power amplification which operates Class C. Since the load is fixed, as the voltage level changes because of the modulation, the tank voltage swing the plate current operating angle and the current pulse form and amplitude change so that the d.c. plate voltage varies linearly with respect to the square root of the power output. This permits distortionless amplitude modulation, but the modulator must supply power equal to one half of the unmodulated carrier power at 100 per cent modulation.

The radio frequency carrier can be expressed as $y = A(t) \cos \gamma(t)$ and in amplitude modulation the signal intelligence (nerve stimulus and response) is made to control the amplitude parameter of the carrier by the relation

$$A(t) = [A_0 + af(t)] \\ = [A_0(1 + ma f(t))]$$

The scheme for the plate operated output stage and a block diagram of the entire system will be found in Fig 1. A complete mathematical analysis of the carrier and amplitude spectra may be found elsewhere³.

The antenna used to recover the signal at a distant point was a vertically mounted dipole designed for optimum reception of the tuned frequency (72.25 Mc/s) fed into a coaxial transmission cable. The intelligence present in the amplitude modulated wave was recovered by impressing the modulated

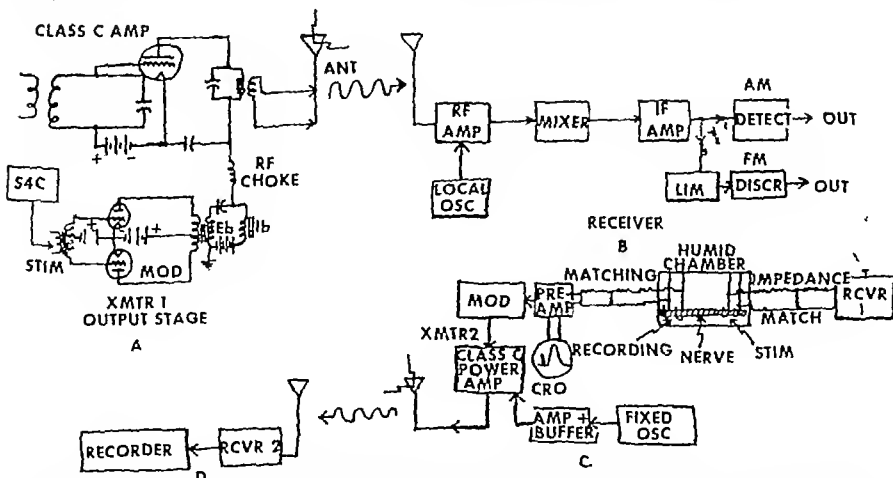


Fig 1 (A) Plate-modulated output stage. Explanation in text. Transmitter I relays stimulus signal to receiver I. (B) Receiver I demodulates signal intelligence and (C) impresses stimulus on to stimulating electrodes via impedance network. Pick up electrodes feed response through matching network to transmitter II, then relay response (also monitored on CRO) back to (D) receiver II where it is demodulated, amplified and drives pen recorder.

wave on a non-linear network which, for low-strength signals, employed a voltage-current characteristic represented by the following terms of a Taylor series

$$i = I_0 + G_1 e + G_2 e^2 \quad (1)$$

where the predominant term is $G_2 e^2$. The carrier and first side-frequency pair which result from the amplitude-modulation of the carrier $E_0 \sin \omega_0 t$ by the modulating wave $ME_0 \cos \omega_1 t$ were impressed at the input of this network. The impressed voltage, containing the stimulus intelligence, can then be written

$$e = E_0 \sin \omega_0 t + \frac{ME}{2\omega} \{ \sin (\omega_0 + \omega_1) t + \sin (\omega_0 - \omega_1) t \} \quad (2)$$

It is found by combination and substitution that the square-law term yields a series of waves. The wave corresponding to the original intelligence is $G_2 ME^2 \cos \omega_1 t$. Its amplitude is proportional to the square of the voltage. This wave was then amplified and fed through a network which matched the output impedance of the receiver to the bipolar stimulating electrodes. In operation, the receiver's *S*-motor was used as a carrier-level indicator for amplitude modulation, and the best records were obtained with the receiver tuned slightly to one side of the carrier frequency. A Ferris model 18-B signal generator was used to align the receiver, which was also a Hallicrafters model *S-27RS*. In later experiments employing frequency modulation a separate stage of the receiver assembly, known as the 'frequency unit', rectified the alternating current output of the receiver, and the d.c. output of the frequency unit was fed to a visual meter and recorder.

The response of the preparation was picked up by silver-silver chloride electrodes, and after source-impedance matching and amplification, modulated another radio transmitter which transmitted the information back to the originating point. Here, after demodulation and amplification, the pulses were used to activate a strip-chart recorder (Leeds and Northrup Speedomax Type *G* Model *S* 60000 series). Sciatic nerves of bullfrogs (*Rana catesbeiana*) and radial or ulnar nerves of dogs (*Canis canis*) were used. A total of 11 nerves was tested. Single motor fibres were used in some experiments, which closely followed the bridge-insulator technique of Tasaki.⁴ Details of those studies will be included in ref. 2. With the distal end crushed, whole nerves were placed on two pairs of electrodes in a humid chamber at 20°C. The location of the active pick-up electrode was 7.5 cm distal to the stimulating cathode and 1.2 cm proximal to the inactive pick-up electrode. The distal electrode was connected to earth and the proximal one was anode during the pulse. The monophasic action potential was monitored at the site of the preparation by d.c. amplification and display on an oscilloscope. The stimulating pulse, measured at the output of the distant receiver, was 0.1–0.5 msec in duration, and its amplitude was adjusted to be supramaximal for beta fibres.

The duration of the responses was 1–3 msec and the maximum amplitude about 30 mV. The wave form of the action-potential was not recorded, but simply the fact of its having occurred. The portion of the record in Fig. 2 shows the responses of the inkwriter to slow stimulation rates, and shows also that the write-out is proportional to amplitude. Thresholds as determined by the onset of activity of the inkwriter varied from 14 to 15 mV, and did not

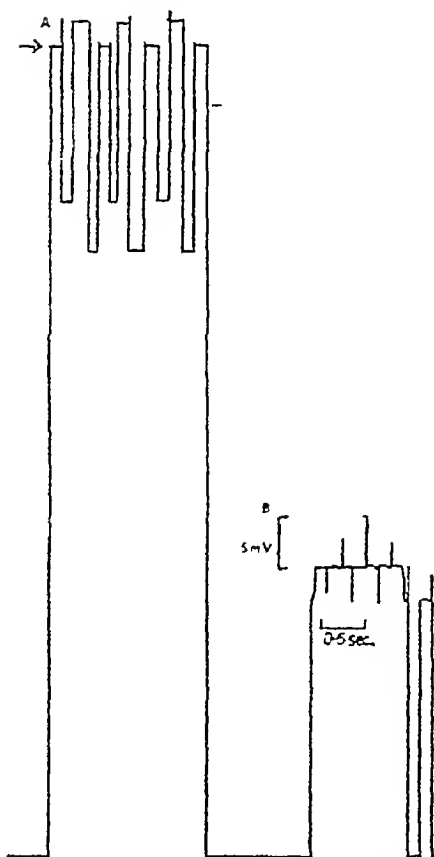


Fig. 2 Photograph of segment of ink write-out showing (A) threshold of 15 mV (at arrow) for a single nerve

differ significantly for amphibian as compared with mammalian nerve.

Conduction velocity was determined by the spacing between the rectangular pulse outlines on the record and ranged in all nerves from 23.5 to 36.8 m/sec. In some experiments reproducible records were easily obtained for 15–20 hr, during part of which the whole system could be left unattended except for changing the paper or filling the ink-reservoir of the recorder. For auditory monitoring during such periods a loudspeaker was connected to the 5,000-ohm terminals of receiver II.

The special problem encountered in this application of telemetry is the matching of receiver output and input impedance-levels to bipolar stimulating and recording electrodes and the matching of the transmitter modulator inputs to the output of the stimulated nerve, with the assumption that the resting resistance is about 20 k-ohms max and that the resistance during activity is no more than 10 per cent of that value.

Theoretically it is possible for the nerve to be stimulated by the carrier wave itself. In general, for carrier frequencies at which losses in the preparation are not too great, the shape of the carrier envelope for the directly applied carrier would be expected to have the same shape as that obtained with a d.c. pulse. Since the response is transmitted over a radio link it is more convenient to use the d.c. pulse for stimulation.

The electrical process of the nerve impulse is a signal similar to those encountered in data handling telemetry systems used for aircraft and missile testing and for satellite experiments. It is now possible to determine the effect on the whole nerve or single fibre (if properly packaged) of magnetic, gravitational or radiation fields at very high altitudes,

in vehicles undergoing changes in acceleration. The long periods of time during which the output of the nerve is relatively constant when stimulated remotely by a constant stimulus assure adequate data for statistical analysis. The method therefore allows measurement of changes in angular acceleration both positive and negative. Basic physiological data which can be collected in such circumstances include threshold, rheobase, chronaxie, strength-duration and strength-latency curves, refractory periods and critical stimulus interval for 2 stimuli. Controlled variation in potentials led from electrodes implanted in animal brains can also be studied by this means either on the ground or in guided or orbital flight. By using a frequency modulated/frequency modulated multichannel system of the type commonly employed in satellite research, the wave form of the action potentials can be recovered with fidelity through high frequency interrogation during the passage of

impulses. Its relationship to environmental variables can then be determined. With interval measuring equipment at present available, nerves might be used in orbital vehicles as biological clocks to determine directly whether or not there is a relativistic shift for excitable tissue*. Thus cannot be done at present with intact animals or astronauts.

I wish to thank Messrs W Boynton R Bottom and A Fisher of the United States Weather Bureau for valuable advice concerning the operation of the transceiver units. Mr P Babv of Electromechanical Research Inc. furnished helpful references.

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COMPOSITION OF A PARAFFIN WAX FRACTION FROM TOBACCO LEAF AND TOBACCO SMOKE

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THE paraffin wax of tobacco leaf and smoke is generally regarded as a mixture of *n*-paraffinic hydrocarbons, with *n*-hentriacontane as the major component¹⁻³. The isolation of pure paraffinic hydrocarbons from both leaf and smoke has been claimed in a number of instances^{4,5}, but it is open to question whether the specimens were, in fact, homogeneous, for in every case the melting point was the only criterion of purity employed and it has been shown that melting points alone do not afford a reliable guide to the purity of paraffinic hydrocarbons⁶.

We have obtained additional evidence of the complex nature of the wax through mass spectroscopic and gas liquid chromatographic analyses of fractions obtained from green tobacco leaf (*Nicotiana tabacum*, Dolores variety), from the 'black fermented tobacco' of a variety of Argentinian cigarettes and from the smoke of these cigarettes. The analyses were very kindly carried out for us at Thornton Research Centre 'Shell' Research, Ltd. through the generosity of Dr R. Graham, and the results shown in Tables 1 and 2, indicate clearly that the wax from each of the three sources is a mixture of broadly similar com-

position. *n*-Hentriacontane is the main individual component, but appreciable quantities of the neighbouring odd numbered homologues and small amounts of the even numbered homologues are present as well. Dr Graham has informed us that the precision of the mass-spectroscopic analysis is not high, and no significance should thus be attached to the apparent small differences in composition of the three waxes. An interesting and novel feature of the results is the high proportion of *iso*-alkanes disclosed by mass spectroscopy. So far as we are aware *iso*-alkanes have not previously been detected in the paraffin wax of tobacco or indeed of other plants, although their presence in cigarette smoke has been noted⁷. (Since writing this article, we have seen a publication by Mme Suzanne Barbozat (*J. Recherches du Centre National de la Recherche Scientifique*, 45 273 1958) in which it is reported that the paraffins of tobacco and tobacco smoke, though predominantly normal, may contain branched chain isomers. Dr A. I. Kosak has also informed us that he and Dr J. S. Swinehart have detected branched chain isomers in the paraffin fraction of cigarette smoke. We are

Table 1 MASS SPECTROSCOPIC ANALYSIS OF PARAFFIN WAXES

| Carbon No. | Source of wax | | | | | | | | |
|------------|---------------------|---------------------|-------|---------------------|---------------------|-------|---------------------|---------------------|-------|
| | Green leaf | | | Fermented tobacco | | | Cigarette smoke | | |
| | <i>n</i> -Alk. anes | <i>i</i> -Alk. anes | Total | <i>n</i> -Alk. anes | <i>i</i> -Alk. anes | Total | <i>n</i> -Alk. anes | <i>i</i> -Alk. anes | Total |
| 25 | 0.0 | 0.0 | 0.0 | 0.7 | 0.0 | 0.7 | 0.0 | 0.0 | 0.0 |
| 26 | 0.5 | 0.0 | 0.5 | 1.3 | 0.0 | 1.3 | 0.5 | 0.0 | 0.5 |
| 27 | 3.0 | 0.0 | 3.0 | 5.9 | 0.8 | 6.7 | 5.2 | 0.8 | 6.0 |
| 28 | 0.1 | 0.0 | 0.1 | 0.9 | 0.0 | 0.9 | 0.5 | 0.0 | 0.5 |
| 29 | 0.6 | 15.0 | 15.6 | 6.3 | 11.0 | 17.3 | 6.2 | 15.3 | 21.5 |
| 30 | 0.0 | 2.5 | 2.5 | 0.6 | 1.6 | 2.2 | 1.0 | 1.5 | 2.5 |
| 31 | 24.1 | 24.4 | 48.5 | 26.6 | 20.4 | 47.0 | 25.0 | 20.2 | 45.2 |
| 32 | 3.0 | 2.4 | 5.4 | 5.1 | 2.0 | 7.1 | 4.3 | 1.9 | 6.2 |
| 33 | 10.8 | 3.3 | 14.1 | 13.1 | 3.9 | 17.0 | 14.3 | 3.5 | 17.8 |
| Total | 50.9 | 49.4 | 100.3 | 60.4 | 29.7 | 100.1 | 56.7 | 43.2 | 99.9 |

The *n*-alkane/*i*-alkane ratio is based on an accepted sensitivity ratio of 2/10

Table 2 GAS-LIQUID CHROMATOGRAPHIC ANALYSIS OF PARAFFIN WAXES

| | Green leaf wax | Fermented tobacco wax | Cigarette smoke wax |
|---|----------------|-----------------------|---------------------|
| Percentage area <i>n</i> -C ₂₅ | — | — | 0.1 |
| <i>n</i> -C ₂₆ | 0.5 | — | 0.6 |
| <i>n</i> -C ₂₇ | 0.3 | 0.3 | 0.4 |
| <i>n</i> -C ₂₈ | 7.5 | 4.4 | 0.3 |
| <i>n</i> -C ₂₉ | 0.6 | 1.0 | 1.1 |
| <i>n</i> -C ₃₀ | 8.8 | 9.2 | 7.4 |
| <i>n</i> -C ₃₁ | 3.9† | 7.1 | 3.8† |
| <i>n</i> -C ₃₂ | 4.0* | 40.5* | 43.4* |
| <i>n</i> -C ₃₃ | 12.5 | 16.0 | 13.0 |
| <i>n</i> -C ₃₄ | 18.0* | 15.5* | 22.8* |
| <i>n</i> -C ₃₅ | — | — | 1.1 |

Column 3 ft. all-glass E 801 on 55-85 mesh 80/100 at 235° C.; nitrogen flow rate 1.5 l./hr.

* These peaks were composed of two unresolved peaks. The results given include both peaks. The impurity is probably a very slightly branched paraffin.

† These peaks were probably due to *n*-C₃₁ paraffins but this was not fully confirmed.

indebted to these authors for telling us of this result before publication) The Thornton workers have interpreted the present results as due to the presence of 2-methylalkanes

For the preparation of the materials for analysis, neutral extracts of the tobacco and a neutral fraction of the cigarette smoke condensate were chromatographed on alumina and the initial waxy fractions eluted with light petroleum (b.p. 40–60°C) were treated with urea in warm methanol⁷. The resulting adducts were washed with light petroleum, decomposed with water, and the recovered paraffins crystallized once from benzene ethanol. The melting points and elementary analyses are shown in Table 3. The waxes showed no light absorption in the ultra-violet, indicating the absence of unsaturated compounds, and their infra-red spectra determined on a Perkin-Elmer 'Infracord' spectrometer were very similar to that recorded for *n*-triacontane⁸. The method of isolation does not rule out the presence of *iso*-paraffins, for it is known that slightly branched paraffins will form urea adducts if the main chain is long enough⁹. Attempts to obtain additional evidence for the presence of *iso*-alkanes by high resolution infra-red spectroscopy in the 1,500–1,300 cm⁻¹ region were inconclusive in the absence of suitable reference compounds

Table 3

| Source of wax | Green leaf | Fermented tobacco | Cigarette smoke |
|---------------------|--------------------|--------------------|--------------------|
| Melting point | 60–63°C | 60–63°C | 61–64°C |
| Elementary analyses | C, 85.4 H, 14.5 | C, 85.4 H, 14.3 | C, 85.4 H, 14.4 |

Little consideration appears to have been given to the possibility that the considerable amounts of paraffin wax in cigarette smoke may play some part in its carcinogenic activity¹⁰. In this connexion, attention might be directed to the report by Horton Denman and Trosset¹¹ that the production of tumours on mouse skin by 3,4-benzpyrene and by 20-methylcholanthrene was considerably accelerated and the tumour incidence increased when the carcinogens were applied in conjunction with a large excess of certain high molecular weight hydrocarbons, including some *n*-paraffinic hydrocarbons. It is not inconceivable that a similar combined action of the paraffins and the carcinogenic aromatic hydrocarbons¹² in cigarette smoke may contribute to the carcinogenic activity towards mouse skin of the smoke, and may account, in some measure, for the fact that the smoke is more potent than might be expected from its very small content of aromatic hydrocarbon carcinogens¹³.

In other experiments we have prepared the methyl esters of acids obtained from the flue-cured tobacco of a variety of British cigarettes, and a fraction of the esters b.p. 190–210°/0.5 mm has also been analysed by mass spectroscopy and gas-liquid chromatography at the Thornton Research Centre. To obtain the esters the tobacco was extracted with chloroform, and the alkali-soluble fraction treated briefly with ethereal diazomethane. The mass spectroscopic results (Table 4) show that methyl palmitate is the major component of the mixture, accompanied by some stearate and smaller amounts of a number of other higher and lower homologues. A considerable amount of C₁₈ unsaturated esters is also present, with methyl linolenate predominating. An essentially similar result was obtained in the gas-liquid chromatographic analysis. Most of the acids corresponding to these esters have already been

Table 4 MASS SPECTROSCOPIC ANALYSIS OF TOBACCO METHYL ESTERS*

| Ester | Acid carbon No | Ester molecular weight | Peak height | Relative sensitivity | Relative quantity |
|--------------|----------------|------------------------|----------------|----------------------|-------------------|
| Caprate | 10 | 186 | 0 | 0.20 | 30 |
| | 11 | 200 | 4 | | |
| Laurate | 12 | 214 | 3 | 0.42 | 7 |
| | 13 | 228 | 0 | | |
| Myristate | 14 | 242 | 7 | 0.63 | 11 |
| | 15 | 256 | 0 | | |
| Palmitate | 16 | 270 | 207 | 0.80 | 352 |
| Margarate | 17 | 284 | 25 | | |
| | 18† | 288 | 12 | | |
| Arachidonate | 18† | 200 | 31 | | |
| Linolenate | 18† | 292 | 115 | | |
| Linoleate | 18† | 204 | 73 | | |
| Ololate | 18† | 206 | 13 | | |
| Stearate | 18 | 208 | 70 | 1.00 | 70 |
| Nonadecylate | 10 | 312 | 7 | | |
| Arachidate | 20 | 326 | 10 | | |
| | 21 | 340 | 4 | | |
| Behenate | 22 | 354 | 11 | | |
| | 23 | 368 | 4 | | |
| | 24 | 382 | 4 ⁹ | | |
| | 26 | 410 | 37 | | |

* Because of lack of knowledge of the relative sensitivities of many of the compounds the results can only be reported incompletely

† Unsaturated

found in cigarette smoke, in which palmitic acid and C₁₈ unsaturated acids appear to be particularly abundant¹⁴. Palmitic acid was also found to be the principal fatty acid of an American bright green leaf by Hollier¹⁵, and it is of interest that the palmitate and linolenate were the main components of a mixture of solanecyl esters recently isolated from an American flue-cured leaf¹⁶. A mixture said to contain methyl laurate, myristate and palmitate has also been obtained from a Japanese flue-cured tobacco¹⁷.

We are very greatly indebted to Dr Robert Graham and the mass-spectroscopic and gas-liquid chromatographic research groups of Thornton Research Centre, 'Shell' Research, Ltd, for the mass spectroscopic and gas-liquid chromatographic analyses. We thank, also, Mr Ivan Neas, director of the Tobacco Research Board of Rhodesia and Nyasaland, for supplying the green tobacco leaf, Dr J. R. Plimmer for the crude wax fraction of the green leaf, and Dr J. W. Cook for his interest in the investigation.

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HÆMOGLOBIN P IN A FAMILY IN THE BELGIAN CONGO

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A SURVEY of abnormal haemoglobins has been carried out on 1,000 African pregnant women visiting the Outpatients Department of the Government Hospital at Stanleyville. The results will be published in detail elsewhere, but it is of interest here that on two occasions haemoglobin P was discovered. Haemoglobin P was first described by Schneider and Haggard¹. On paper and open boundary electrophoresis at alkaline pH, haemoglobin P moves more slowly to the positive pole than haemoglobin A and separates from that pigment. It moves faster than haemoglobin S but does not separate from a mixture of S and P. Under these conditions it cannot be distinguished from haemoglobin L. On electrophoresis in acid pH, either in citrate agar or by the open boundary technique and in resin chromatography, haemoglobin L separates widely from haemoglobin A, whereas haemoglobin P does not separate. Thus haemoglobins L and P can be differentiated by these procedures.

In one of the findings of haemoglobin P an extensive family study was made (Fig. 1). The proband was a 24-year old Bantu female of pure Lokele descent. Originally the Lokele lived on the River Congo, but the proband and her family had settled in Stanleyville. She was eight months pregnant when first seen and seemed perfectly well. She had three children who were alive and healthy. Laboratory examinations revealed the presence of P¹ falciparum in her blood and ankylostoma ova in her stools. She suffered from a moderate hypochromic anaemia which was corrected by treatment with antimalarials and iron, and the mean corpuscular haemoglobin concentration rose from 26 to 31.8 per cent and the mean corpuscular haemoglobin from 24.3γ to 31γ. Her serum iron level at the end of the treatment was 117, per 100 ml.

On paper electrophoresis at alkaline pH her haemoglobin separated into two fractions, one haemoglobin A and another moving more slowly in

Table 1 FINDINGS IN A FAMILY IN WHICH HÆMOGLOBINS A, S AND P ARE FOUND AS ADULT VARIANTS AND IN WHICH A PROPORTION OF THE MEMBERS OF THE FAMILY SHOW SIGNIFICANT TRACES OF HÆMOGLOBIN P WITHOUT MICROCYTHAEMIA

| Pedi- gree designa- tion | Name | Sex | Age | Sickle- cell trait | Adult hæmo- globin | Alkaline red- ant hæmo- globin (per cent) | Red cells (per cu. mm.) | Cell volume (per cent) | Hæmo- globin (gm./ 100 ml.) | M.C.H.C. (per cent) | M.C.V. (cu. μ) | M.C.H. (γ) | Reti- culo- cyte (per cent) | Blood group |
|-----------------------------------|------------------------------|-----|-----|--------------------------|--------------------------|--|-------------------------------|------------------------------|--------------------------------------|------------------------|-------------------|------------------|--------------------------------------|----------------|
| I 1 | KAMAKO | M | 65 | 0 | AP | 1-6 | 4,400,000 | 41.8 | 13.8 | 33 | 93.8 | 31 | 0-0 | A, N, ccDE |
| I 2 | MALASI | M | 65 | 0 | AP | 1-6 | 4,385,000 | 40 | 18-6 | 33.7 | 91.2 | 30-6 | 0.3 | A, M, CcDe |
| II 1 | SALUMU Boniface | M | 31 | + | APS | 3-0 | 6,080,000 | 47 | 16.1 | 33.1 | 92.5 | 29.7 | 1 | A, M, CcDe |
| II 2 | PATIMA Julienne | F | 28 | 0 | A | <1.5 | 3,780,000 | 38 | 11 | 23.9 | 100-5 | 20.1 | 0 | 0, MN, ccDe |
| II 3 | YAWKWA Hilary | F | 27 | 0 | A | <1.5 | 4,570,000 | 42 | 14.3 | 34 | 91.9 | 31.3 | 0 | A, MN, ccDE |
| II 4 | RAPIT Salini | F | 25 | 0 | AP | 5 | 2,880,000 (3,600,000) | 36.2 (11.4) | 9.4 (31.8) | 28 (97.5) | 93.4 (31) | 24.3 | 0.5 | A, MN, CcDE |
| II 5 | BERNARD | M | 26 | 0 | A | <1.5 | 4,480,000 | 43 | 12.1 | 30.5 | 90 | 29.3 | 0-0 | 0, MN, ccDe |
| II 6 | KILLOHO Alphonse | M | 22 | + | AS | <1.5 | 5,600,000 | 46 | 14 | 30-4 | 82.1 | 26.7 | 0.2 | A, MN, ccDE |
| II 7 | ARIZA Marie Louise | F | 19 | 0 | A | <1.5 | 4,025,000 | 39 | 12.7 | 32.5 | 96.8 | 33.1 | 1 | 0, MN, ccDe |
| III 1 | SALUMU Albert | M | 12 | 0 | AP | 3.1 | 4,000,000 | 40 | 12.7 | 31.7 | 86-0 | 27-6 | 0.3 | A, MN, CcDe |
| III 2 | SALUMU Melanie | F | 9 | 0 | AP | 7.3 | 4,370,000 | 33 | 13.1 | 34.5 | 86-0 | 30 | 0-0 | A, MN, CcDe |
| III 3 | SALUMU Ercell | M | 7 | + | AS | <1.5 | 4,390,000 | 37 | 13.1 | 35.5 | 84.3 | 29-9 | 0 | A, MN, CcDe |
| III 4 | SALUMU Tabu | F | 6 | + | AS | 1-6 | 3,560,000 | 30 | 8.7 | 29 | 60.3 | 25-0 | 2 | A, MN, CcDe |
| III 5 | SALUMU Pauline | F | 5 | 0 | AP | 1.7 | 4,085,000 | 37 | 11.3 | 30.5 | 90.5 | 27-6 | 2 | A, MN, ccDe |
| III 6 | SALUMU Cécile | M | 2 | + | AS | <1.5 | 3,690,000 | 32.5 | 10.7 | 32-0 | 90.2 | 29.7 | 0 | A, MN, ccDe |
| III 7 | NOULALAT Boniface | M | 7 | 0 | AP | 5-2 | 3,640,000 | 30 | 9.4 | 31.4 | 78.1 | 24-5 | 1.1 | A, MN, ccDE |
| III 8 | NOULALAT Christine | F | 5 | 0 | AP | 3-0 | 3,500,000 (4,620,000) | (32) (39) | (10.4) (11.5) | (32.4) (31) | (81.1) (80.2) | (29.0) (26.5) | 0.3 | A, MN, ccDF |
| III 9 | NOULALAT Marie Colette | F | 2 | 0 | A | 19.8 | 4,520,000 (4,250,000) | 37 (37-5) | 11.7 (12.2) | 31-6 (32.5) | 81-8 (88) | 26.8 (28.6) | 0.4 | 0, MN, ccDE |
| III 10 | KIDITHO Marguerite | F | 2 | 0 | A | 2.5 | 4,225,000 | 30.5 | 12 | 30-4 | 93.4 | 29.4 | 0.3 | 0, MN, ccDL |
| III 11 | KIDITHO Valérie | F | 12 | + | AS | 3.1 | 4,400,000 | 35 | 11.1 | 30.8 | 81.8 | 25-2 | 0.2 | 0, MN, ccDF |

* Key M.C.H.C. mean corpuscular haemoglobin concentration M.C.V. mean corpuscular volume M.C.H. mean corpuscular haemoglobin

† The figures in brackets show the results after the removal of hookworms and treatment with antimalarials and iron. In all subjects nothing abnormal was seen in the white cell count and the serum bilirubin level was raised.

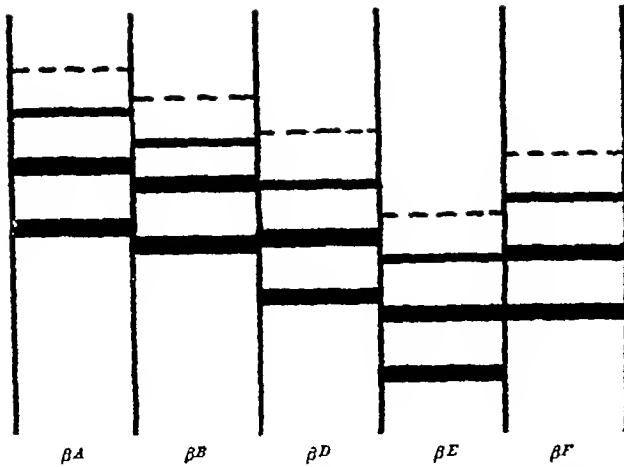


Fig 1. Relative mobility in starch gel of the four zones produced by each β globulin allele in cattle. The anodic side of the gel is at the top of the diagram, only the β -globulin zones being shown.

zones controlled by the five alleles are shown in Fig 1. It will be seen that the zones controlled by β^D are intermediate in mobility to those produced by β^A and β^D , while β^F gives rise to zones intermediate in mobility between those produced by β^D and β^E .

Previous experience has shown that each β -globulin genotype formed from the alleles β^A , β^D and β^E gives only one phenotype¹. Fifteen phenotypes would therefore be expected from five alleles, fourteen have been found so far. The homozygote of the infrequent allele β^D has not yet been seen. The appearance of the phenotypes (Fig 2) was anticipated

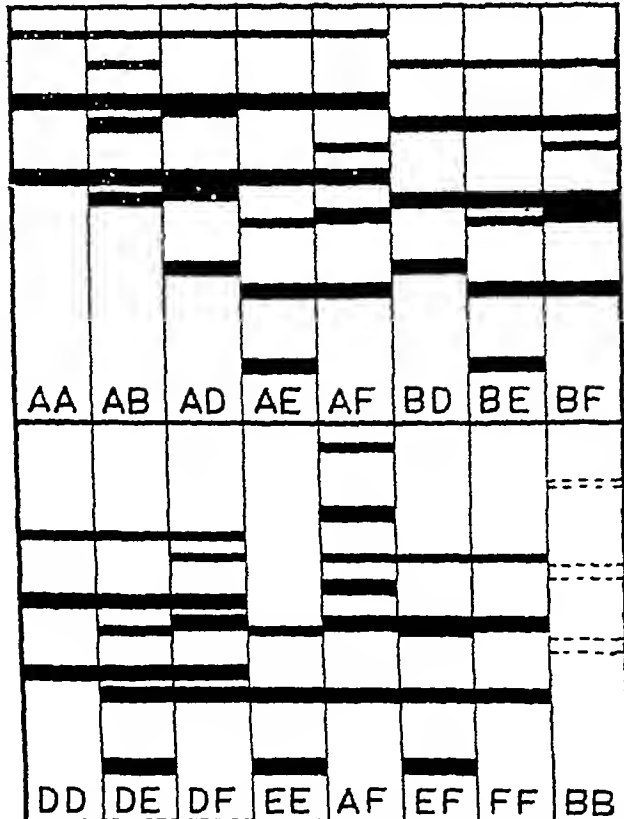


Fig 2. The fourteen cattle β globulin phenotypes. The anodic side of the gel is at the top of each portion of the diagram, only the β globulin zones being shown. The fast moving faint band produced by each allele (cf. Fig 1) is not shown. For AA, AB, etc., read $\beta^A\beta^A$, $\beta^A\beta^B$, etc. The dotted zones for $\beta^D\beta^D$ (bottom right) show the expected appearance of this phenotype, which has not yet been found.

in the main from the knowledge that the pattern given by a heterozygote is indistinguishable from that given by a simple mixture of the corresponding homozygous sera^{1,2}.

Data from matings between Sindhi \times Sindhi, Sahiwal \times Sahiwal, Sindhi \times Jersey and Sahiwal \times Jersey cattle confirm that the previously unrecognized phenotypes represent individual genotypes formed from five alleles (Table 1).

Table 1. DISTRIBUTION OF PHENOTYPES FROM MATINGS INVOLVING THE CATTLE β GLOBULIN ALLELES β^D AND β^F .

| Parents | | Offspring | | |
|---------|------|-----------|-----------|--------------|
| Dam | Sire | Like dam | Like sire | Recombinants |
| AA* | AF | 3 | 3 | — |
| AA | BF | — | — | 1 AB |
| AD | AF | 1 | 9 | 3 AA, 5 DF |
| AD | BF | — | — | 1 AB, 1 BF |
| AD | FF | — | — | 1 DF |
| AE | AF | 5 | 0 | 0 |
| BF | AF | 1 | 0 | 0 |
| DD | AF | — | — | 1 AD, 4 DF |
| DD | DF | — | — | 1 DF |
| EF | AF | 0 | 1 | 1 FF |
| EF | DF | 1 | 1 | 0 |

* For AA, AF, etc., read $\beta^A\beta^A$, $\beta^A\beta^F$, etc.

The frequency of each allele for several breeds and crossbreeds of cattle from two herds is shown in Table 2.

Table 2. SHOWING β -GLOBULIN GENE FREQUENCIES FOR SOME BREEDS AND CROSS-BREDS OF CATTLE AT F. D. McMASTER FIELD STATION (TOP) AND NATIONAL CATTLE BREEDING STATION (BOTTOM).

| Breed | No of animals | Gene frequency | | | | |
|-------------------------------|---------------|----------------|-----------|-----------|-----------|-----------|
| | | β^A | β^B | β^D | β^E | β^F |
| Sindhi | 14 | 0.57 | 0.04 | NII | 0.28 | 0.11 |
| Sindhi \times Jersey | 20 | 0.52 | NII | 0.24 | 0.12 | 0.12 |
| Sahiwal | 10 | 0.10 | 0.20 | NII | 0.15 | 0.55 |
| Sahiwal \times Jersey | 31 | 0.33 | 0.05 | 0.28 | 0.03 | 0.31 |
| Jersey | 61 | 0.51 | NII | 0.49 | NII | NII |
| Hereford | 27 | 0.39 | NII | 0.52 | 0.09 | NII |
| Shorthorn | 18 | 0.50 | NII | 0.39 | 0.05 | NII |
| Hereford \times Shorthorn | 10 | 0.45 | NII | 0.55 | NII | NII |
| Brahman \times Shorthorn | 14 | 0.28 | NII | 0.43 | 0.18 | 0.11 |
| Brahman \times Hereford | 15 | 0.40 | NII | 0.24 | 0.20 | 0.16 |
| Africander \times Shorthorn | 13 | 0.19 | NII | 0.50 | 0.31 | NII |
| Africander \times Hereford | 15 | 0.23 | NII | 0.47 | 0.30 | NII |
| Brahman* | — | 0.3 | NII | 0.1 | 0.3 | 0.3 |
| Africander* | — | NII | NII | 0.4 | 0.6 | NII |

* Approximate frequencies computed from remainder of data.

It has been suggested previously^{1,3} that the frequency of β^E within a breed may reflect the climatic or ecological stress to which the breed is subjected. Thus, the frequency of β^E increases in a northerly direction in the British Isles, both within and between breeds. The high frequency of β^E in all the zebu breeds examined is particularly interesting therefore in view of the well-known climatic and ecological tolerance of these cattle.

I thank the Officer-in-Charge of the F. D. McMaster Field Station of the Commonwealth Scientific and Industrial Research Organization, Badgery's Creek, New South Wales, and of the National Cattle Breeding Station of the Commonwealth Scientific and Industrial Research Organization, 'Belmont', Rockhampton, Queensland, for supplying blood samples, and C. Bloomfield for technical assistance.

¹ Ashton, G. C., *Nature*, 182, 370 (1958).

² Ashton, G. C., and McDougall, E. I., *Nature*, 182, 945 (1958).

³ Ashton, G. C., *Nature*, 183, 404 (1959).

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LETTERS TO THE EDITORS

TERMINOLOGY

Retentate a New Scientific Term

ANYONE who has resorted to the technique of dialysis will be aware of an odd and inconvenient gap in the terminology relating to the process. For the substances which pass through the dialysis membrane there is a generally accepted term 'dialysate'.

Exception has been taken to this word by the editors of the *Biochemical Journal*¹. Such exception may be justified on etymological grounds as the purist finds unpalatable a word compounded of a Greek stem and Latin suffix. But the alternative, 'diffusate', selected by the said editors may be objectionable scientifically.² As dialysate has other wise received universal acceptance and usage, it is best retained despite its hybrid origins.

On the other hand, to our knowledge no suitable or generally accepted term exists to describe the material which is retained by semi permeable membranes. Herbertson *et al.*³ have recently referred to the retained material as the 'core', but there seems little logic or justification for the selection of this word, which has other recognized connotations. Most authors have bridged the existing terminological gap by circumlocution, for example, the non dialysable material, the substances which remain in the dialysis bag (tube), etc. Altogether, the situation is unsatisfactory.

After due deliberation, in which several alternative possibilities were considered, we propose the term *retentate* to designate those substances which are retained by semipermeable membranes in the course of dialysis.

Though we recognize the term is of Latin derivation, while being applied in a process which is designated by a word derived from Greek, we feel this is less heinous than the hasty already committed in the percentage of dialysate. We further feel *retentate* has the advantages of (1) ready recognition being descriptive of the events concerned, and (2) uniqueness, inasmuch as it has not hitherto been used in any other sense.

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¹ The *Biochemical Journal* Suggestions to Authors" revised 1957

² *P. 10*
³ *Editor Immunology* 2 1 (1959)

⁴ Herbertson, J. Forsyth, J., and Colldahl H. *Acta Chem Scand* 12 757 (1958)

CHEMISTRY

Concentration of Stearic Acid in Monolayers Adsorbed from Solution

MATHIESON¹ has recently obtained electron micrographs of oleophobic stearic acid films adsorbed on mica from hexadecane solution. These show islands of stearic acid in the monolayer, with only about one third of the surface covered. The observations are in good agreement with the results reported by Cook and Ries² for the adsorption of radioactive stearic acid on mica and gold from hexadecane solutions. They too found that only 20-30 per cent of a close packed monolayer of stearic acid molecules was adsorbed on these inert substrates. Mathieson also points out that island structures are not formed when adsorption of stearic acid proceeds from the melt. These authors have interpreted their observations in terms of a solvent solute interaction whereby stearic acid molecules adsorbed from solution are surrounded by hexadecane molecules in an oriented array.

We have recently found that the adsorption of radiostearic acid from nitromethane solutions leads to similar results. Oleophobic films of $C_{18}H_{37}COOH$ formed on mica platinum and chrome plated steel substrates by immersion in saturated nitromethane solutions for periods of 1 min - 2 hr contained 0.1-0.4 of a close packed monolayer of stearic acid. The high degree of association in liquid nitromethane (*b.p.* 101°C) and the lack of correlation between the amount of stearic acid adsorption and possible adsorption sites on the solids studied suggests a solvent solute interaction mechanism in this case, too.

These observations are being reported and discussed in more detail elsewhere.³

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September 11

¹ Mathieson, R. T. *Nature*, 183, 1893 (1959)

² Cook, H. D., and Ries, H. E., *J. Phys. Chem.*, 63, 226 (1959)

³ Gaines, G. L., *Ann. American Chemical Society* 130th National Meeting, Atlantic City September 1959 (to be submitted to *J. Phys. Chem.*)

A Radiochemical Tracer Study of the Relative Stability of the Halogenoplatinates

IN view of the recent classification of metals into two types, partly on the basis of the relative stabilities of their halogen complexes we wish to report the direct measurement of the relative stabilities of the chloro bromo and iodo platinate in aqueous solution. These stabilities can be used to obtain the differences of bond strength between the various complexes. An earlier attempt by Schlossinger and

Palmateer² to measure the stabilities spectrophoto-metrically gave only semi-quantitative results.

The addition of iodide solutions labelled with iodine 131 to PtCl_6^{2-} Cl^- and PtBr_6^{2-} Br^- mixtures followed, after equilibrium was attained, by precipitation of the mixed complex as the cesium salt, enabled the ratio of free to ligand iodide to be measured radiochemically. This method provides a quick and accurate analysis of small amounts of iodide, in the complex or free state, in the presence of much larger amounts of chloride or bromide. (A similar procedure has been used to study the relative stabilities of the chloro- and bromo-platinates by Dunning and Martin³, to whom we are indebted for a preprint of their forthcoming paper). In this way, curves relating $\log \{[\text{Cl}^-] / [\text{I}^-]\}_{\text{free}}$ or $\log \{[\text{Br}^-] / [\text{I}^-]\}_{\text{free}}$ to the average number of iodide ligands in the complex were obtained at 0, 25 and 44.5°C. From each curve the six equilibrium constants for successive substitutions by iodide were derived using Bjerrum's method⁴. For the purpose of comparison, only the overall constants $K_{\text{Cl } 1}$ and $K_{\text{Br } 1}$ will be considered, where $K_{\text{Cl } 1} = [\text{PtI}_6^{2-}][\text{Cl}^-]^6 / [\text{PtCl}_6^{2-}][\text{I}^-]^6$. At 25°C, $\log K_{\text{Cl } 1} = 18.25$ and $\log K_{\text{Br } 1} = 16.19$. The solution had an ionic strength of 0.5, but since the equilibria involve interchange of quite similar ions, it is probable that the concentration constants measured are close to the thermodynamic constants. The variation of $\log K$ with temperature leads to values of ΔH° for the total replacement, by iodide, of chloride or bromide in the complex.

For the overall reaction $\text{PtCl}_6^{2-} + 6\text{I}^- \rightarrow \text{PtI}_6^{2-} + 6\text{Cl}^-$, ΔH° is made up by (a) the difference between the total heats of hydration of the six chloride ions and the six iodide ions (b) the difference between the heats of hydration of the two complex ions, and (c) the difference between the total heat contents of the six Pt-I bonds and the six Pt-Cl bonds. (b) can be calculated to be of the order of 22 kcal/gm. ion, using the Born equation⁵ and a radius estimated from known bond-lengths⁶ and ionic radii. (a) is -112 kcal (ref. 7) and the overall measured value of ΔH° is -19 kcal. (c) is therefore +71 kcal/gm. ion, and the average individual Pt-I bond is of the order of 12 kcal weaker than the corresponding Pt-Cl bond. Similar calculations based on our ΔH° experiment show that the Pt-I bond is 4-5 kcal weaker than the Pt-Br bond.

Value of ΔH° is therefore determined by the difference between two large terms. One, the change in heat of hydration of the system favours the iodide as the more stable complex, and the other, the change in bond-strengths, favours the chloride. In the case of metals where the stabilities in aqueous solution of the halogen complexes are in the order $\text{I} < \text{Br} < \text{Cl}$, the relative bond-strengths are decisive. As the M-I bond becomes relatively less weak the iodide complex will become relatively stronger, and when it is less than about 10-15 kcal weaker than the M-Cl bond the order of stability will become $\text{I} > \text{Br} > \text{Cl}$. The exact point of the reversal of the order of stability, as measured by equilibrium constants will of course, depend also on entropy factors. Since platinum (IV) is a typical member of the $\text{I} > \text{Br} > \text{Cl}$ class, it is likely that the bond-strength order is $\text{I} < \text{Br} < \text{Cl}$ in all halogen complexes; but, provided the inequality is not too great, the order of stability can be the reverse of this. The border-line between the two classes of metals will only fortuitously be the same, when defined by

this criterion (which is highly dependent on the solvent), as when defined by the relative stabilities of unchanged group 5 or group 6 ligand atoms, where solvation effects will be much smaller.

The importance of solvation effects seems to have been first pointed out by Kazarnovskii⁸ in 1947. The above treatment follows that of Grinberg and Nikol'skaya⁹, who showed how it explained the apparent anomaly whereby the order of lability of platinum complexes is $\text{I} > \text{Br} > \text{Cl}$ even though this is also the order of their thermodynamic stabilities in aqueous solutions.

A more detailed account of this work will be given elsewhere.

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BIOCHEMISTRY

A New Enzyme System in the Tamarind

A NEW polysaccharide has been demonstrated to be active in the seed kernel of the tamarind (*Tamarindus indica*, Linn.) during germination. It was purified as follows. The ground kernel was extracted successively by petroleum ether (b.p. 60-80°C), chloroform and absolute ethyl alcohol. One per cent of the solution from the residues was centrifuged three times, precipitated by an equal volume of 95 per cent ethyl alcohol and filtered through linen and dried. This was repeated twice and the fibrous product extracted in a Soxhlet apparatus by absolute alcohol for more than 48 hr. The pure polysaccharide (yields, 51.0 per cent, ash. 0.0) was shown to be homogenous by obtaining ten fractions as solutions by successive treatments of two samples with water at different temperatures one from low to high and the other from high to low. Each fraction of solution gave the same polysaccharide which yielded on chemical hydrolysis, the same ratio of sugars (glucose, galactose, xylose, 3:1:2), as demonstrated by chemical and chromatographic methods. In several series of quantitative experiments of isolation, no other polysaccharide was detected in the kernel.

Neither diastase (B.D.H.) nor germinated barley malt could hydrolyze this polysaccharide at temperatures ranging from 30-70°C: but taka diastase (Parke-Davis) did hydrolyze it at these temperatures.

That this enzyme system differed from taka diastase, was shown as follows. Germinated seeds (20 gm.) were ground with 25 ml. distilled water in a glass mortar. The resulting slurry with 175 ml.

water was stirred mechanically for 30 min and filtered through linen. This extract (10 ml per sample) was allowed to hydrolyze different samples (each 25 ml) of the taramind polysaccharide solution (0.25 per cent), at different temperatures in the range, 31–60°C for 18 hr. The enzyme was active between 31° and 46°C, with an optimum at 38°C and it rose to a maximum in the pH range 4.0–5.0. The enzyme was found to be inactive in the dried seed, and to gain maximum activity after the seed coat was abraded and before initiation of leaves. This enzyme system, hydrolytic and protein in nature, as well as not precipitable by ammonium sulphate, is also effective on starch in optimum conditions. The synthetic enzyme system could not even be found in the seeds of growing fruit from initial stages.

Further details will be published elsewhere. We wish to thank Dr M. Qudrat-i-Khuda and Dr Salimuzzaman Siddiqui for their encouragement.

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A Lipoperoxidase Factor in Soya Extracts

Most studies on lipoxidase have been carried out on material from soya extracts. Lipoxidase catalyses the oxidation of pentadiene fatty acids such as linoleic acid, forming conjugated diene hydroperoxides. Haematin compounds such as haemoglobin, catalase and cytochrome c also catalyse the oxidation of these fatty acids. A recent study of this type of haematin action has been made by Maier and Tappel¹. (For convenience we use the term 'haematin' for iron porphyrin compounds irrespective of iron valency.)

We have been interested in determining whether extracts of soya bean and other plant materials owe some of their unsaturated fat oxidase activity to the presence of haematin as well as to lipoxidase. We used cytochrome c as catalyst in a system previously devised as an assay for soya lipoxidase². In this system the degree of oxidation of linoleate by lipoxidase is indicated by the secondary destruction of β -carotene, and the resulting colour change is a measure of lipoxidase activity. At pH 5.4, using freshly prepared sodium linoleate and β -carotene at levels of $0.7 \times 10^{-4} M$ and $1.1 \times 10^{-6} M$ respectively, in the system there was virtually no reaction but with slightly oxidized linoleate cytochrome c caused considerable carotene destruction. With excess cytochrome c ($0.8 \times 10^{-7} M$) the bleaching was proportional to the concentration of conjugated diene between diene levels of $0.1 \times 10^{-6} M$ and $4 \times 10^{-6} M$ in the system. With an excess of conjugated diene ($10^{-3} M$) the destruction of carotene was proportional to the concentration of cytochrome c at levels of between 0.4 and $4 \times 10^{-8} M$. Cytochrome c in the system. The reaction was completed within less than a minute; no further bleaching occurred if the reaction were prolonged for several minutes. When the reaction was carried out in the absence of β -carotene and measurements of conjugated diene made at 234 m μ , a fall in the level of conjugated diene was observed.

Under the conditions described the cytochrome c bleaches carotene by the destruction of preformed

peroxide rather than by the coupled concurrent oxidation of linoleate whereas lipoxidase causes increase of conjugated diene in the presence of β -carotene³.

On examining defatted soya under similar conditions we found that distilled water extracts differ in nature from pH 4.5 acetate buffer extracts as indicated in Table 1.

Table 1. PERCENTAGE β -CAROTENE DESTROYED IN 1 MIN BY 0.2 ML SOYA EXTRACT (2 GM/100 ML)

| Concentration of linoleate hydroperoxide in reaction system | Water extract | pH 4.5 buffer extract |
|---|---------------|-----------------------|
| Less than $6 \times 10^{-5} M$ | 7.4 | 14 |
| $6 \times 10^{-5} M$ | 7.8 | 43 |

These figures, typical of results obtained in many experiments, suggest that there are two factors in soya, one predominating in water extracts little affected by preformed diene the other, in buffer extracts more active in the presence of preformed diene. With fresh substrate in the absence of β -carotene the ratio of diene conjugation produced by the water extract to that produced by the buffer extract was about 5:1. This is of the order of the comparable ratio for carotene bleaching as shown in Table 1. With preformed peroxide in the system the diene conjugation ratio is not lowered while the carotene destruction ratio falls to about 1.5:1 as shown in the table and may be further lowered if greater amounts of peroxidized linoleate are present.

It would appear that the buffer extracts differ from the water extracts in having more lipoperoxidase activity (similar to that of cytochrome c) in that they use preformed linoleate peroxide to bleach β -carotene, and in consequence destroy much more of the pigment when auto-oxidized substrate is used. The water extracts appear to bleach carotene mainly by concurrent oxidation of linoleate. The activities of both extracts were destroyed by heating at 80°C for 3 min.

In this system we find that haemoglobin and cytochrome c are most active about pH 3.8. Howthorn and Todd⁴ observed a similar optimum for catalase. However buffer extracts of soya have a pH optimum between 5 and 6 in the system. So that while the lipoperoxidase factor resembles the haematin mentioned in acting on linoleate peroxide, it appears to differ in its response to hydrogen ion concentration.

A full account of this work will be published elsewhere.

One of us (J. A. B.) wishes to thank the Department of Scientific and Industrial Research for partial financial support of this work and Miss Thelma Carnegie for technical assistance.

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α -Oxidation of Indoleacetonitrile

It is known that certain plant tissues can convert 3-indolylacetonitrile to the highly active plant growth substance 3-indolylacetic acid¹⁻³ and we have shown that other plant tissues are able to bring about an α -oxidation of 3-indolylacetonitrile to yield 3-indolylcarboxylic acid which is inactive^{3,4}. A recent publication by Thimann and Mahadevan⁵ describing the extraction of what is believed to be a hydrolytic enzyme from the stems and leaves of certain monocotyledons (Gramineae), which is capable of converting 3-indolylacetonitrile to 3-indolylacetic acid, prompts us to report upon experiments using a cell-free extract of etiolated stems of a dicotyledon (*Pinus*). A clear demonstration of the α -oxidation of 3-indolylacetonitrile to 3-indolylcarboxylic acid is given by this extract.

Pea seedlings (var Alaska) were grown at 25°C in red light and harvested when 12 cm in height. About 100 gm of stems from which the terminal 5 mm had been removed, were frozen at -15°C and then ground at this temperature. The tissue was allowed to thaw, 25 ml of phosphate buffer (pH 7.0, 0.025 M) added, and the crude extract strained. This extract was centrifuged in nylon tubes for 25 min at 11,000 r.p.m. (approx. 14,000 g) in a refrigerated centrifuge at 2°C. The cell-free supernatant liquid was pipetted from the centrifuge tubes and used immediately for the metabolic studies. 3-Indolylacetonitrile was dissolved in 0.2 per cent aqueous acetone to give a 20 p.p.m. solution. A 25 ml quantity of this nitrile solution was mixed with 25 ml of the cell-free extract in a 200 ml glass stoppered tube and incubated for 12 hr at 25°C in darkness. The contents of the tube were then acidified to pH 2.8-3.1 and extracted with peroxide-free ether. The presence of 3-indolylcarboxylic acid in this extract was shown on a two-dimensional paper chromatogram developed first in isopropanol/ammonia (0.880)/water (10.11) and then in isopropanol/acetic acid (glacial)/water (4.11). After spraying the chromatogram with Ehrlich reagent, a pink spot which gave a characteristic red fluorescence in ultraviolet light slowly appeared. This chromatogram was compared with one bearing synthetic 3-indolylcarboxylic acid developed simultaneously. A comparison of the 3-indolylcarboxylic acid content of different extracts was made possible by applying the extracts to the starting line of a chromatogram which was then developed once in the ammoniacal solvent and sprayed with Ehrlich reagent to give pink spots (R_F 0.18).

In addition to showing the degradation of 3-indolylacetonitrile to 3-indolylcarboxylic acid evidence was obtained of the presence of an aldehyde (R_F 0.79) on chromatograms developed in isopropanol/ammonia/water and sprayed with a solution of 2,4-dinitrophenylhydrazine hydrochloride. This aldehyde was inseparable from synthetic 3-indolealdehyde by two-dimensional chromatography and it is likely that this compound, which was also found in our earlier metabolic studies⁶, is an intermediate product in the conversion of 3-indolylacetonitrile to 3-indolylcarboxylic acid.

The α -oxidation of 3-indolylacetonitrile was prevented by boiling the cell-free extract for a period of 1-2 min prior to the addition of the nitrile solution, the amount of 3-indolylcarboxylic acid found in the other extract was then no greater than the trace

normally found in extracts of pea tissue. The natural occurrence of other extractable 3-indolylcarboxylic acid in pea tissue has previously been reported⁷. Considerably reduced amounts of it were produced from 3-indolylacetonitrile when the enzyme inhibitors, iodoacetate and phenyl mercuric nitrate, were added to the solutions before incubation, and these indications that sulphhydryl groups may be involved in the α -oxidation are being further investigated.

By subjecting the cell-free extract to increasing concentrations of ammonium sulphate at pH 7.0, a series of precipitates was obtained, one of which contained most of the enzyme activity. This active fraction, which was precipitated when the ammonium sulphate concentration of the extract was raised from forty per cent to sixty per cent saturated, was readily redissolved in phosphate buffer for metabolic studies. Since a quantity of material was precipitated at ammonium sulphate concentrations below forty per cent saturated, this procedure proved to be a useful purification method.

Whilst the efficiency of conversion of 3-indolylacetonitrile to 3-indolylcarboxylic acid was greatly increased by using this purified preparation, there was still no evidence on the chromatograms for the production of 3-indolylacetic acid. This confirms the work of Thimann¹ and Seeley *et al.*² and is in marked contrast to the behaviour of 3-indolylacetonitrile in wheat and maize coleoptiles³ and with enzyme extracts of *Avena* and *Hordeum* tissue⁸ where conversion to 3-indolylacetic acid readily occurs.

All these results correlate well with those of biological tests, thus, for example, 3-indolylacetonitrile is highly active at low concentrations as a plant growth substance in tests using the coleoptiles of Gramineae, but at these concentrations is completely inactive in tests using pea tissue^{1,2,8}.

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Reaction of Formyl Porphyrins with Acetone-Hydrochloric Acid

ACETONE-HYDROCHLORIC acid has been widely used to split haemoproteins, including cytochromes of the α type which contain formyl substituents in their prosthetic groups. Results reported below show that formyl porphyrins and haemins react with acetone-hydrochloric acid, and hence it is necessary to exercise caution in the use of this reagent. Fortunately the reaction between formyl porphyrins

and acetone hydrochloric acid is a slow one (48–72 hr being necessary for complete conversion at room temperature) so that if the temperature is kept low and only a relatively short time is allowed for cleavage of hemoprotein the amount of alteration of a formyl group is negligible.

A small amount of the porphyrin under investigation was allowed to stand at room temperature, in the dark, in acetone containing 0.7 per cent (w/v) hydrochloric acid, any change in the spectroscopic properties of the porphyrin being noted by alteration of the position of the absorption bands. When the reaction was completed, as evidenced by the constant position of these absorption bands the porphyrin was returned to other and the reaction product purified by alumina chromatography of the methyl ester. Paper chromatography, according to the method of Chu Green and Chu¹, showed that the product was homogeneous.

This reaction was carried out with five formyl porphyrins (monoformyl and diformyl-deuteroporphyrin, chloroacetoformylporphyrin, porphyrin *a*¹, and cryptoporphyrin *a*²), and with monoacetyl and diacetyl-deuteroporphyrin. All the formyl porphyrins were shown to react with acetone hydrochloric acid while the acetyl porphyrins were recovered unchanged from the reaction mixture. It was also established that the use of iron complexes instead of the free porphyrin did not alter the result of the reaction. The absorption maxima of the acetone condensates of the formyl porphyrins are recorded in Table 1 together with the corresponding data for the parent formyl porphyrin.

Although aldol condensations are usually associated with alkaline pH's, it is known that similar type condensations can occur under acidic conditions³, and this seems to offer a probable explanation of the reaction of acetone hydrochloric acid with formyl porphyrins. Thus the reaction might be summarized as:

$$-\text{CHO} + \text{CH}_3\text{COCH}_3 \rightarrow -\text{CH}=\text{CH}-\text{CO}-\text{CH}_3 + \text{H}_2\text{O}$$

and such an alteration is in accord with observed spectroscopic properties of the resulting porphyrins. Further evidence in support of this explanation has been obtained by the treatment of the acetone condensate of monoformyl-deuteroporphyrin with sodium hydroxide-iodine (iodoform reaction) from which reaction monoacetyl acid deuteroporphyrin has been obtained. The identity of this degradation product was established by comparison of its

trimethyl ester with an authentic sample of this compound. Both samples had the same *R_F* value in two solvent systems¹, and had identical visible spectra (Table 1).

I would like to thank Dr R. Lemberg for his encouragement and advice and Mr J. Barrett for a sample of monoacrylic acid deuteroporphyrin trimethyl ester. A grant from the National Health and Medical Research Council of Australia is gratefully acknowledged.

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Pyridoxal Phosphate a Coenzyme for Histidine Decarboxylase

ALTHOUGH the role of pyridoxal phosphate as a coenzyme of amino acid decarboxylases is generally recognized attempts to demonstrate its participation in the enzymic decarboxylation of histidine have hitherto been unsuccessful¹.

We have been able to demonstrate an activation of mastocytoma histidine decarboxylase by pyridoxal phosphate. The enzyme source was the supernatant fraction obtained by centrifugation of a 1 in 2 homogenate of mouse mastocytoma² in 0.3 M sucrose at 140 000 *g* for 2 hr followed by dialysis for 60 hr at 0° C against frequently changed distilled water. Dialysis served to remove not only pyridoxal phosphate but also histamine and other amines present in this tissue.

Tubes containing 0.3 ml samples of enzyme solution were incubated at 37° C in 0.2 M phosphate buffer at pH 7 with several different concentrations of L (-) histidine (70, 140, 280, 560 $\mu\text{g}/\text{ml}$) both with and without the addition of 30 $\mu\text{g}/\text{ml}$ of pyridoxal phosphate. The total volume of incubation mixture in each tube was 1.5 ml. 0.3 ml samples were removed at 1, 60 and 120 min after beginning the incubation and acidified to stop the reaction. After neutralization the samples were diluted with Locke solution and the histamine content of each sample was estimated by bioassay on a strip of isolated guinea pig ileum suspended in Locke solution.

The results of a typical experiment are shown graphically (Fig. 1).

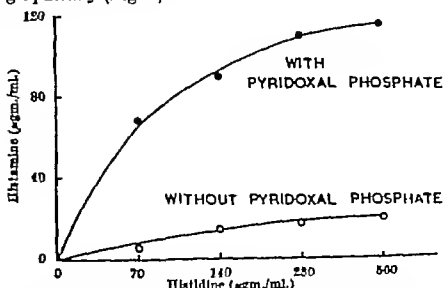


Fig. 1. Graph showing the formation of histamine by a preparation of mouse mastocytoma as a function of histidine concentration. The enzyme was incubated in the presence of different concentrations of L (-) histidine with and without the addition of pyridoxal phosphate.

TABLE 1

| Porphyrin | Absorption Bands mμ | | | | | III/IV |
|--|---------------------|-----|-----|-----|--|--------|
| | I | II | III | IV | | |
| Monoformyl deuteroporphyrin | 641 | 678 | 655 | 615 | | 1.70 |
| Acetone condensate of | 637 | 675 | 651 | 610 | | 1.49 |
| Diformyl deuteroporphyrin | 648 | 693 | 662 | 625 | | 0.64 |
| Acetone condensate of | 643 | 687 | 667 | 619 | | 1.06 |
| Chloroacetoformylporphyrin | 642 | 683 | 659 | 610 | | 1.36 |
| Acetone condensate of | 639 | 681 | 656 | 614 | | 1.22 |
| Cryptoporphyrin <i>a</i> | 642 | 684 | 660 | 610 | | 1.30 |
| Acetone condensate of | 639 | 682 | 655 | 616 | | 1.21 |
| Porphyrin <i>a</i> | 646 | 688 | 668 | 617 | | 2.30 |
| Acetone condensate of | 645 | 679 | 655 | 612 | | 1.83 |
| Synthetic monoacrylic acid deuteroporphyrin trimethyl ester | 650 | 674 | 644 | 605 | | 1.24 |
| Degradation product from acetone condensate of monoformyl deuteroporphyrin | 650 | 675 | 644 | 605 | | 1.15 |

With the exception of porphyrin *a*, its condensate and the two samples of monoacrylic acid deuteroporphyrin where either was the solvent used all spectroscopic data were determined in chloroform solution.

This experiment has been repeated a number of times with the same result, namely that after prolonged dialysis pyridoxal phosphate must be added to the incubation medium for full activity of the enzyme to be observed. On the other hand, after dialysis for less than 24 hr, adequate to remove the amines, full or almost full activity of the enzyme can be observed without the addition of pyridoxal phosphate².

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Reaction of Mercuric Chloride with Plasmalogen

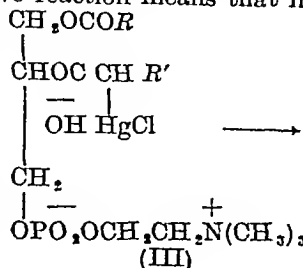
It has been found that aqueous mercuric chloride reacts with the enol-ether double bond of plasmalogen¹ to form a mercury-organic compound. This reaction clarifies the mercuric chloride catalysis in the Feulgen-Voit-Schiff identification of plasmalogen².

Filter paper is spotted with 70 μgm (2 μl of solution) of a commercial preparation of beef heart lecithin ('Lecithin' (ex beef), Sylvania Chemical Co., Orange, New Jersey) in 95 per cent ethanol which assays 52 per cent choline plasmalogen. This paper is immersed for 30 sec. in 1 per cent aqueous mercuric chloride. Excess mercuric chloride is removed with five washes in 1 per cent sodium chloride and five washes in distilled water. The presence of mercury in the lipid spot is detected by immersing 2 min. in a 0.1 per cent solution of diphenyl carbohydrazide in 70 per cent ethanol which is 0.1 N in potassium hydroxide. After washing thoroughly in water to remove excess diphenyl carbohydrazide reagent, a deep purple spot of the mercury salt is observed against an unstained background. This test is sensitive to 1.0 μgm of plasmalogen in a spot of 1 cm diameter. Other agents for detecting mercury may be used, for example hydrogen sulphide or dithizone, but these are less sensitive.

The following lipids were tested by the same technique and were found to be negative: sphingomyelin, cerebroside, cholesterol, strandin, oleic acid, linoleic acid, linolenic acid, stearic acid, methyl oleate, myristic aldehyde, linseed oil and olive oil.

The site of reaction of mercuric chloride with the lecithin-plasmalogen mixture was determined in the following ways. A negative reaction means that no formation of the mercury-diphenyl-carbazide salt was detected in the lipid spot.

(A) When the beef heart lecithin-plasmalogen mixture was treated either (1) by hydrolysis in 90 per cent acetic acid³, 1 hr. at 50°C or (2) by hydrogen-



ation with platinum oxide, 1 hr. at 50°C, and the total products spotted on filter paper, the mercuric chloride reaction carried out as described above was negative.

(B) Filter papers after being spotted with the beef heart lecithin-plasmalogen mixture were subjected to the following separate treatments:

- (1) 0.1 N aqueous iodine, 2 min. at 25°C
- (2) 0.1 N hydrochloric acid, 1 hr. at 50°C
- (3) 0.1 N aqueous bromine in 2 per cent potassium bromide, 2 min. at 25°C

After a thorough water wash the papers were treated with mercuric chloride and then with diphenyl carbohydrazide as described above. In each case the reaction was negative.

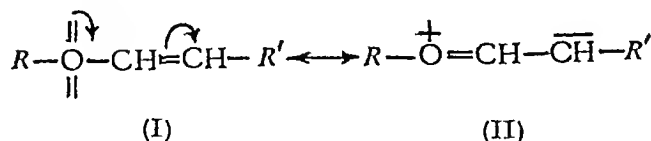
(C) Filter papers spotted with the beef heart lecithin-plasmalogen mixture and treated with 1 per cent mercuric chloride were then subjected to the following separate treatments:

- (1) 5 per cent potassium cyanide, 5 min. at 25°C
- (2) 0.1 N aqueous iodine, 5 min. at 25°C
- (3) 0.1 N hydrochloric acid, 5 min. at 25°C

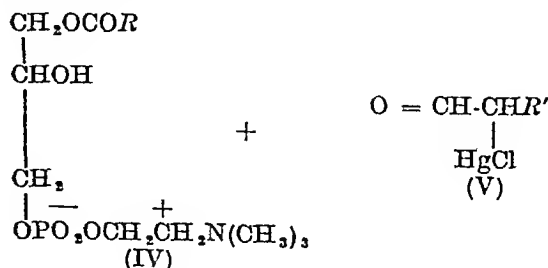
In each case a negative reaction was obtained with diphenylcarbohydrazide.

All the above series of reactions have been duplicated on a chloroform-methanol extract of total rat brain lipids⁴ which contains plasmalogens to the extent of 10 per cent of the total lipids.

These reactions are consistent with the view that the mercuric chloride is reacting with a double bond which is labile to acid hydrolysis and mild iodine treatment. The mercuric chloride adduct formed is labile to acid and mercuric complexing agents. The reaction of mercuric chloride with the enol-ether of plasmalogens is analogous to the reaction of more ionic mercury salts with normal olefins⁵. Mercuric chloride reacts slowly or not at all with simple olefins⁵, probably because of the low concentration of HgCl_2^+ ions. The resonance form (II), of the enol-ether structure increases the negative charge on the β carbon making it much more reactive to electrophilic additions of this type.



Preliminary quantitative studies of the uptake of mercury in lipid spots indicate that the reaction with the α , β -unsaturated ether is almost instantaneous. However, after about 60 sec. in 1 per cent mercuric chloride a slow reaction with other unsaturated bonds begins. If the product of the mercuric chloride catalysis of the Feulgen-Voit-Schiff reaction² initially formed is the hemiacetal (III), this exists in equilibrium with the free aldehyde (V), and lysolecithin.



This hypothesis has been verified by the chromatographic identification in the products of the plasma logen mercurio chloride reaction, of a free fatty aldehyde containing mercury and lysocleithin. Also we have isolated in 21 per cent yield β -chloromercuroacetaldehyde* from the reaction of the model system, butyl vinyl ether plus aqueous mercuric chloride.

This reaction with mercurio chloride has been developed for histochemical localization of plasma logen (unpublished work).

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Hydroxylation of Proline in Vitro

WHILE carrying out a study of hydroxyproline synthesis in biological media, by hydroxylation of proline or peptides containing proline we have also investigated the possibility of hydroxylation of pyrrolidine ring in vitro. We commenced our study by ascertaining^{1,2} whether or not cortisone inhibited the formation of free hydroxyproline in animal tissues during their embryonal development and thus interfered with the biosynthesis of collagen.

The possibility of incorporating free hydroxyproline^{3,4} (and hydroxylysine in analogy^{5,6}) into collagen proteins was denied in most papers. However in a recent study by Mitoma *et al.*⁷ on the same experimental material as in our case, proofs are presented that bound hydroxyproline also originates from free hydroxyproline. Furthermore the central significance of hydroxylation of proline for the synthesis of collagen arises in the papers of Robertson^{8,9} and Gould¹⁰ who have found proof for hydroxylation inhibition of proline in the case of ascorbic acid deficiency. The possibility of hydroxylation of both aromatic¹¹ and sterol rings¹² has been proved by many authors.

Our experiments have shown that in the reactive medium containing ethylene diamine tetraacetic acid sodium salt Fe^{++} , ascorbic acid, hydrogen peroxide and proline, a substance forms which can be determined by specific reaction on hydroxyproline¹⁴. By means of paper ionophoresis partition chromatography, as well as by isolation of hydroxyproline in the form of reneekate and by measuring the absorption curves, we have found that the substance formed has properties inherent to hydroxyproline. Hydroxylation does not occur either in the absence of ascorbic acid or hydrogen peroxide. Ethylene diamine tetraacetic acid sodium salt and Fe^{++} are not essential, but in their presence, however, hydroxylation becomes more intensive.

Hydroxylation is almost completed within three

minutes if the incubation lasts for more than 30 min. the amount of hydroxyproline formed decreases. The presence of pure oxygen in the reactive medium, instead of hydrogen peroxide, also brings about the formation of hydroxyproline, however, the reaction rate is slow and not intensive.

We have found that the optimal concentration of substances in the reactive medium and the optimal conditions of reaction are 8×10^{-2} M ferrous sulphate, 2.6×10^{-2} M ethylene diamine tetraacetic acid sodium salt, 8×10^{-4} M ascorbic acid, 4.7×10^{-2} M hydrogen peroxide, 0.1-0.15 M solution of phosphate buffer, pH in the range 4.5-5.0. There is a definite relationship between the temperature and degree of hydroxylation (studied up to 55°C). The amount of hydroxyproline formed is related to the concentration of proline in the reactive medium and the degree of conversion is in the region of 2-4 per cent. We have also studied the possibility of hydroxylation of polyglycine and polyglutamyglycine and have found the same degree of conversion as in proline.

Thus we have been able to show that in the reactive medium of the same composition as was used before by Udenfriend *et al.*¹⁵ for the hydroxylation of the substituted aromatic ring, hydroxylation of proline also occurs.

Further experiments aiming at the biological utilization of these results are being carried out.

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Microbial Degradation of Rutin

COMPARATIVELY little work on the metabolism of rutin has been published. 3,4-dihydroxyphenyl acetic acid and homovanillic acid are found in urine after oral administration of rutin to the rat^{1,2} and protocatechuic acid accumulates in rat kidney homogenates in the presence of quercetin³.

We have shown⁴ that a fungus, *Pullularia fermentans* var. *candida*⁵, forms phloroglucinol, protocatechuic acid and an unknown substance when cultivated in aqueous rutin solution. This unknown substance has now been identified as 2-protocatechuyl phloroglucinol carboxylic acid.

The organism (about 50 mgm wet weight) was incubated with rutin (1 gm) in 1 l of 0.003 M phosphate buffer (pH 6.0) at 25°C for 5 days and the liquid was extracted with ether. After removal of ether, the remaining mass was dissolved in hot water (80°C), and about 0.1 gm substance was obtained in white needles after cooling in a refrigerator. When subjected to paper chromatography the R_F value of this substance agreed well with that of the unknown

substance, as was reported previously, both in *n*-butanol/acetic acid/water (4:1:2) and in 80 per cent phenol.

This substance, after recrystallization from hot water, contained 2.5 mol of water of crystallization and melted, effervescing at 174°C, and produced dark green dyes and red orange dyes with ferric chloride and with benzidine diazo reagents⁶, respectively.

When hydrolyzed with 10 per cent potassium hydroxide, the substance gave phloroglucinol and protocatechuic acid and it dissolved in a sodium bicarbonate solution evolving carbon dioxide, suggesting the presence of a carboxylic group in its molecule. These facts suggest that this substance is identical with a protocatechuoyl phloroglucinol carboxylic acid (anal. calc. for $C_{14}H_{10}O_8 \cdot 2.5H_2O$, C, 47.87, H, 4.30, found C, 48.44, H, 4.39).

Since this substance easily loses the carboxyl group on heating to 100°C, it was methylated with an excess of diazomethane and the methyl ether methyl ester was obtained as colourless needles, which melted at 144°C after recrystallization from absolute alcohol (anal. found C, 60.91, H, 5.16). When admixed with 2-veratroyl 4,6-dimethoxyphloroglucinol carboxylic acid methyl ester (anal. calc. for $C_{14}H_{10}O_8$, C, 60.63, H, 5.36, found C, 60.69, H, 5.02), which had been synthesized from 2,4-dimethoxyphloroglucinol carboxylic acid methyl ester and veratroyl chloride, this methyl ether methyl ester did not show any depression of melting point, suggesting the identity of these substances.

From these results it is evident that the substance produced by the fungus is identical with 2-protocatechuoyl phloroglucinol carboxylic acid.

We are grateful to Mr M. Yoneyama, Biological Laboratory, University of Hiroshima, for identifying the fungus and to Dr M. Hasegawa, Government Forest Experiment Station, for his helpful advice.

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Chemical Nature of a Plant-Virus Inhibitor from Rice

THE inhibition of tobacco mosaic virus infection of primary bean leaves (*Phaseolus vulgaris* L. var Pinto) by extracts of various portions of rice plants has been described recently¹. The inhibitor or inhibitors present in rice resemble those derived from other plants such as spinach (*Spinacea oleracea* L.)², poke weed (*Phytolacca acinosa* Roxb. var *esculenta*)³, New Zealand spinach (*Tetragonia expansa* Murr.)⁴, and sweet william (*Dianthus barbatus* L.)⁵, in that the infection of test plants is inhibited when the plant extract and virus inoculum are mixed and applied simultaneously. The inhibitor in rice extracts differs in that it protects bean leaves against tobacco mosaic virus infection even when applied to the leaves (which are then rinsed with water) 1-3 days prior to inoculum application. In so far as we are aware, the only other plant extracts that protected test plants

against virus infection were derived from carnation (*Dianthus caryophyllus* L.)⁶, but the time between inhibitor application and inoculation was only 1-3 hr.

Experiments were conducted to determine the general chemical nature of the inhibitor as a basis for subsequent more detailed chemical investigation. The source of the inhibitor used was rice polish, since the inhibitor is concentrated in this readily available by-product in the milling of rice. The antiviral activity of the various chemical fractions of rice polish was determined by the local-lesion bioassay described by Holmes⁷. In these assays one member of each pair of opposite primary bean leaves was rubbed with the preparation plus tobacco mosaic virus and the opposite member with a comparable untreated control inoculum.

The inhibitor could be extracted from the polish with water, but not with methanol, and addition of methanol to the water extract caused complete inactivation with the formation of a precipitate. Centrifugation of the cloudy aqueous extract at 15,000 r.p.m. for 30 min gave a clear, slightly yellow solution retaining all its activity. Addition of 20 per cent trichloroacetic acid to a final acid concentration of 10 per cent in the extract completely destroyed the activity of the inhibitor, with the formation of a slight precipitate. Addition of cold saturated ammonium sulphate solution to cold rice-polish extract to 80 per cent saturation, followed by centrifugation, gave a precipitate that was found to be active. Very slow addition of cold absolute ethanol to cold rice-polish extract, to give a final ethanol concentration of 40 per cent, followed by centrifugation, gave an active precipitate. By mixing the aqueous extract with various powdered adsorbents, it was found that the inhibitor was adsorbed on alumina, magnesium oxide ('Sea Sorb'), and charcoal, but not on silica ('Celite'). The inhibitor failed to pass through a Visking membrane in 4 hr after the extract was placed in a stainless steel ultrafiltration apparatus and 40 lb of nitrogen per square inch was applied.

These preliminary experiments indicate that the virus inhibitor in rice polish is probably a protein, with a molecular weight greater than 13,000.

The aqueous extract of rice polish loses its activity slowly upon standing, even at 5-7°C, with the formation of a precipitate which may be denatured protein. The fresh extract is approximately neutral in reaction, but on standing, either in the cold or at room temperature, it becomes acidic, with consequent loss in activity.

Further investigation of this virus inhibitor is in progress.

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Release of Non-Esterified Fatty Acids from Adipose Tissue in Normal and Diabetic Rats

From a number of recent papers it appears that the mobilization and transport of fat from fat depots to sites of its further utilization take place mostly in the form of non-esterified fatty acids¹. Evidence that this is so is provided by Dale² and Gordon³ who observed during states with an inadequate utilization of carbohydrates an elevated blood level of non-esterified fatty acid. When the utilization of carbohydrates was increased (after ingestion of glucose or after administration of insulin) the blood level of non-esterified fatty acids decreased. Experiments with adipose tissue *in vitro* also confirmed that under certain conditions non-esterified fatty acids can be released. The amount released depends on whether at the moment the animal was killed the energy requirements were satisfied from reserves. Gordon and Cherkas⁴ have demonstrated an increased release of non-esterified fatty acids from incubated epididymal fat at fasting rats, while during satiety the release was insignificant. It was also revealed that the release of non-esterified fatty acids from incubated adipose tissue of normal animals is increased by various hormones added *in vitro*: adrenalin⁵, noradrenalin, corticotropin^{6,7}, while its release is arrested after the addition of insulin⁴. Thus, it can be assumed that the adipose tissue of diabetic animals, which must mobilize fat reserves will also, *in vitro*, release more non-esterified fatty acids than the tissue of healthy animals. Our experiments confirm this assumption.

For our experiments we used intact white rats and rats with alloxan diabetes weighing 100–120 gm. The animals were killed after 10 hours fasting and a slice of about 50 mgm of epididymal fat was incubated for four hours in 4 ml of pooled post-absorptive human serum at 37° C with constant agitation. The initial and final concentration of non-esterified fatty acids in the medium was estimated using Dole's method⁸; the blood sugar level by Hagedorn and Jensen's method. The results are expressed in micro-equivalents of non-esterified fatty acids released after 1 hour per 1 gm of fresh tissue \pm standard error.

We performed two separate experiments under the same conditions. In the first experiment, however, we used diabetic rats 8 days after the administration of alloxan, in the second experiment rats 15 days after the administration of alloxan, the human serum used as medium being from a different group of donors. From the tissue of the control animals in the first experiment 2.32 ± 0.31 μ equiv non-esterified fatty acids were released during the incubation, while in the diabetic rats the corresponding figure was 4.07 ± 0.41 μ equiv. In the second experiment we obtained the following results: control animals 5.21 ± 0.51 μ equiv non-esterified fatty acids, diabetic animals 8.58 ± 0.52 μ equiv non-esterified fatty acids. The blood sugar level of the diabetic rats was 170–340 mgm per cent immediately before the beginning of the experiment, of the control animals 70–110 mgm per cent. The results are shown in Table 1.

From these experiments it appears that in animals with alloxan diabetes the release of non-esterified fatty acids from the adipose tissue is significantly higher. In earlier experiments we established the direct correlation between non-esterified fatty acids level and blood sugar level in diabetic animals⁹. In the experiments carried out during the present work

Table 1 NON-ESTERIFIED FATTY ACIDS RELEASED FROM FATTY TISSUE OF NORMAL AND ALLOXAN DIABETIC RATS

| Experiment No | Group | Number of rats | Non-esterified fatty acids production μ equiv./gm tissue/hr | Mean \pm S.E. | Statistical significance |
|---------------|----------|----------------|---|-----------------|--------------------------|
| 1 | Control | 12 | 2.32 \pm 0.31 | 4.6 \pm 0.41 | P < 0.001 |
| | Diabetic | 8 | | | |
| 2 | Control | 8 | 5.21 \pm 0.51 | 8.58 \pm 0.52 | P < 0.001 |
| | Diabetic | 8 | | | |

however, no relation between the release of non-esterified fatty acids from the tissue and the blood sugar level in the alloxan diabetic animals was confirmed. To elucidate the mechanism of the difference of non-esterified fatty acids release from adipose tissue in normal and alloxan diabetic rats it will be necessary to direct attention to changes in the tissue lipoprotein lipase activity, this being the subject of our current work.

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Distribution of Enzyme Systems Responsible for Steroid Metabolism in Different Tissues and Subcellular Fractions

From their studies of the *in vivo* metabolism of various biologically active and inactive 11 oxygenated steroids, Bush and Mahesh¹ believe that the glucocorticoid activity of these steroids is due to the specific interaction of an 11 β hydroxy group on the steroid molecule with the receptor sites for such hormones and that such an interaction does not involve oxidation-reduction at C-11. However, Talalay and co-workers² observed that various hydroxy steroids including the 11-oxygenated ones, can act as co-enzymes in the transfer of hydrogen between pyridine nucleotides in the presence of suitable steroid dehydrogenases and they suggest that this is the mode of action of steroid hormones. In the present study, the metabolism of cortisol and cortisone has been investigated in various tissues in order to determine the distribution of enzyme systems responsible for the metabolism of the steroids, with the view of finding out whether steroid metabolism is directly involved in hormone action or whether it represents stages in their detoxication and removal from the body.

The diaphragm of the unfasted male albino rat was the first tissue to be studied. One gram of the tissue was incubated with 100 μ gm of cortisol in 10 ml of Krebs Ringer phosphate buffer (pH 7.0–7.1) at 37° C for two hours in an atmosphere of 100 per cent oxygen and the steroids were extracted and then chromatographed on paper according to the methods described by Bush and Mahesh¹ with minor modifications.

Steroid metabolites were detected and estimated using blue tetrazolium reagent for a ketone group.

sodium hydroxide fluorescence for Δ^4 -3-ketosteroids and Zimmerman's reagent for 17-ketosteroids

Since there was very little metabolism in the diaphragm, even in the presence of 5×10^{-4} M triphosphopyridine nucleotide, the study was extended to rat heart, leg muscle, brain, stomach, small intestine, large intestine and kidney. In these tissues, with the exception of the kidney, there was very slight reduction at C-20 and oxidation at C-11, even with the addition of triphosphopyridine nucleotide or reduced triphosphopyridine nucleotide, and no detectable amounts of ring A reduced C-21 steroids or 17-ketosteroids were found. In the kidney, the main metabolites of cortisol were cortisone, 11β 17 α 20 21-tetra-hydroxy-pregn-4-en-3-one and 17 α 20 21-trihydroxy-pregn-4-en-3 11-dione

In the kidney, slices were most active in metabolism, mince was intermediate, and homogenate was the least active. In two experiments, the average C-20 reduction in slices, mince and homogenate was 48.2, 26.5 and 1.8 per cent respectively of the total recovered metabolites, whereas oxidation in the 11-position was 62.5, 46.7 and 22.2 per cent respectively. The losses of activity in the mince and homogenate were only partly recovered by the addition of triphosphopyridine nucleotide or reduced triphosphopyridine nucleotide. Schneider and Horstmann⁴ also observed a similar loss of metabolic activity in liver and kidney mince as compared to the respective slices.

In order to investigate further the different metabolic activities of the various kidney preparations, the distribution of the enzyme systems in various sub-cellular fractions was studied. Nearly all of the oxidation of cortisol at C-11 occurred in the particulate fraction when the homogenate was centrifuged at 104,000 g for 1 hour. When the whole homogenate was separated by differential ultracentrifugation into nuclear particles, mitochondria, microsomes and supernatant fractions, the activity was mainly associated with the nuclear particles and microsomes, and there was very little activity in the mitochondria. There was a 13-fold increase in the amount of cortisone formed when 100 μ gm of cortisol was incubated with the nuclear fraction obtained from 1 gm of kidney in the presence of 5×10^{-4} M triphosphopyridine nucleotide. In two experiments, the average amount of cortisone formed from 100 μ gm of cortisol was 38.8 μ gm in the nuclear fraction, 8 μ gm in the mitochondria and 20.5 μ gm in the microsomes.

In order to determine whether the nuclei were responsible for the metabolism of cortisol by the kidney nuclear fraction, these particles were isolated by the method of Dounce⁵. The nuclei exhibited very little metabolic activity as compared to the whole nuclear fraction. The part of the nuclear fraction remaining after removal of the nuclei, and presumably consisting mainly of cell membranes, was highly active in metabolism. This would suggest that the enzyme responsible for C-11 oxidation is linked with the cell membranes and is destroyed partly by destruction of the cell structure.

When cortisone was incubated with various kidney preparations and cell fractions, the main metabolic reaction was reduction in the C-20 position which took place to a much greater extent than with cortisol. Furthermore, in the presence of reduced triphosphopyridine nucleotide, reduction at C-11 appeared to be less than 10 per cent as compared to a 60 per cent oxidation of cortisol to cortisone in the presence of triphosphopyridine nucleotide. This would indicate

that the enzyme system is not freely reversible, a property which was not observed in the corresponding liver enzyme described by Hurlock and Talalay⁶.

A detailed report of this investigation will be presented elsewhere. This work was supported in part by grants from the American Cancer Society and the National Institute of Arthritis and Metabolic Diseases.

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An Effect of Selenium and Cystine on Lipide Peroxidation in Tissues Deficient in Vitamin E

Two vitamin E deficiency syndromes in the chick are preventable by nutrients other than α -tocopherol. Exudative diathesis does not occur when the deficient diet contains trace amounts of selenium. With diets simultaneously low in tocopherol and sulphur amino-acids, muscular dystrophy occurs which can be prevented by cystine, methionine, or vitamin E, trace amounts of selenium (<0.5 ppm) are ineffective. The mechanism by which selenium and sulphur amino-acids replace vitamin E is unknown. Since the only established biochemical action of tocopherol is that of an antioxidant, it appeared that possibly these other nutrients may in some way affect peroxidation of unsaturated fatty acids. Thiobarbituric acid has been shown to be a sensitive reagent for determining the extent of peroxidation in autoxidizing tissues^{1,2}. Using this test as described by Tappel and Zalkin³, we have found that dietary selenium and cystine significantly reduce peroxidation in certain tissues of vitamin E deficient chicks.

Day-old chicks were fed either of two vitamin E-deficient diets for 28 days. Diet A contained 30 per cent of purified soybean protein, 6 per cent of salts, 1 per cent of 'stripped' lard, 0.3 per cent of cystine, and all vitamins except E. Diet B contained 15 per cent of purified casein, 10 per cent of gelatin, 4 per cent of lard, 6 per cent of salts, and all vitamins except E. Glucose, to make 100 per cent, was the carbohydrate in both diets. Control groups on each diet received α -tocopherol in the diet. Diet B, which was low in sulphur amino-acids, produced white muscle striations in all chicks. The extent of peroxidation in liver and breast muscle homogenates was determined as indicated in Table 1. Three separate experiments with each diet gave similar results; the data from one typical experiment are shown in Table 1.

Tissues from chicks fed either diet A or B with vitamin E gave no pink colour with thiobarbituric acid when incubated alone or with ascorbic acid⁴. The low values given for these groups (3 and 6) represent faint yellow solutions uncorrected for the reagents. Aliquots of homogenates from vitamin E-deficient livers or muscles, before incubation, gave faint colours with thiobarbituric acid which were predominantly yellow. After incubation, bright pink or red colours were formed with thiobarbituric acid.

Table 1 PEROXIDATION IN HOMOGENATES OF TISSUES AS DETERMINED WITH THIOBARBITURIC ACID (TBA)*

| Diet | Group No | Addition | No of chicks | Mean TBA units \pm standard error† | | | |
|------|----------|---------------------------|--------------|--------------------------------------|-------|--------------|-------|
| | | | | Liver | P | Muscle | P |
| A | 1 | None | 7 | 373 \pm 73 | <0.01 | 181 \pm 12 | 0.70 |
| A | 2 | 0.5 p.p.m. E ₂ | 7 | 185 \pm 12 | | 155 \pm 8 | |
| A | 3 | 100 mcgm. vit. E/kgm. | 4 | 71 \pm 16 | | 67 \pm 18 | |
| B | 4 | None | 7 | 302 \pm 78 | 0.5 | 171 \pm 13 | <0.01 |
| B | 5 | 0.3 per cent L-cystine | 7 | 248 \pm 49 | | 117 \pm 5 | |
| B | 6 | 100 mcgm. vit. E/kgm. | 3 | 57 \pm 10 | | 38 \pm 3 | |

* Two ml. of a 5 per cent homogenate in 0.1 M phosphate buffer pH 7.4 were incubated in air in a 60 ml. stoppered flask at 37°C with shaking in a water bath for 1 hr. One ml. was then removed, deproteinized with 10 per cent trichloroacetic acid and the reaction with thiobarbituric acid run on 1 ml. of supernatant.
† One TBA unit = absorbancy $\times 100$ at 535 m μ /gm. fresh tissue.
‡ Added as sodium selenite.

With diet A, livers from chicks ingesting selenium (group 2) produced significantly less 'peroxides' than did the control group (1). Three of these chicks had evidence of mild exudative diatheses. The difference between the muscles from these groups was not significant.

In group 4 which had diet B alone, all chicks had varying degrees of muscle atrophy. These tissues gave thiobarbituric acid values significantly higher than those of the chicks in group 5 receiving dietary cystine (muscles without striations). With the doubly deficient muscles there was no correlation between the severity of striations and the thiobarbituric acid values. The livers from groups 4 and 5 produced amounts of 'peroxides' not significantly different.

It is important to note that these observed effects of selenium and cystine are independent of each other. Selenium shows an effect only with diet A which contains added cystine, and the liver but not the muscle is involved. Cystine shows its effect exclusively with diet B and only in the muscle. As mentioned above, dietary levels of selenium below 0.5 p.p.m. are ineffective in preventing the muscular dystrophy. It should be pointed out that diet A is inadequate with respect to essential fatty acids but growth is normal at this age.

Homogenates of heart and brain have been studied to a limited extent. It is of interest that although hearts from chicks fed vitamin E did not form 'peroxides' as tested above brains from such chicks gave just as high thiobarbituric acid values as did brains from vitamin E deficient birds. This tissue also formed more 'peroxides' than any of the other tissues tested. It would appear that tocopherol does not pass the blood brain barrier.

These studies indicate that selenium and cystine in some way alter the composition of tissues so that the capacity to peroxidize lipids is reduced. This is not a direct action since we have found that selenium and cystine when added *in vitro* to homogenates do not reduce peroxidation. Machlin *et al.*³ have reported a similar lack of effect for selenium. It is also not probable that selenium is acting by sparing tocopherol since our experience has indicated that the rate of depletion of vitamin E from tissues is not influenced by biologically active selenium.⁴

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PHYSIOLOGY

Effect of Prolonged Thyroid Administration on Aged Male Rats

THE second phase of an earlier study has been completed and it was felt that a brief note of the results would complement the first report.¹ Male Holtzman strain rats (400 gm.) were given orally purified thyroid extract (Proloid[†] Warner Chilcott) from 12 months of age until death at 21 months in three daily dosage series A, B, and C, equivalent to 15, 60, and 240 mcgm respectively for a 70 kgm human. At necropsy, all the principal organs (the same as those examined in the first phase¹) after gross examination were fixed in buffered 10 per cent formalin, paraffin processed, and stained in the usual way and histochemically for elastic collagenic, and reticular tissues and for neutral and acid polysaccharides, as in the first series of experiments.¹⁻⁴ Sections were compared with each other, with those of untreated control animals of equal age, and with sections obtained from rats with hypothyroidism induced by iodine 131. Organs from 84 experimental animals were studied with special regard to the vascular structures and the connective and epithelial tissues.

The examination of alterations in the cardio vascular sections (heart and all vascular levels) was interesting in that the hyper and hypo thyroid physiological states were not reflected histologically, with the exception of an increase of intimal acid polysaccharides in the larger vessels of the hyper thyroid animals (most marked in B series) and in consistent medial fibrosis (aortic) in series B and C. Heart sections demonstrated no consistent architectural or histochemical alteration. Study of the various connective tissues indicated that other than the usual changes of age no consistent variations from normal were present. Polysaccharide changes in ground substance were minimal between series and not consistent. Basically it appears that under the conditions of this experiment, experimentally altered thyroid function does not affect the fundamental integrity of the connective tissues of the aged rat or alter the basic histological structure of the vascular organs.

Microscopical examination of the various epithelial structures in the series indicated that the abnormal thyroid physiological states were not reflected histologically in any consistent manner other than the expected alterations of extreme hyperthyroidism in series C. The only major pathological state observed was inconsistent patchy degenerative changes in the supranuclear medullary regions in series C animals. It would appear that in common with the vascular and connective tissues, induced hyperthyroidism under the conditions of this experiment has little effect on the overall epithelial structures in the gastro intestinal, genito-urinary, pulmonary, and exocrine glandular organs and only the usual effects of time hyperthyroidism on the endocrine epithelial tissues in series C.

When these results are evaluated in combination with those of the first phase, it would appear that in spite of physiological manifestations of experimentally altered thyroid function, the basic architecture of the tissues and organs of the aged rat will not be affected except for certain endocrine organs in extreme toxic states.

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Blood Keto-acids in Kwashiorkor

DURING desalting in an electrolytic desalter (Shandon Scientific Co Ltd, London) of urines from kwashiorkor patients, it was observed that a considerable amount of a black mercury amalgam was invariably formed. Estimation of the concentration of ammonia in these urines confirmed that the amalgam formation was due to a high ammonia content. This was in agreement with a report made earlier by Platt and Heard that ammonia excretion was increased in protein malnutrition. It was suspected at the time that this increased ammonia output may be the result of an acidification defect due to reduced hydrogen ion excretion by the renal tubules or else to the excretion of increased amounts of organic acids. Afterwards, while measuring serum transaminase levels by the spectrophotometric method¹ it was noted that on the addition of malic or lactic dehydrogenase and reduced diphosphopyridine nucleotide to the buffered serum, the specimens from cases of kwashiorkor consumed more reduced diphosphopyridine nucleotide than normal serum. In many instances more than 30 min were required to produce equilibrium conditions and in most cases extra reduced diphosphopyridine nucleotide would have to be added in order to produce a steady state and a high enough initial spectrophotometric reading. With normal serum on the other hand, equilibrium was usually attained in less than 10 min and it is unusual for extra reduced diphosphopyridine nucleotide to be required. This observation pointed to the probability that ketoacids which are substrates for malic dehydrogenase and lactic dehydrogenase must accumulate in the blood in kwashiorkor.

Paper chromatography of ketoacid hydrazones according to the procedure of McArdle² confirmed that pyruvate mainly, and in some case α -ketoglutaric acid were present in increased concentration in the blood in kwashiorkor. Blood pyruvate was then determined by the enzyme spectrophotometric method of Segal *et al*³. All the normal children and adults examined by this method had fasting blood pyruvate concentrations of 0.40–0.85 mgm/100 ml. The twenty-five kwashiorkor patients examined had fasting blood pyruvate levels ranging from 0.50 mgm/100 ml to 2.8 mgm/100 ml, the value was more than 1.00 mgm/100 ml in 14 of the 25 patients. There was no correlation between blood pyruvate concentration and the clinical assessment of the severity of the case.

α -Ketoglutaric acid was determined in the perchloric acid extract used for pyruvate estimation by measuring the yellow colour of the hydrazone after pyruvate had been destroyed with lactic dehydrogenase. Normal values ranged from 0.08 to 0.22 mgm/100

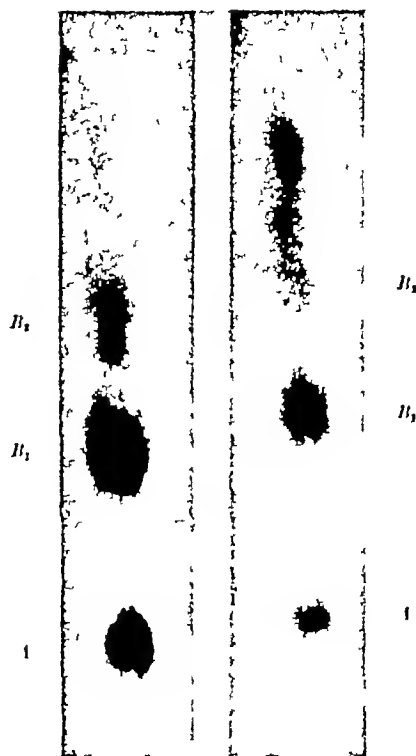


Fig. 1. (1) Chromatogram of blood ketoacids on admission. The equivalent of 0.8 ml blood was applied. (2) Chromatogram of blood ketoacids after patient had been given the methionine supplemented high carbohydrate diet. Same quantity of blood as in (1).

A, ketoglutaric acid spot, B₁ and B₂ pyruvate spots

ml. The kwashiorkor cases showed much variation but in only five of the twenty-five cases was α -ketoglutaric clearly above the normal range.

When patients are successfully treated with milk and vitamin supplements the blood pyruvate returned to normal level. When they were fed for three days with a standard diet of high carbohydrate and low protein content supplemented with 25 mgm thiamine daily by intramuscular injection as well as other vitamins by mouth the blood pyruvate did not show any significant change. In two cases fed for three days with the same standard diet to which was added 3 gm DL-methionine daily, the blood pyruvate showed dramatic reduction. The chromatograms of one of the cases is shown in the accompanying photographs (Fig. 1), which were taken under ultra-violet light after the papers were treated with 2 per cent sodium hydroxide in 90 per cent ethanol. The blood pyruvate in this case was 2.6 mgm/100 ml on admission. After three days on the diet supplement with methionine, the value had fallen to 1.2 mgm/100 ml. There is thus evidence that the accumulation of pyruvate may be due, at least in part, to deficiency of sulphhydryl groups. The matter is being further investigated in this laboratory.

I am indebted to Dr W. R. F. Collis, head of the Department of Child Health in the College, for clinical facilities to carry out this investigation.

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Effect of Acetylcholine and Eserine on the Spawning of *Hydractinia echinata*

It is usually considered that the responses of coelenterates are not mediated by acetylcholine¹ because (1) there is no evidence of significant amounts of acetylcholine or choline esterase in their bodies, (2) neither these substances nor atropine nor curare affects their neuromuscular activities². However I have recently found that acetylcholine (Roche) and physostigmine (eserine, B D H) affect the spawning activity of *Hydractinia echinata*.

As previously reported^{3, 4} spawning is induced by a suitable periodicity of lighting darkness conditioning the response which is triggered by light. When isolated gonophores are subjected to sea water containing either acetylcholine (concentration 5×10^{-4}) or eserine (concentration 10^{-4}) during the periods of darkness discharge is inhibited in 50–80 per cent of the mature gonophores, but a number of treated gonophores both male and female spawn in the dark without light treatment. Concentrations of both substances above 10^{-3} inhibit spawning completely and those below 10^{-4} are ineffective.

As neither of the drugs acts when introduced at the beginning of illumination or even 5 min before the illumination is due to start it is clear that the triggering process is insensitive to them.

Thus they appear to act in two ways: in one, by interfering with the increase in photosensitivity during darkness and in the other by triggering off the final process of spawning. It is also worth noting that sensitivity to either acetylcholine or eserine coincides in time with sensitivity to calcium⁵.

Whether a true cholinergic mechanism exists, and how it is related to calcium remains to be discovered.

The work was done whilst holding a research fellowship of Bedford College and I am greatly indebted to Dr C H Mortimer and the members of the staff of the Millport Marine Station for providing facilities.

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Transmission of Passive Immunity in an Insectivore

THE hypothesis¹ that antibodies are not transmitted through placenta of the epitheliochorial and syndesmochorial types and are transmitted through haemochorial and haemoendothelial types was at one time widely accepted. More recently it has been demonstrated in the rabbit² and guinea pig³ in which the placenta are haemochorial that the transmission of antibodies occurs exclusively via the yolk sac. In the rat transmission occurs by way of the yolk-sac endoderm and by way of the gut and in this species some transmission across the haemochorial placenta could not be excluded⁴.

In the hedgehog the placenta is haemochorial and in the young of animals immunized against *Brucella abortus* specific agglutinins could not be detected in the sera before suckling. The females received immunizing injections before and during pregnancy and the maternal antibody titres during pregnancy were of the order 1/640 to 1/1280. The sera of 10 young derived from 6 litters which were removed

from their mothers before suckling occurred gave negative results at dilutions of 1/10. In this species the yolk sac persists to term and its embryonic wall remains intact⁵ whereas in the rabbit guinea pig and rat the yolk sac is of the inverted type in which the embryonic bilaminar segment is broken down and the yolk sac splanchnopleur is exposed to the uterine lumen.

The young of ruminants horse and pig are born without antibodies and in these species a rapid uptake of antibody occurs from the colostrum and milk during a 36 hr period after birth. During this period the antibody titre of the serum of the young animal increases to become approximately equivalent to that of the maternal serum. The antibody of the colostrum in these animals attains titres which equal or exceed those of the maternal serum. In the hedgehog the antibody titre of the first milk closely approximates the maternal serum titre but with suckling the titre declines so that in the nursing female six days after parturition it is about 25 per cent of the maternal serum titre. In this species there is an uptake of antibody from the milk by the gut but even after several days the titre attained in the serum of the young hedgehog is only a small fraction of that in the maternal serum. The highest serum titre so far obtained in a young animal is 1/20 with partial agglutination at 1/40 at 64 days of age. The titres of the maternal serum and milk being 1/640 and 1/160 respectively. In this representative of a primitive mammalian order transfer of anti-*Brucella* agglutinins does not occur prenatally, and the postnatal transmission is of a very low order when compared with other species in which the young obtain passive immunity after birth.

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Release of Histamine from Rat Mast Cells by Blood Treated with Dextran

HALPERN¹ has shown that the injection of dextran into albino rats causes increased capillary permeability and shock. Coincident with the appearance of shock there is a massive release of histamine into the blood stream of injected animals. The liberated histamine probably accounts for the greater part of the increased capillary permeability and shock resulting from the administration of dextran. It seemed of interest therefore, to investigate the mechanism of the release of histamine. It was found that dextran reacts with a plasma protein to produce a substance which acts on mast cells to release histamine.

Peritoneal cavity cells including mast cells, were obtained from the rat by a method previously described². To detect mast cell disruption one drop of the cell suspension was added to one drop of rat serum or serum fraction at room temperature and the preparations were examined under the microscope. Histamine assays were performed by the method of Lowry *et al.*³

Satisfactory results were obtained only when the solutions had a pH of less than 7.5. For this reason blood was collected and centrifuged into paraffin.

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A substance causing disruption of mast cells and release of histamine was present in the sera of rats 60 min after intraperitoneal injection and 30 min after intravenous injection of dextran ('Dextraven' in physiological saline, 30 mgm dextran/100 gm body-weight). Greater concentrations of this active principle appeared more rapidly in the sera of adrenalectomized rats after injections of similar amounts of dextran. Death occurred within 30 min in these animals. Intraperitoneal injections of hydrocortisone sodium succinate ('Solu Cortef', Upjohn, 200 mgm/kgm) given daily for 5 days prior to challenge with dextran prevented death of the adrenalectomized animals. The sera of these animals was comparable in its activity on mast cells with sera from dextran-injected normal rats.

The active principle was also produced *in vitro* when dextran was added to serum from normal rats, adrenalectomized rats and hydrocortisone-treated adrenalectomized rats. Its concentration was greater when the serum was obtained from adrenalectomized rats than when obtained from normal and hydrocortisone-treated adrenalectomized rats. The histamine-releasing substance was produced rapidly at room temperature when the pH of the serum-dextran mixture was between 7.0 and 7.5 but did not appear when dextrose (2 mgm/ml) was added to the dextran solution before this was placed in contact with the serum. The addition of hydrocortisone *in vitro* did not affect the concentration of the active principle. Again, its production was not inhibited by inactivation of serum complement (60°C for 5 min) or by iodoacetate, phenylmercuric acetate, sodium fluoride or soya bean trypsin inhibitor (Nutritional Biochemicals).

A β - and γ -globulin fraction of rat serum prepared by precipitation with 25 per cent ethanol at -5°C did not disrupt mast cells when dissolved at pH 7.0. Addition of dextran to the fraction produced an active histamine release substance but the presence of dextrose inhibited the interaction. Similar results were obtained when another polysaccharide (zymosan, Nutritional Biochemicals, 5 mgm/ml serum) was added to rat serum *in vitro* and to the β - and γ -globulin preparation.

In earlier work it was shown that a polypeptide from nucleated cells acts on mast cells *in vitro* and causes them to disrupt with the release of histamine^{2,4}. The substance responsible for disrupting the mast cells is probably a histone or histone breakdown product. The mechanism suggested by the present work involves the release of an active substance from rat serum or a serum fraction. The active principle is produced in the serum of rats following injections of a polysaccharide (dextran). It is also found in rat serum in the absence of cells, when dextran or another polysaccharide (zymosan) is added to the serum *in vitro*.

While it may be tempting to suggest that an antigen-antibody reaction is involved (dextran versus a normal antibody to dextran in rat serum), there is no proof that this is the mechanism.

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Transformations of Myxoma into Vaccinia or Ectromelia Virus in Tissue Culture

THE Berry-Dedrick transformation¹ is known as the first instance of what is called genetic interaction between animal viruses, but the investigation of this phenomenon has been restricted to a combination of active fibroma and heat-killed myxoma, except for some studies on recombination of the influenza group^{2,3}. In a previous paper⁴, a new example of viral transformation was demonstrated using active ectromelia and heat-inactivated vaccinia. The present investigation was undertaken to see if the same phenomena could occur between the other viruses classified in the pox group.

The IHD strain of vaccinia or the Biken strain of ectromelia was heat-inactivated and myxoma was used as live virus (Table 1).

Table 1. COMPARISON OF CHARACTERISTICS OF VIRUSES USED

| Virus | Pathogenicity | | Viral growth in tissue culture | |
|------------|----------------------------------|--------------|--------------------------------|---------|
| | Rabbit* Skin tumour lethal | Effect No | FL† + | L‡ - |
| Myxoma | | | | |
| Vaccinia | Skin lesion not lethal | No | | + |
| Ectromelia | No | Lethal | + | + |

* Intradermal injection

† Intraperitoneal injection

‡ Growth medium: 0.5 per cent lactalbumin hydrolysate in Earle's balanced salt solution with 15 per cent bovine serum.

§ Growth medium: 0.5 per cent lactalbumin hydrolysate and 0.1 per cent yeast extract in Hanks's balanced salt solution with 5 per cent bovine serum.

Myxoma virus obtained from skin tumours of domestic rabbits was passaged twice in the human amnion cell (FL strain), where the virus could be propagated forming cytoplasmic inclusion bodies. 7 days after inoculation the titre of intracellular virus reached about 10^6 ID (in rabbit)^{5,6}.

Vaccinia and ectromelia were used after serial passage in L cells. The infected monolayers were freeze-thawed in the presence of growth medium and centrifuged at 3,000 r.p.m. for 5 min. The supernatant fluids from this centrifugation, which contained on the average about 10^6 TCID₅₀/ml of virus, were heated at 56°C for two hours (vaccinia) or one hour (ectromelia). At this temperature, vaccinia can be inactivated to a survival of less than 10^{-6} within 30 min, while ectromelia can be inactivated within 15 min. No active virus was found in tissue culture or in the respective host animal inoculated with these heated preparations.

The transformations were carried out in FL cells grown in 200 ml prescription bottles. Cellular monolayers (about 5×10^6 cell/bottle) were exposed to a mixture of 1 ml of infectious myxoma (10^5 - 10^6 ID in rabbit) and 1 ml of heat-inactivated virus preparation of vaccinia or ectromelia which had been added to 8 ml of growth medium. Culture medium was changed twice weekly with fresh medium containing 1 ml of heat-inactivated virus preparations. 7 days after inoculation, infected cells were disrupted by freeze-thawing, and centrifuged 3,000 r.p.m. for 5 min. One ml of the supernatant was transferred into monolayers of L cells.

The cytopathic change similar to those of vaccinia or ectromelia was shown after 2 or 3 days. This would indicate that the transformation of myxoma into

vaccinia or ectromelia had taken place. The transformed virus was purified twice by limiting dilution passages. The purified viruses had the same pathogenicity for rabbits and mice as each original virus strain.

Preliminary work using fibroma virus showed that fibroma also could be transformed into vaccinia by the similar procedure.

With heat-killed vaccinia, poliomyelitis (Type 1, Brunhilde strain) and measles (Edmonston strain) could not lead to transformation when used as active virus. Recently it was shown in our laboratory that myxoma was closely related serologically to vaccinia and ectromelia.⁷ These results may suggest that there is a correlation between transformation and cross immunity.

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Protein Synthesis in Macrophages containing *Elmeria tenella*

RECENT studies on bacteriophage have shown that the virus may stimulate anabolic protein metabolism in the parasitized bacterial cell and furthermore defect metabolic processes towards the production of bacteriophage nucleoprotein.

This is a preliminary report of a similar phenomenon in intestinal macrophages of the chick which have become invaded by the sporozoan *Elmeria tenella*. Briefly the process of infection consists of swallowing the oocyst which breaks down in the small intestine, liberating sporozoites. These invade the cells in the

caecal wall and undergo schizogony within the cells, liberating merozoites which re-invade the gut wall.

This process was studied by standard histological methods and by histochemical methods in the caeca taken from a chick seven days after oral infection. The parasite can be seen in large macrophages which often entirely replace the lamina propria mucosae adjacent to this there is a conspicuous exudate composed mainly of red cells with a moderate number of eosinophil leucocytes. The adjacent epithelial cells of the gut show numerous mitotic figures and many contain globules of secretion.

The parasitized macrophages are considerably enlarged (Fig. 1) and filled with protein most of which appears to be ribonucleic acid as judged by the 'tetratozo' method and by pyronin staining using ribonucleosides as a control measure. In the early stages the ribonucleoprotein collects at the centre of the cell surrounded by a palisade of developing schizonts. Later the cell fills with schizonts and the ribonucleoprotein is presumably incorporated within them.

The nuclei of the macrophages are greatly enlarged displaced to the side of the cell and show two or three big nucleoli. This is an index of intense protein synthetic activity by the cell. The fate of the macrophages is, at present, uncertain since it is unusual to find evidence of damage to these cells. They may liberate the merozoites and serve as a breeding ground for even more.

The histological appearances suggest an enhanced ribonucleoprotein production within chick macrophages parasitized by *Elmeria tenella*, and further more that this new protein is incorporated into the newly formed merozoites.

Further confirmation of this view will be attempted by the use of fluorescent conjugates of chick and *Elmeria* protein and the results will be reported in due course.

We are grateful to Dr J. Beattie and Dr L. Horton Smith for the opportunity to study this material.

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HISTOLOGY

Histochemical Use of the Cyanocarbon Organic Compounds

MEMBERS of the new group of organic compounds called 'cyanocarbons'¹ appear worthy of investigation as histochemical localization reagents on the basis of preliminary studies made with one of the series, tetracyanoethylene. These compounds are chemically quite active and will take part in a large number of organic reactions.¹⁻⁴ For example tetracyanoethylene may in proper circumstances, react through additions to its double bonding with such radicals as dienes ketones and hydrogen, and through replacement of cyano groups it will react with the alkoxy hydroxy and aminoaryl radicals. The products of many such reactions are coloured. Tetracyanoethylene produces an intense yellow colour with benzene orange with toluene, and red with xylene. Reactions with certain amines will produce 4 tetracyanovinylamines, a class of brilliant orange to blue dyes.

Experiments utilizing animal and human necropsy tissues 10 per cent buffered formalin and Bouin's



Fig. 1. T.S. of chick caecal wall seven days after oral *E. tenella*. Parasites in macrophages (upper part of picture). Haemorrhagic exudate in submucosa (lower part of picture) (H. and E., $\times 410$).

fluid fixed and paraffin processed, suggest that tetracyanoethylene may well be an interesting protein localization reagent. In general, fairly good colorations are found at tissue sites usually associated with such complexes. This does not, however, preclude its use in the localization of other tissue components. The solvent problem is a serious one with tetracyanoethylene since it will react with most organic solvents. Best results have been obtained with 0.5–2 per cent solutions in tetrahydrofuran, ethyl acetate dimethylsulphoxide, or dimethylformamide⁵. Only the finest grades of these solvents should be used since impurities will introduce complicating side-reactions. Staining times vary and depend upon the strength of the staining solution but sections treated 2 hr in a 0.5 per cent solution at room temperature show adequate coloration regardless of solvent used. Care must be taken during staining to avoid contamination of the solutions because of the active chemical nature of tetracyanoethylene. The dehydration process after staining should be done without unnecessary delay. The localizations are usually yellow, suggesting the benzene ring, and at times are transient. Especially strong colorations are frequently obtained at the sites of iron pigments. It is important to remember that certain of the solvents may be quite toxic, and special care to avoid their fumes is necessary during the staining procedure. The use of a hood is recommended. Detailed experiments on the histochemical value of this series of compounds are now in progress. Unfortunately, cyanocarbon chemicals are still in the experimental stage and are not readily available commercially. However, in the near future they probably will be placed on the market and may be easily obtained by interested persons.

I would like to express my appreciation to Dupont de Nemours and Co for providing the tetracyanoethylene used in these experiments, to Dr B. C. McKusick and Dr T. C. Cairns for their helpful comments on the nature of tetracyanoethylene, and to note that this investigation was supported by research grant H-1907 (C 3, 4), National Heart Institute, National Institutes of Health, United States Public Health Service.

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Mast Cell Population of Lung of the Guinea Pig and other Tissues

In 1941 Jacques and Waters mentioned the degranulation of mast cells in the liver of a dog undergoing anaphylactic shock¹. In 1952 Stuart stated that the shock organs of anaphylaxis in the dog, rabbit, and guinea pig all contain mast cells which degranulate when a sensitized animal is injected with antigen². Unfortunately, no details were given of the histological techniques he used.

More recently, Mota and Vugman have reported some experiments from which it was concluded that anaphylaxis in the lung of the guinea pig caused a marked reduction in the number of mast cells histologically demonstrable in that organ³.

In this laboratory an attempt to demonstrate mast cell degranulation in guinea pig lung following antigen administration to a sensitized animal led to a series of surprising observations. All the tissues used in these investigations were fixed for 24 hr in absolute ethyl alcohol. Pieces of lung, liver and skin were embedded in paraffin and examined as sections 10 μ thick. Spreads of connective tissue or pleura were examined directly. In all, four different stains were used to demonstrate mast cells in the tissues. These were (1) thionin as a saturated solution in 50 per cent alcohol, (2) toluidine blue as a 0.5 per cent solution in 50 per cent alcohol, (3) polychrome methylene blue as an aqueous solution, (4) acetylated sudan black as a saturated solution in 70 per cent alcohol. The first three stain metachromatically the heparin in the mast cell granules and the last-named stains the phospholipid in the mast cell granules.

Using these stains, mast cells were readily discernible in most of the tissues examined. Abundant mast cells were found in the mesentery of the hamster, and a slightly smaller number in the cheek pouch of that animal. Spreads of mouse mesentery were found to contain a slightly smaller number of mast cells than hamster cheek pouch, and so also were sections of the abdominal skin of the rat. A similar number of mast cells were observed in omentum, mesentery and pleura of the guinea pig. In the parenchyma of the lung around the major blood vessels and air passages no mast cells were visible in sections taken from either normal or sensitized unshocked guinea pigs. They were also absent in sections of guinea pig skin. It was thus not possible to demonstrate mast cell degranulation in lung tissue of sensitized guinea pigs after intravenous challenge with antigen. Whereas mast cells in the omentum or mesentery of the guinea pig showed no change after anaphylactic shock a large number of the mast cells seen in guinea pig pleura were disrupted or degranulated after antigen challenge. Mast cells were observed in normal dog liver. They were slightly less numerous and not quite so well differentiated as in other tissues. Only about half the normal number were visible in sections taken from dog liver 1 hr after intravenous challenge under pentobarbitone anaesthesia with a shock dose of antigen causing an immediate fall in blood pressure from 130 to 10 mm mercury. No mast cells could be demonstrated in rabbit lung adjacent to the point of entry of the pulmonary artery.

These observations invite one or two obvious conclusions. Mast cells in the liver of the dog undergo degranulation and disruption during anaphylactic shock thus confirming the observation of Jacques and Waters. The same is not true of the lung of the guinea pig or rabbit, since, contrary to Stuart's suggestions, in these experiments mast cells appeared to be absent from the respective shock organs. It thus seems not unlikely that the histamine which causes rapid onset of fatal bronchoconstriction in the guinea pig during anaphylaxis is derived from some structure other than the connective tissue mast cell. Anaphylactic histamine in the rabbit is also most probably not of mast cell origin.

It is possibly relevant that Mota and Vugman who reported high mast cell counts in the lung of the guinea pig, used as a fixative a 4 per cent solution of lead subacetate in 50 per cent ethanol containing 0.5 per cent acetic acid. They then prepared frozen sections of the lung 50 μ thick which were stained with toluidine blue. Gomori condemns the use of lead in frozen sections and states that whereas lead adsorbed in paraffin sections can be readily washed out by dilute acetic acid, frozen sections may hold lead so stubbornly that even prolonged washing in strong acetic acid cannot remove it completely.⁴ It is surprising therefore, to be confronted with evidence implying that mast cells in the lung of the guinea pig can only be detected after prior treatment of the tissue with lead even though they can be readily observed elsewhere without such prior treatment, but worth noting, however, that Bloom has reported that metrial gland cells of the rat uterus show definite metachromasia after fixation in lead acetate, a very faint metachromasia after fixing in methanol and no metachromasia at all after fixation in other fixatives (Bloom personal communication). Alternatively, Mota and Vugman succeeded in staining with toluidine blue lead which had been adsorbed on to some morphological structure which was not a connective tissue mast cell.

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RADIOBIOLOGY

Effect of the Level of Microbial Population on Isotopically Exchangeable Phosphate in Soil

If a soil is shaken with a phosphate solution labelled with phosphorus-32 the specific activity (phosphorus-32/phosphorus-31) is reduced in consequence of isotopic exchange with the exchangeable phosphate in the soil. At equilibrium the following relationship holds: phosphorus-32/phosphorus-31 in the solution = phosphorus-32/phosphorus-31 in the exchangeable form in the soil. The specific activity in solution can be determined by assay while the phosphorus-32 in the soil can be calculated by the difference between the initial and final phosphorus-32 contents of the solution. The amount of phosphate in the soil which has exchanged isotopically under the conditions of the experiment can readily be calculated.¹ It is also possible to calculate the quantity of phosphate which is removed or sorbed² by the soil from the change in concentration of inactive phosphate in the solution. The amount of phosphate which plants will absorb does not always bear a simple relationship to these quantities, but knowledge of exchangeable or sorbed phosphate in the soil can be of value in the study of factors which control the availability of phosphate to plants.

It has been assumed by previous investigators that the value of isotopically exchangeable phosphate would be unaffected by the level of microbial population in the system during the period of equilibration. Until recently the evaluation of the effects of micro-organisms has been difficult to make since conventional methods for destroying micro-organisms in soil for

example by means of steam or chemicals may well modify surfaces on which the exchange of phosphate occurs. The γ rays from cobalt-60 now, however, provide a convenient physical method for reducing the level of microbial population without causing an appreciable rise in temperature of the soil during the period of irradiation. Accordingly the determination of isotopically exchangeable phosphate by the method of Russell *et al.*³ has been investigated both in the normal air-dry soil and in soil previously irradiated with γ rays from cobalt-60.

Samples of the selected soil a Middle Lias loam from Banbury, Oxfordshire (pH 7.6), were sealed into glass ampoules which were themselves sealed into separate polythene envelopes. After irradiation with 10^4 reps of γ rays from cobalt-60 the ampoules were removed from the polythene envelopes under aseptic conditions and put into tubes containing labelled phosphate solutions which had been sterilized in an autoclave at 15 atmospheres for 20 min. Sterile rubber bungs with glass rods projecting from their lower surfaces were inserted into the tubes and the ampoules were broken by shaking them sharply against the rods. The irradiated soil was thus introduced into a sterile solution with the minimum risk of microbial contamination. Control samples which had not been irradiated were transferred in the same way.

Microbiological assay and measurements of exchangeable and sorbed phosphate were made after different intervals of time in two experiments (Table 1). Using a dilution plate method the microbial population was shown to consist almost entirely of bacteria; very few fungi were detected (<1 colony per plate at the highest concentration). For the purposes of the present investigation therefore the bacterial plate count has been taken as an index of microbial activity and while the shortcomings of this method were appreciated it was considered an adequate indication of the relative abundance of viable micro-organisms. Complete sterility was not achieved by irradiation but a reduction of the bacterial population by a factor greater than 1,000 was achieved in tubes examined after one day. The population thereafter increased due apparently to the multiplication of bacteria which survived irradiation but in all cases the bacterial population was very small by comparison with that in the tubes which had not been irradiated. Irradiation had no statistically significant effect on the values for exchangeable or sorbed phosphate although there was a tendency for the latter value to be decreased.

These experiments give clear evidence that bacteria and probably other micro-organisms present during

Table 1. EFFECT OF IRRADIATION WITH γ -RAYS ON EXCHANGEABLE AND SORBED PHOSPHATE AND BACTERIAL POPULATION AFTER DIFFERENT PERIODS OF SHAKING

| (Values for exchangeable and sorbed phosphate in mgm./15 gm. soil) | | | | | S.D. ($P=0.05$) |
|---|--|----------------------------------|--------------------|--------------------|----------------------|
| | | Duration of shaking (days) | Irradiated | Control | |
| Exp. 1 | Exchangeable phosphate | 1 | 0.63 | 0.63 | 0.17 |
| | | 7 | 1.10 | 1.20 | |
| | Sorbed phosphate | 1 | 1.85 | 1.80 | 0.07 |
| | | 7 | 2.16 | 2.29 | |
| | Bacterial population (per gm. soil) | 1 | 5.4×10^4 | 1.2×10^5 | |
| | | 7 | 4.0×10^4 | 1.1×10^5 | |
| Exp. 2 | Exchangeable phosphate | 7 | 1.07 | 0.94 | 0.12 |
| | | 14 | 1.40 | 1.36 | |
| | Sorbed phosphate | 7 | 2.91 | 2.36 | 0.07 |
| | | 14 | 2.57 | 2.44 | |
| | Bacterial population (per gm. soil) | 7 | $<1 \times 10^4$ | $<1 \times 10^4$ | |
| | | 14 | $<0.1 \times 10^4$ | $<0.1 \times 10^4$ | |

the period of equilibration cannot account for any large fraction of isotopically exchangeable phosphate in this soil as determined by this method

We are indebted to Dr R Scott Russell for much useful discussion and to Mr W Hutchinson of the Technological Irradiation Group of the Isotope Division, Atomic Energy Research Establishment, for carrying out the irradiation of the samples

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Pharmacological Suppression of Increased Capillary Permeability following Irradiation of the Intestine of Rats

THE syndrome of acute intestinal lesions due to ionizing radiation leading to an early death of the animals has been described by many workers¹⁻⁵. The present work is concerned with the increase of the capillary permeability in the intestinal tract of rats after irradiation and the suppression of this phenomenon by the action of drugs affecting the esterase systems

The increased capillary permeability following turpentine-induced pleurisy^{6,7} and thermal burns in rats^{8,9} can be inhibited by pretreating the animals with antihistamines and anti-esterase drugs

The increased permeability due to irradiation was investigated in male rats weighing 200-250 gm, which were exposed, under nembutal anaesthesia to a dose of 1,500r or 200 kV X-rays given in 11 min over a circular abdominal field of 1.5 in diameter. At intervals of 1-4 days after exposure a solution of trypan blue was injected into the tail vein and the animal killed 30 min later⁶. In the irradiated animals the dye left the capillaries and stained the intestine blue. This phenomenon began after 24 hr and reached its maximum after 3 days. The staining in different regions varied in intensity and in order to evaluate it the affected length was expressed as a percentage of the total length of the intestine

Animals irradiated with no pretreatment showed a progressive increase in the intensity and length of the intestine that was stained, at 24 hr 37.7 per cent, 48 hr 73.4 per cent and 72 hr 92.0 per cent of the gut was affected

Pretreatment of the animals immediately before irradiation with a single intramuscular injection of di-isopropylfluorophosphate, 3 mgm/kgm body weight in arachis oil, suppressed the staining of the intestine completely after 24 hr and at 48 hr reduced the length stained to only 20 per cent of the whole. Similar results were obtained with (a) quinine dihydrochloride (125 mgm/kgm injected immediately before irradiation, a further dose of 40 mgm/kgm given at 24 hr and 5 mgm/ml added to the drinking water), (b) quinidine sulphate (250 mgm/kgm in propylene glycol given before irradiation plus 150 mgm/kgm at 24 hr after irradiation), (c) chloroquine sulphate 'Nivaquine', (40 mgm/kgm, before radiation plus 25 mgm/kgm at 24 hours)

Pretreatment with mepyramine maleate, 'Anthisan' (1 mgm/kgm and subsequently administered in the drinking water 1 mgm/ml), reduced the length of the intestine stained to 10 per cent of the total length of 24 hr, but had no observable effect after 48 hr. despite repeated administration of this drug. Pretreatment with 2-bromo-*d*-lysergic acid (BOL 148) had a slight effect on the length of the intestine stained at 24 hr. following radiation but no effect at 48 hr

The results, which will be published in detail elsewhere, are strikingly similar to those obtained with similar pretreatments to thermal burns. Since the effective drugs inhibit pseudo cholinesterase, their action may be due to suppression of an esterase system

I wish to thank Dr. H B Foll and Dr A Glucksmann for their advice and encouragement, and Messrs Sandoz for the gift of BOL 148

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Decrease in Radiosensitivity of the Intact Mouse Spleen produced by Hypoxia

THE radio-protective effects of low oxygen tensions in tissues during exposure to X-rays has been described by Gray and his associates¹. Wright and Howard-Flanders² have demonstrated the protective action of severe hypoxia on the irradiated mouse-tail, and Wright³ has observed increased resistance of the intact mouse thymus, irradiated while the animal was breathing nitrogen

An attempt has been made to determine the effects of severe hypoxia on the intact spleen of irradiated mice. 60-70-day old T O strain male mice, weighing 22-24 gm were anaesthetized with an intraperitoneal injection of 7.5 mgm 'Avertin' (tribromoethanol) in a volume of 0.3 ml. In one group of animals at laparotomy a soft catgut noose threaded through a polyethylene sleeve was placed around the splenic pedicle, drawn tight and held with a bulldog clip. The spleen was then returned to the peritoneal cavity which was closed with sutures. After 10 minutes at room temperature, by which time the spleen was almost black, the animals were exposed to 800 r whole-body irradiation. The ligatures were then removed and the wound sutured. Another group of animals had their splenic pedicles ligated after irradiation. A third group of mice was irradiated after laparotomy alone, and a fourth untreated group acted as control

All mice were killed by cervical dislocation 5 days after treatment. Their spleens were removed and fixed overnight in Bouin's fluid, weighed after blotting dry and later examined histologically. The assessment by weight of irradiation damage to the spleen has been described by Carter, Harris and Brennan⁴. The splenic weights are shown in Table 1, together with their standard deviations and the numbers of animals used in brackets

Table 1 MEAN WEIGHTS OF FIXED SPLEENS (MGM) WITH THEIR STANDARD DEVIATIONS, FIVE DAYS AFTER IRRADIATION

| Untreated controls | Irradiation only | Spleen ligated then irradiated | Irradiation then ligation |
|--------------------|------------------|--------------------------------|---------------------------|
| 63 ± 8 (12) | 24 ± 8 (9) | 70 ± 14 (8) | 22 ± 7 (7) |

As vascular disturbances followed ligation of the splenic pedicle, direct comparison of splenic weights was only considered profitable between the two ligated groups. A *t* test shows that the spleens of animals ligated and then irradiated weigh significantly more than those irradiated and then ligated ($t=7.2$ with 13 degrees of freedom, $P<0.001$).

Histological examination of the spleens confirms that the heavier group of spleens are less damaged than the lighter group. In the animals which had the ligature applied after irradiation, no primary lymphatic nodules are present. Groups of small and a few medium size lymphocytes are observed in narrow perivascular cuffs. No lymphoblasts and very few megakaryocytes can be seen. This group closely resembles the group irradiated after the sham operation.

In the spleens of mice irradiated while the ligatures were in place, the normal follicular architecture has disappeared. However, groups of lymphoblasts large and small lymphocytes, megakaryocytes, myeloblasts and polymorphonuclear leucocytes are seen and mitotic figures are present. Vascular engorgement is an outstanding feature of this group in comparison with the previous one, and must account for some of the difference in weight between them.

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PALAEONTOLOGY

Conchiolin Remnants in Mother-of-Pearl from Fossil Cephalopoda

DECALCIFICATION of mother-of-pearl from recent molluscs leaves soft stratified membranes of conchiolin. These membranes cleaved and broken by ultrasonic vibrations, appear in the electron microscope as fragments of lace like reticulated sheets or perforated leaflets¹. The pattern of these structures differs with the groups and species of molluscs. Three main patterns (nautiloid gastropod and pelecypod) have been provisionally recognized¹. Replicas of surfaces of mother-of-pearl prepared before and after corrosion by decalcifiers have shown that the reticulated sheets correspond to the conchiolin membranes which alternate with the mineral lamellae in the stratified nacreous configuration and which separate the individual crystals of aragonite disposed side by side in each lamella².

The three patterns of structure of conchiolin have been also detected in mother-of-pearl from Palaeocene to Jurassic molluscs³.

The latter investigations have been extended to 40 specimens from 18 genera of Liocene Cretaceous, Jurassic, Pennsylvanian and Ordovician Cephalopoda (Ammonoidea and Nautiloidea). In preliminary observations, reticulated sheets exhibiting the nautiloid pattern altered in different ways, were found in mother-of-pearl from 3 specimens of *Eutrophoceras*

(including *E. dekeyi*), *Platoniceras* (Cretaceous), *Leioceras opalinum* Reinecke (Jurassic), *Eoceras anales* (?) sp. *Pseudorthoceras knoxense* an undetermined nautiloid (Pennsylvanian), *Dolorthoceras sociale* (Ordovician).

Fig. 1 shows in decalcified mother-of-pearl from *Nautilus macromphalus* Sowerby (Recent) a reticulated sheet consisting of sturdy trabeculae separating elongated or rounded openings of irregular outlines. Fig. 2 represents a reticulated sheet from an unidentified Pennsylvanian nautiloid collected in the asphaltic formations near Sulphur (Oklahoma) a locality in which the original mineralogical structure of aragonite has been preserved unaltered⁴. Comparison between Fig. 2 and Fig. 1, gives evidence of a great similarity of structure between Recent and Pennsylvanian nacreous conchiolin membranes. In some areas of the fossil material the fabrics appear shrunk or flattened. However these modifications were also observed in the sheets of the recent *Nautilus*

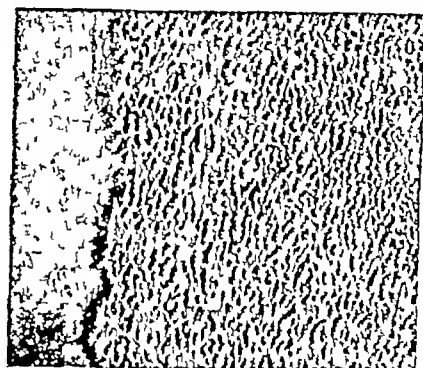


Fig. 1. *Nautilus macromphalus* Sowerby (Recent). Decalcified mother-of-pearl. Fragment of a reticulated sheet of conchiolin, collapsed by desiccation on to a Formvar support and shadow cast with palladium. ($\times 12,000$).



Fig. 2. Unidentified nautiloid (Pennsylvanian). Decalcified mother-of-pearl. Fragment of an interlamellar reticulated sheet lying on a perforated membrane of Formvar and shadow cast with palladium. The areas corresponding to the crystals of aragonite of a lamella, originally superimposed on the organic sheet and by the decalcifier as white ridges, erected the sh. ($\times 12,000$).

The results so far obtained indicate a great stability of the conchiolin patterns throughout considerable periods of time, in favourable burial conditions, as in Sulphur (more than 200 millions of years in the Pennsylvanian specimens). The results suggest also that recordings of the micro-architecture of conchiolin remains might give useful information about the identity of fossil shells, in which the fragments of the test available are too small or too dissociated to be studied by the classical methods of palaeontology.

I am grateful to Prof Tove Birkelund, Dr G Arthur Cooper, Prof William M Furnish, Dr P L Maubeuge, Prof Norman D Newell, Prof A Rosenkrantz and to Prof Dr O H Schindewolf for gifts of generous collections of finely preserved mother-of-pearl of Cephalopoda.

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BIOLOGY

Discarded Blood Bank Blood as a Source of Protein for Cultivation of HeLa Cells

Most mammalian cell cultures require serum protein for continued survival and growth. Serum protein is probably the most expensive component of tissue and cell culture media, especially if human cells are cultivated in homologous serum. We have studied the possibility of employing outdated blood bank blood as a possible source of the protein necessary for the growth of HeLa cells. Such discarded blood is available in fairly large quantities and if it could be successfully employed for cell cultures an expensive bleeding programme could be dispensed with.

In order to ascertain whether the fluid portion of such blood would support the growth of HeLa cells it was necessary to free the plasma of the citrate ion used as an anticoagulant. Plasma was removed from the blood and placed in large 'Cellophane' dialysing tubes, 80 mm flat diameter. Plasma was dialysed against 6 to 7 volumes of demineralized water. The dialysing water was changed 6 times at 6-12 hour intervals. Finally, the plasma was dialysed against Hanks's balanced salt solution overnight which replenished the calcium and magnesium ions and permitted the plasma to clot. Serum protein was removed and sterilized by filtration through 'Selas' unglazed porcelain candles, 02 porosity. Such dialysed preparations obtained from blood bank blood were tested for their ability to support growth of HeLa cells and were compared with medium containing serum from fresh undialysed blood and also with Eagle's medium¹. Since dialysable components of serum are necessary for the growth of HeLa cells, the dialysed serum was supplemented with yeast extract which has been shown to have a serum-sparing effect². Yeast extract contains many amino-acids and vitamins, is economical, and can be autoclaved and retain its serum sparing effect.

For the tests, aliquots containing 80,000 trypsinized HeLa cells each were dispensed into 100 screw-capped test-tubes, 16 × 125 mm. The medium employed for

dispensation was 30 per cent processed blood bank serum protein supplemented with 0.2 per cent yeast extract in Hanks's balanced salt solution. On the following day, medium was decanted and cells washed 3 times with balanced salt solution and the indicated media added. Tubes were placed in the roller drum and replicate tubes removed and counted at the times indicated. Each count represents the average of three tubes. Media was replaced every 48-72 hours. The results, represented in Table 1, indicate that such processed serum protein, when supplemented with yeast extract, compares favourably with whole serum in the ability to support the growth of HeLa cells. It is also interesting to note that the dialysed components of serum can be replaced by yeast extract. The failure of Eagle's medium to support growth of HeLa cells when supplemented with such serum proteins is unexplained but may be due to the extensive dialysis. The Eagle's formula which we employed did not contain inositol³ which has been shown to be necessary when extensively dialysed serum is used.

TABLE 1

| Medium Composition | Cell Count* | | |
|---------------------------------|-------------|---------|---------|
| | 48 hr | 120 hr | 216 hr |
| Dialysed Serum 30% (a, b) | 81,000 | 138,000 | 221,000 |
| Dialysed Serum 10% (a, b) | 75,000 | 152,000 | 169,000 |
| Whole serum 30% (b) | 80,000 | 160,000 | 247,000 |
| Whole serum 10% (b) | 57,000 | 172,000 | 200,000 |
| Eagle's medium 90% ³ | | | |
| Dialysed serum 10% (a) | 20,000 | 10,000 | 13,000 |

* Average per three tubes.

(a) Processed from outdated human blood bank plasma.

(b) With yeast extract, 0.2 per cent. Hanks's balanced salt solution.

Such dialysed serum preparations have been used exclusively in this laboratory for over a year for the cultivation of HeLa cells with a considerable savings of expense. Large pools of plasma are processed and the resultant serum proteins frozen until used.

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Age Determination in Wild Rabbits

POPULATION studies of the wild rabbit (*Oryctolagus cuniculus*) in New Zealand and elsewhere have emphasized the need for reliable methods of age determination. Since weight is a satisfactory criterion of the age of young rabbits up to 3-4 months, when they become sexually mature¹, the sequence of epiphyseal fusion of bones was examined in an attempt to determine the age of older animals. This work was initiated by Watson and Tyndale-Biscoe², who found that the epiphysis at the head of the tibia fused at 41 weeks (range 33-44 weeks). Further work by Tyndale-Biscoe³ (and unpublished work) showed that the epiphyses of all other long bones unite at about the same age or earlier than do those at the head of the tibia, but that the epiphyses of the verte-

bra do not fuse to the centrum until later in life and could therefore provide an age criterion for older animals

An attempt has now been made to determine the timing of epiphyseal fusion of the vertebrae and the extent of individual variation. The ideal method would be to recapture from a wild population rabbits of known age that had been marked and released when very young, but this was impracticable. No wild population free from control by man was available, and moreover, it would have been necessary to mark very large numbers of young, since only about 2 per cent are likely to survive until 2 years old⁴. For these reasons it was decided to base the work on skeletal material from captive animals of known age. It had been found that growth in captivity did not effect the age of fusion of the tibial epiphyses² like wise, in the present study the bone fusion of two wild rabbits marked and released as young and recaptured when 16 and 33 months old respectively, was similar to that of captive rabbits of comparable age.

Young wild rabbits were obtained and their age assessed in one of the following ways (a) captured when the tibial epiphyses were still unfused and their age (± 6 weeks) determined by recording the time of fusion using X rays²⁻⁴, (b) dug out of burrows soon after weaning and aged (± 1 week) by weight⁴ or (c) bred in captivity from wild parents, and exact age known.

In young rabbits the disk shaped epiphyses are separated by cartilage from the anterior and posterior faces of the centrum. Fusion is a gradual process and all stages exist between epiphyses that are entirely separated by cartilage and those that are indistinguishable from the rest of the centrum. For the present purpose an epiphysis has been considered as fused only when the line of fusion could no longer be detected. The anterior lumbar epiphyses are the first to fuse followed by the posterior lumbar, anterior thoracic and posterior thoracic generally in that order. Within each of these groups the epiphysis of the most posterior vertebra fuses first and the others in order anteriorly.

Altogether 47 skeletons of rabbits of known age have been examined, and these are grouped in Table 1.

Table 1 STAGE OF FUSION OF LUMBAR VERTEBRAL EPIPHYSES OF 47 WILD RABBITS GROUPED ACCORDING TO AGE

| Age (months) | No. examined | No. of rabbits with epiphyses fused | | | | | | | | | | | | | | |
|--------------|--------------|-------------------------------------|----|----|----|---|---|---|---------------------|---|---|---|---|---|---|--|
| | | Anterior epiphyses | | | | | | | Posterior epiphyses | | | | | | | |
| | | - | 0 | 6 | 4 | 3 | 2 | 1 | 7 | 6 | 6 | 4 | 3 | 2 | 1 | |
| 0-14 | 10 | | | | | | | | | | | | | | | |
| 15-20 | 13 | | 13 | 0 | 6 | 2 | | | | | | | | | | |
| 21-26 | 11 | | 11 | 11 | 10 | 9 | 5 | 4 | 3 | 2 | | | | | | |
| 27-32 | 6 | | 0 | 6 | 6 | 0 | 0 | 0 | 0 | 0 | 1 | | | | | |
| 33-38 | 7 | | 7 | | | | | | 7 | 0 | 2 | 2 | 1 | 1 | | |

according to age; the number of rabbits with each lumbar epiphysis fused being shown. The earliest fusion occurred at fifteen months, and although there was considerable variation with age, fusion of the anterior epiphyses progressed anteriorly until all were fused at the age of 26 months. The posterior epiphysis of the 7th lumbar vertebra was first recorded fused at 26 months, and that of the 6th lumbar vertebra at 32 months, and was fused in all rabbits over 34 months old. For practical purposes any rabbit with both epiphyses of the 6th and 7th lumbar vertebra can be considered as over 33 months of age. In two races of laboratory rabbits complete fusion of all epiphyses is said to occur between 26 and 27 months⁶, though this does not appear to take place in

the wild rabbit till much later in life.

The present results make it possible to divide a sample of wild rabbits into four age groups based on the degree of epiphyseal fusion of the tibia and lumbar vertebrae.

(1) Less than 10 months proximal tibial epiphyses unfused.

(2) 10-25 months tibia fused all posterior epiphyses of lumbar vertebra unfused.

(3) 26-33 months posterior epiphyses of the 7th lumbar vertebra fused posterior epiphyses of the 6th lumbar vertebra unfused.

(4) More than 33 months posterior epiphyses of the 6th lumbar vertebra fused.

Further work is in progress to obtain more precise information on the extent of individual variation and the ages at which fusion of other vertebral epiphyses occur.

Age determination based on epiphyseal fusion has already been found useful in studies of the reproduction⁷ and parasite burden⁸ of wild rabbits and also in assessing natural mortality⁴ and effects of control measures¹⁰. The main limitation of skeletal criteria lies in their restricted value for field examination of live animals. However a completely unfused tibial epiphysis can be felt with the thumb nail in a living rabbit², but unfused vertebral epiphyses cannot be detected in this way nor are they easily seen in X ray photographs. On the other hand a method of age determination based on skeletal features has the advantage that it can still be used long after the death of the animal concerned.

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Asexual Reproduction in the Enchytraeidae (Olig.)

ASEXUAL reproduction has only recently been recorded in the *Enchytraeidae*¹. This inability of *Enchytraeidae* to reproduce asexually is in sharp contrast with the situation within the families of Anisidae and Aelosomatidae. We have however found asexual reproduction to occur in three species of *Enchytraeidae* among the 78 Danish species listerically examined. In one species asexual reproduction by fragmentation and regeneration is the only mode of reproduction whereas the two other species are able to reproduce sexually as well as asexually.

Gognettia sphagnetorum (Ejd.) augm./Nielsen and Christensen² comprises two cytotypes $n=54$ and $n=160$. Asexual reproduction was suspected to occur in this species because sexually mature worms are very rare at any season of the year in spite of the high population densities encountered³ (about 120 000 per sq. m), similar densities were found in moorland in Britain (personal communication by Dr. J. Peaches). In the few sexually mature specimens which have

been available for examination it was found that the eggs laid by the 54-chromosome type develop up to a certain stage but that the embryos never hatch, the chromosomes of blastomere mitoses are highly condensed and their number is very variable. In the 160-chromosome type either one or two polar bodies are extruded. In the former case a few cell divisions, with more than 300 chromosomes in the metaphase plates, take place, in the latter case division does not occur, and the pronucleus remains in interphase. In all cases the eggs die within a day or two. In this species sexual reproduction is, therefore, entirely absent and fragmentation is the only means of multiplication. The fragmentation is not preceded by the formation of a special budding zone and the fracture is always located near the middle of a segment. The wound is closed by contraction of the body wall, a blastema grows forward and forms a new body wall, the alimentary canal which becomes attached to the blastema forms a solid strand of cells, at an early stage its dorsal region differentiates into the pharynx, at the same time the brain and blood vessel is formed, when the regenerate has reached a length of about two normal segments, it is sub-divided into 8 segments (sometimes only 7) by transverse grooves visible on the outer surface. Internal septa are formed between segments iv and v and backwards to viii/ix, shortly afterwards septal glands become visible as paired cellular aggregations on all newly formed septa, meanwhile the formation of setae commences from segment ii and proceeds backwards to viii, the oral opening, buccal cavity and oesophageal lumen are differentiated from the solid cord which represents the prospective alimentary canal, the differentiation is now complete, and the worm begins to feed.

Among a total of 44 immature worms kept in cultures only 5 did not fragment within a month, the remaining 39 yielded 124 smaller fragments, all in the process of regeneration. Direct observations in the breeding chambers⁴ showed that the worms divided simultaneously into several fragments: one fragment consisting of the original anterior end which only has to regenerate a new posterior end, a varying number of intermediary fragments which regenerate segments at either end and, finally, the original posterior end. Only the foremost fragment is able to move about immediately after the fragmentation, the others remain immobile for a while and are incapable of moving until the regeneration is nearly complete, thus forming a chain of fragments. Even an intermediary fragment consisting of only two intact segments and half a segment at either end is able to regenerate completely.

In *Cognettia glandulosa* (Mich.) the number of mature worms is high for a short period during the autumn. The chromosome number is $n \sim 54$ and $2n \sim 108$, the eggs develop parthenogenotically and the diploid number is restored by fusion of second polar body and pronucleus. In addition *glandulosa* is able to fragment and to regenerate a new anterior end, as in the former species by the addition of 8 new segments. In breeding experiments running for one month 28 mature worms resulted in 25 worms of normal size, 10 fragments (derived from only 3 worms), 120 cocoons (which were used for cytological purposes) and 30 newly hatched worms.

Buchholzia appendiculata (Buchholz) ($n=19$ and $2n=38$) also possesses the ability to fragment and regenerate. Preliminary experiments have shown that the eggs hatch normally, hence, like *O. glandulosa*, this species is able to reproduce both asexually and via eggs but it remains unknown whether it reproduces

parthenogenotically.

The three species reproducing asexually represent two different genera but they are unique in having the genital organs displaced towards the anterior end by three or, occasionally, four segments. The ovaries are attached to the posterior side of the septum between segments viii and ix, and the testes to septum vii/viii. The gonads, therefore, always arise from new tissue formed during the regeneration.

The cytology of parthenogenesis and histology of regeneration will be dealt with in greater detail elsewhere.

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Variations in Early Cleavage of the Zebra Fish

LIVING eggs of the zebra fish, *Brachydanio rerio* (Hamilton, formerly Buchanan), have been studied to detect variations in the rates of cleavage between eggs in the same batch and between different batches. In this tropical fresh-water fish a symmetric pattern of cleavage favours the prompt recognition of impending cytoplasmic furrows up to the 32-cell stage¹, beyond which the stratification of blastomeres and their diminution in size make sufficiently precise observations impossible. Cell division is synchronous in all blastomeres from the 2- to the 32 cell stage.

The stock fish were maintained in aquarium tanks, each sex separately. For any one experiment, eggs were obtained from the mating of one male and one female brought together in a special breeding tank. Egg-laying usually occurs within the 2 hr after sunrise, and by persistent observation during this time the eggs could be seen dropping through the water or, more usually, at the moment of their arrival on the blackened floor of the tank. Six eggs were transferred to a 'Porspox' observation chamber mounted on a stereoscopic microscope stage. Each egg was placed in a separate concavity in the floor of the chamber, and afterwards could be identified by a letter engraved in the adjacent 'Porspox'. All six eggs could be seen simultaneously in the field of view at magnifications of $\times 8$ or $\times 16$. The transfers must be completed before the first cleavage plane has formed, a period of about 30 min from laying.

The temperature of the breeding tank was controlled at $27.25 \pm 0.5^\circ\text{C}$ by a mercury-toluene thermoregulator. The observation chamber received its heat from an outer jacket, through which circulated water from an external thermostat controlled by a mercury contact thermometer. The temperature of the water in the chamber was measured to 0.1°C at frequent intervals throughout each experiment, either by using a copper-constantan thermocouple, or later a thermistor. In both cases a suitable circuit was arranged to show the thermal fluctuations as deflections of a galvanometer needle. The water in the chamber was kept within the limits of $27.25 \pm 0.5^\circ\text{C}$ except during the restoration of water lost by evaporation, when the limits were temporarily exceeded. Rapid cytolysis of whole batches of eggs

during preliminary experiments showed the need for active aeration of the ambient water. This was provided as a stream of air bubbles which by its agitation also facilitated thermostats.

The galvanometer readings and a coded commentary on the progress of cleavage in each egg were recorded on magnetic tape. An audible time base, in the form of a 'click' at 30-sec intervals, was superimposed on the commentary and the base provided with a calibration point, by recording the General Post Office 'speaking clock' once during every uninterrupted run of tape. Using this method, developmental events could be timed to the nearest minute. Since the moment of fertilization was not known, the times of formation of cleavage furrows were measured from the appearance of the first.

The individual developments of 30 eggs have been studied in 5 batches of 6. 8 eggs did not cleave, 21 progressed to the 32-cell stage and beyond, 1 cleaved abnormally with asymmetry. An analysis of variance was performed on the duration times of the 2, 4, 8 and 16-cell stages within each batch. In no batch was there any significant difference ($P > 0.05$) between eggs, so the data within batches were pooled and the mean duration times of each stage for each batch is shown in Table 1. There were, however, significant differences between stages in batch 3 ($P < 0.001$) and batch 4 ($P < 0.01$). The existence of interstage variation made it necessary to compare batches stage by stage. For example when this was done for batches 1 and 2, by using a t test, a significant difference was found but only between the 16-cell stages ($P < 0.01$).

TABLE 1

| Batch | Number of eggs | Number cleaving | Stage | Stage and its mean duration (min.) | | | |
|-------|----------------|-----------------|-------|------------------------------------|------|------|----|
| | | | 2 | 4 | 8 | 16 | 32 |
| 1 | 6 | 3 | 14.3 | 15.7 | 14.7 | 15.7 | |
| 2 | 6 | 6 | 14.3 | 16.8 | 15.7 | 17.8 | |
| 3 | 6 | 6 | 9 | 14.8 | 15.4 | 14.6 | |
| 4 | 6 | 2 | 10.6 | 10.6 | 10.0 | 12.0 | |
| 5 | 6 | 6 | 10.8 | 16.4 | 16.4 | 16.0 | |

These eggs were already in the 2-cell stage when first observed.

The variations may be due to the biological material the experimental conditions or both. There were differences in parentage, and, perhaps in preconditions of the eggs within the ovary. It is also possible that some compensatory control of cell division is operating during cleavage. Records of temperature fluctuations within the desired limits during each experiment, establish the existence of a different thermal history for each experiment and for most eggs (since not all the eggs in a batch develop in phase). Finer temperature control and recording will be necessary to assess the importance of these differences as a cause of variation. It has been shown for sea urchins of the genus *Arbacia* that the oxygen tension has a limiting effect upon the rate of cell division when the partial pressure in the gaseous phase falls below a value which Amberson² places at cell division, when the partial pressure in the gaseous phase falls below a value which Amberson² places at 11.5 and Clowes and Kral³ at 15 mm mercury. In the present experiments aeration of the water was as turbulent as was compatible with other requirements.

Cleaving eggs of the zebra fish have been used for the bio assay of cellular poisons.⁴ In any refinements of this technique aimed at quantitative comparison of cytologically active chemicals the possible existence of normal variations should be taken into account.

I wish to thank Mr G M Clarke of the Long Ashton Research Station for statistical advice.

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The Sea Anemone (*Calliactis parasitica*) and the Hermit Crab (*Eupagurus bernhardus*)

In the well known associations between hermit crabs and sea anemones, the crab is generally assumed to play an active part in establishing and maintaining the relationship. This has been demonstrated for *Adamsia palliata* and *Eupagurus prideauxi*,¹ for *Calliactis parasitica* and *Pagurus arrosor*,² and for *O. parasitica* and *P. stratus*.³ From this it might be expected that the large hermit crab of British waters, *Eupagurus bernhardus*, also actively assists the settlement of *O. parasitica* on its shells. Brief comments in a note by Brightwell⁴ and a review by Davenport⁵ suggest however, that these authors never observed such behaviour in *E. bernhardus* since they both state that the belief that this crab places anemones on its shells requires verification.

I have investigated the relationship between these two animals by introducing shells occupied by *E. bernhardus*, and/or unoccupied shells, into containers where a number of *Calliactis* had settled on the walls, floor, or on objects such as stones, scallop shells or slates. Several different experimental arrangements were used, and in all, I recorded about 250 transfers of *Calliactis* to the shells from their original positions. Many of these were followed visually but in no case was a crab seen to play any part in the process. The anemone, by sticking to the shell by its tentacles and spreading the oral disk over a wide area, then detaching the pedal disk and by bending the column double bringing the pedal disk over to the shell, climbed on shells entirely unaided by the crab.

The visual experience was confirmed by results which show that *Calliactis* transfer to unoccupied shells just as frequently and as rapidly as they do to shells occupied by *Eupagurus*. In experiments where choices were given, and in successive trials where occupied or unoccupied shells were presented under otherwise identical conditions, there were 153 records of settling on unoccupied, and 149 on occupied, shells. Moreover *Calliactis* which had settled on unoccupied shells showed no tendency to desert these for occupied shells which were presented later.

E. bernhardus is generally found in empty *Buccinum* shells carrying several *Calliactis* but living *Buccinum* are seldom found in Nature with the anemone on the shell. Yet in these experiments, *Calliactis* settled very readily on shells of living *Buccinum* and did not desert these later for shells occupied by *Eupagurus* when the latter were introduced.

The tendency for *Calliactis* to settle on occupied or unoccupied shells is abolished if these shells have been thoroughly cleaned by boiling in caustic soda. This indicates that the stimuli which elicit this remarkable behaviour pattern have a chemical component arising from the organic matter adhering to the surface of the shell.

A full account of the work will be published elsewhere. It was done at the Marine Biological Laboratory, Plymouth, and I thank the Director and staff for facilities and help. I also thank the Council of the Royal Society for a grant from the Browne Fund, part of which was used for this investigation.

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Acanthocottus lilljeborgi (Collett) in British Seas

THE Norway bullhead, *Acanthocottus lilljeborgi* (Collett, 1875), is a marine cottid (Teleostei-Scelopari) endemic to the European boreal region. It closely resembles *A. bubalis* (Euphr.) (= *Cottus bubalis* Euphr.) in general appearance, wide attachment of branchiostegous membrane to isthmus, number and arrangement of opercular spines, and possession of a small barbel at each corner of the mouth, but is readily distinguished from *A. bubalis* by the presence of a second longitudinal row of ossicles, dorsal and parallel to that along the lateral line, a difference in pelvic fin formula (I2 instead of I3) and smaller maximum size (60 mm against 170 mm)¹. The distribution and development of *A. lilljeborgi* have been reviewed by Bruun^{2,3}. Demersal juveniles and adults of this small fish are not often taken, and most records refer to pelagic postlarvæ. Outside British seas, the species is known from the south and west coasts of Iceland, the Faeroes, Rockall Bank, Great Fisher Bank, the Norwegian coast to 65° N, and the Skagerrak and Kattegat.

Past British records are very few, and bottom living older stages have been recorded only from the Clyde sea area, where small numbers have been found at depths of 10-47 fathoms (18-87 m)^{4,5}. The only definite British record of postlarvæ is given by Bal⁶, who obtained them off Port Erin, Isle of Man, in May, 1939. However, postlarvæ from the west coast of Ireland (Tory Island and Donegal Bay in the north, Valentia Island in the south) and the east coast of Scotland (St Andrews Bay and neighbourhood)^{7,8}, all originally identified as *Oncocottus quadricornis* (L.) (= *Cottus quadricornis* (L.)), have been assigned to *A. lilljeborgi* by Bruun.

In the Irish Sea, within the past eighteen months, demersal examples of *A. lilljeborgi* have been taken by scallop-dredge in depths from 15-28 fathoms (28-51 m) off the south end of the Isle of Man. Standard lengths ranged from 30 to 44 mm. The bottom deposit at the places of capture is coarse, being mainly composed of dead shells and stones, except in one locality where there is a characteristic *Modiolus* epifauna⁹. The relatively wide distribution of the species over this coarse ground, and the evidence of breeding in the region (occurrence of postlarvæ and similarity of some of the demersal specimens to the mature male described by Bruun²) suggest that *A. lilljeborgi* is an established inhabitant of the Irish Sea.

I am grateful to Mr R. G. Hartnoll, of the Biological Station, Port Erin, for providing most

the Manx material, and to Dr D. W. Tucker, of the British Museum (Natural History), for confirming the identity of four of these fishes.

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Defensive Acid-Secretion in Some Marine Gastropods

It has been known for many years¹ that the opisthobranchiate gastropod *Pleurobranchus membranaceus* (Montagu) is able to produce acid secretions if roughly handled, and the obvious inference is that these secretions deter would-be predators (especially carnivorous fish). More recently, this inference was given a scientific basis in experiments with pleurobranchids and marine fish in the Port Erin Aquarium². During the past few months an attempt has been made to ascertain whether acids were secreted by gastropods other than *P. membranaceus*, and the purpose of this communication is to present some preliminary findings.

It has been found that acid fluids of approximately pH 1 can be secreted by the mantle and foot of *Berthella plumula* (Montagu) (Opisthobranchia: Pleurobranchidae), *Lamellaria perspicua* (L.) (Prosobranchia: Lamellariidae) and *Velutina velutina* (Müller) (Prosobranchia: Lamellariidae). The pH estimations were made with Johnson's and B. D. H. pH papers. The acid secretion is produced only after rather violent treatment of the area of skin to be tested.

In experiments with hungry fishes (including cod *Gadus morhua* (L.), pollack *Pollachius pollachius* (L.), shanny *Blennius pholis* (L.), father lasher *Cottus bubalis* Euphrasen and plaice *Pleuronectes platessa* (L.)), these gastropods were invariably rejected as food. Rejection frequently occurred only after the gastropod had been in the fish's mouth for some seconds. Of the truth of the inference that it is the acid secreted by the gastropods which is responsible for their rejection there can be little doubt, since Bateson³ found food soaked in a dilute acid for a few seconds to be repellent to a variety of fishes.

One of the most remarkable features of these tests is that the gastropod seldom shows any sign of damage, even though the treatment it appears to receive from the hungry fish is violent in the extreme. It is also worthy of note that the ability to secrete an acid seems to have evolved quite separately at least twice, for the Pleurobranchidae and the Lamellariidae, although superficially exhibiting many parallels, are in the opinion of modern malacologists not at all closely related.

The work here described is financed by a grant from the Leverhulme Trust and is part of an investigation into defensive adaptations in naked gastropods.

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Albinism in Coconut Seedlings

In an article on inducing chlorophyll in albinic citrus seedlings Minessy¹ has recently shown by suitable grafting methods that chlorophyll formation was not blocked in the normal plant and that no chlorophyll irregularities appeared when albinos were grafted on to green ones. He mentions that this result apparently seemed to contradict the somewhat accepted view that albinism is due to recessive genes as was claimed by Torres for the Szinko mandarin. Several other workers, Petel² in the case of the coconut Bull³ in the case of the African oil palm, Posnette and Cropley⁴ in the case of the strawberry Riek *et al.*⁵ in the case of the tomato, also believed that the cause of albinism was due to certain disturbed genetical factors brought together by cross pollination. Some botanists have attributed the lack of chlorophyll to infection with an unknown disease. Pretreating citrus seeds with disinfectants such as Ceresan⁶ and 'Agrosan' resulted in the production of seedlings which were nearly all green. Albino avocado seedlings were shown by Wallace and Drake⁷ to result both from seeds originating from off bloom or late set fruit as well as from matured fruits. Teger and Cameron⁸ on the other hand, found that albinism could be eliminated in citrus seedlings by the removal of seed coats before sowing, indicating that the inhibitor of chlorophyll formation resided in the seed coats. Furtado⁹ has mentioned coconut seedlings exhibiting complete shoot albinism, attributing this to some internal factor and chlorosis due to lack of ferruginous products in the endosperm.

The logical inference from the above review is that there is yet some other factor which induces albinism in plants. Indeed some of the evidence reported in the case of complete or partial lack of chlorophyll in leaves refers to inadequate functioning of some physiological mechanism essential for the development of plastid colour, a condition which is also brought about by the genetic composition of the plant. That this physiological mechanism appears to be the proper and optimum utilization of iron (and probably nitrogen and magnesium) is apparent from the results we have obtained in several attempts made to induce chlorophyll in albinic coconut seedlings. Although calcium, phosphorus and iron do not enter into the composition of the chlorophyll their variations in the soil are generally known to influence its production. This also appears to depend upon the general vigour and tone of the plant which in their turn are influenced by the optimum availability and/or utilizability of certain combinations and concentrations of these elements.

The albino coconut leaf tissue contained rather high iron and high phosphorus contents. The possibility of preventing the high phosphorus content hampering the availability of iron for the biosynthesis of the pigment by side tracking the iron as iron phosphate was therefore examined in three ways. Iron (and magnesium) were supplied to the soil every week in the form of chelates (Iron green 330 Fe NaFeO as well as Na₂Mg) singly and in different combinations to pot-established albino coconut seedlings. Dilute aqueous solutions (2 per cent) were used. It was observed that the central shoots began to develop green colour from about the end of the second week and steadily progressed until the whole leaf appeared healthy and green. The green tint developed from the base of the leaf, proceeding to the tip, petiole and midrib portions almost

simultaneously. Even from the time of appearance the emerging inner shoot had developed chlorophyll just as the normal leaf. Although development of chlorophyll and health of the seedlings progressed with the chelate application the plants gradually faded and eventually died.

In a second series of experiments the tip of one of the albino leaves was just out and the cut end kept dipped in a 2 per cent cane sugar solution. On continuing the feeding of the leaf with sugar for a week it was observed that the inner leaves which developed afterwards had green colour even as a normal leaf. This may be attributed to the organic matter suitably chelating the iron present in the leaf and rendering the nutrients in an available form thus paving the way for normal physiological processes to occur. In the third experiment the cane sugar was substituted by a 2 per cent solution of potassium chloride for the foliar feeding since it is known¹⁰ that iron precipitation by phosphorus could be prevented by a possible conversion of inorganic to organic phosphorus in the leaf and/or by secondary effects on the organic acid status and cell sap pH. There was a remarkable response to the potassium treatment in that there was a progressive greening of the inner shoot and inner whorl of leaves.

These results show that inadequate availability of iron due probably to the incapacity of the plant to utilize the iron already present in the leaf determines the albino condition. The requisite mobilization of the iron appears to be the factor controlled by the recessive gene or genes since albinism is an inherited character. Albinism in the coconut thus appears to follow the general biochemical pattern of nutrient maladjustment which when corrected could orientate the recessive genetical factors to re-adjust properly the physiological processes concerned in the biosynthesis of chlorophyll to their usual and normal courses. Planned experiments to elucidate further these aspects are in progress and will be reported elsewhere.

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Capsicum Species of West Africa

There is still considerable confusion in the classification of the genus *Capsicum*. While some authorities disagree as to whether all the cultivated varieties should belong to a single variable species or to the two species, *C. annuum* and *C. frutescens* recognized by Linnaeus¹⁻⁴, others have recognized more species⁵⁻⁷. The number of pedicels per leaf axil has been one of the main characters used in the classification of the genus. Recently Wilson⁸ following Smith and Heiser⁹, has used 3-5 pedicels at each node and the circular constriction at the base of the calyx in fruit

to distinguish a third species *C. sinense* Jacq in West Africa

In the past two years I have collected Nigerian 'peppers' and also have in my collection three types of *C. sinense* Jacq received, among other species, from the United States by the kindness of Prof P G Smith of the University of California. I have found, under fertile medium and favourable growth conditions both outdoors and in an insect-proof greenhouse, that plants of the *C. sinense* Jacq type have 1, 2 and occasionally 3 pedicels at each node. I have observed that there are, as a rule, two opposite leaves or stem branching with opposite or near opposite leaves wherever the number of pedicels at each node exceeds 3. Since *Capsicum* plants have alternate leaves, these nodes with opposite or near opposite leaves may be regarded as cases of short internodes¹¹. There have not been more than 5 pedicels in any such case. The maximum number of pedicels per leaf axil or true node appears therefore to be 3.

I have also observed circular constriction of the calyx in the fruit of varieties with 1, 2 or 3 pedicels per leaf axil. Varieties with the constriction commonly have the greenish yellow or greenish white corolla typical of *C. frutescens* L.

Although embryo abortion of the 'somatoplastic sterility' type¹⁰ has been found in some crosses of *C. annuum* L and *C. frutescens* L, the two commonly recognized species of the genus, the species are, however, not completely intersterile, and their *F*₁ hybrids have shown regular pairing suggestive of homologous chromosomes¹¹. So far I have found no cause to think that the reported sterility barrier between *C. sinense* Jacq and *C. frutescens* L, which it resembles in every aspect, approaches the degree of intersterility found between *C. annuum* L and *C. frutescens* L. The basis of separation of *C. sinense* Jacq as a distinct species from *C. frutescens* L appears rather inclusive at least in the West African species. Now that the species *C. abyssinicum* A Rich, *C. baccatum* L Holl, and *C. cordiforme* Mill listed for West Africa¹² are no longer regarded as distinct¹³, it is suggested that until further work provides conclusive evidence of the existence of other species, the West African 'peppers' should be limited to *C. annuum* L and *C. frutescens* L on the following basis. *C. annuum*, usually 1 and rarely 2 pedicels per leaf axil, white corolla. Generally has thrifty growth for one season. *C. frutescens*, frequently 1 and 2, and occasionally 3 pedicels per leaf axil, light greenish yellow to greenish white corolla. Generally has thrifty growth for more than one season.

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ENTOMOLOGY

Central Control of Interactions between Behaviour Patterns in a Hemileucine Moth

PREVIOUS publications have described the relation between precurrent flight performance and the strength of a subsequent rhythmic settling response ('rocking') in the neotropical saturniid moth *Automeris aurantiaca* Weymer (Hemileucine¹)². The strength of the rocking response, measured as the number of complete oscillations of the rhythm, increases linearly with duration of flight, and in the absence of further flight responses is stable to retesting for periods of at least 90 min. The mechanism by which flight performance is thus registered and expressed in the subsequent settling behaviour is of particular interest, for the relationship is similar to that between the flight activity of foraging honey-bees, and the rhythmic distance-specific components of the communication dance².

Three factors other than flight duration influence the strength of the rocking response: (1) age from eclosion, (2) the presence of competing reproductive responses, themselves released by precurrent flight², which may be eliminated by removal of the abdomen, either before flight, or between flight and testing, (3) the proximity in time between flight and the settling response, close temporal proximity between the two acts tends to diminish the strength of the rocking response.

If these three factors are controlled by appropriate techniques, the number of oscillations which will be performed after a given duration of forced, tethered flight² can be predicted within very narrow limits.

The following operations performed before flight fail to interfere with the process of registration: (1) removal of the antennae, including Johnston's organ, followed by the ablation, by scraping, of the wind-sensitive hairs of Eltringham's organ, and the painting of the entire head with a layer of shellac varnish, (2) section of the indirect flight muscles, with or without bilateral excision of the wing-bases, and removal of the abdomen. Thus neither exteroceptive nor proprioceptive feed-back from flight-performance can mediate registration. This conclusion is reinforced by the fact that registration proceeds at the same rate in free-flying and tethered, de-alated moths.

After flight, (3) removal of the abdomen, followed by perfusion with Ringer's solution alone, and with amounts of up to 60 gm/l of added glucose or trehalose fails to interfere with the stability of the response, even after recovery from the osmotic shock caused by the stronger solutions. Since the mouthparts are vestigial, and the moths do not feed, these perfusion tests confirm that registration cannot be mediated by the interoception of the state of metabolic reserves.

The mere removal of tarsal support in the absence of an ensuing flight response is insufficient to induce registration. No afferent pathways other than those implicated by the release of flight need to be stimulated for registration to take place, moreover, activation of the central neural units which mediate the excitation and maintenance of flight is a necessary part of the process.

For technical reasons, it is unlikely that experiments of this type can be applied to the honey-bee communication dance, even in more moderate form. Nevertheless, the present results allow a strong presumption that the distance-specific components of the bee's dance may be controlled by similar

central interactions. Such a hypothesis at least has the merit of economy, in comparison with the alternative hypotheses requiring feed back from the metabolism or aerodynamic consequences of flight.

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Insecticidal Effects of Activated Charcoal and Clays

BRISCOE¹, Kitchner *et al.*², Wigglesworth³ and Parkin⁴ have studied the inert⁵ dusts for their insecticidal action. Reports on the insecticidal properties of inert⁵ dusts, particularly of silica, coal ash, diamond, Carborundum⁵ dusts from blast furnaces, flint, feldspar magnesite and dolomite are available.¹⁻⁴ While screening samples of various clays, decolorizing carbon, gas absorbing carbon, silica gel and commercial soil conditioners for insecticidal effects, it was observed that most of the dusts passing through a 300 mesh had various degrees of insecticidal effects on *Tribolium castaneum* Hbst adults, but activated charcoal and decolorizing clays exhibited in general, quicker effects on insects than unactivated dusts. Samples of wood shavings, sawdusts, coconut shells and kaolin clays were activated therefore, for further studies on their insecticidal properties. Activated charcoals were prepared by the zinc chloride activation method⁶ and kaolin clays were activated by acid treatment⁷.

Dusts passed through a 300 mesh were used for this work. The insecticidal properties of the activated and inactivated samples were tested against *T.*

castaneum by releasing adults on the dusts applied on glazed porcelain test plates and enclosing them in glass rings for different exposure periods. At the end of exposure periods mortality counts were recorded. Gas absorbing capacities of the samples were determined by Mantell's method⁸. Decolorizing properties of charcoal samples were determined by suspending 0.1 gm samples in 10 ml of 0.01 per cent methylene blue solution in distilled water for 30 min and per cent transmission readings were taken in a Lumitron photoelectric colourimeter using a 650-mμ filter on the filtered aliquot diluted to 10 times its volume with distilled water. Bleaching qualities of clays were assessed by the method of the American Oil Chemists Society.⁹ The results obtained with the activated and inactivated charcoal and clay samples on their gas absorbing, decolorizing and insecticidal qualities are presented in Tables 1 and 2.

Activated charcoal and clay samples showed in general high degrees of insecticidal activity (Tables 1 and 2). On activation the gas absorbing capacity was increased in the samples as compared with the inactivated samples. The decolorizing property was also improved by the activation treatments of the charcoal and clay samples. The results indicated that the insecticidal potency of the dusts is related to either the decolorizing property or the gas absorbing capacity or both. These aspects require further elucidation. Activated charcoals were found to be better insecticides than the activated clays or silica gel. In our experiments, gas absorbing carbon of the type used in a gas mask canister resulted in 100 per cent mortality of the test insects within 4 hr exposure, while the inactivated charcoals from different tumbars gave 30 per cent or less mortality even after 24 hr exposure of the test insects. The clays on activation exhibited high degrees of insecticidal properties although the inactivated parent materials did not show appreciable insecticidal actions (Table 2). However, prolonged exposures of 24 and 48 hr on unactivated clays and 0 day's post exposure incubation of the test insects on wheat flour, resulted in 10-80 per cent mortality.

In a further study it was interesting to note that activated charcoal samples exhibited comparatively

Table 1. INSECTICIDAL, GAS-ABSORBING AND DECOLORIZING PROPERTIES OF CHARCOAL SAMPLES

| SAMPLE | Mortality % <i>T. castaneum</i> exposure (hr at 26°C., 65% R.H.) | | | | CCl ₄ adsorptive capacity gm./gm. of charcoal, 25°C | Decolorizing power Lumitron % Transmission, 650 mμ filter |
|---|---|-----|-----|-----|--|--|
| | 4 | 8 | 16 | 24 | | |
| Canister carbon 1 | 100 | 100 | 100 | 100 | 1.23 | 100 |
| Canister carbon 2 | 48 | 83 | 100 | 100 | 0.95 | 100 |
| Activated carbon (Aferok) | 28 | 79 | 100 | 100 | 0.79 | 100 |
| Coconut shell carbon (I.A.) | 0 | 0 | 0 | 30 | 0.07 | 26 |
| Coconut shell carbon (A) | 30 | 75 | 100 | 100 | 0.74 | 100 |
| <i>Dalbergia latifolia</i> charcoal (I.A.) | 0 | 0 | 23 | 0 | 0.20 | 20 |
| <i>Dalbergia latifolia</i> charcoal (A) | 30 | 64 | 83 | 100 | 0.02 | 01 |
| <i>Tectonia grandis</i> charcoal (I.A.) | 0 | 0 | 0 | 20 | 0.04 | 18 |
| <i>Tectonia grandis</i> charcoal (A) | 25 | 30 | 68 | 100 | 0.59 | 54 |
| <i>Anogeissus latifolia</i> charcoal (I.A.) | 0 | 0 | 0 | 30 | 0.50 | 20 |
| <i>Anogeissus latifolia</i> charcoal (A) | 0 | 15 | 25 | 66 | 0.56 | 24 |
| Coal (I.A.) | 0 | 0 | 0 | 0 | 0.03 | 18 |

I.A., inactivated; A., activated; * 14 (control)

Table 2. INSECTICIDAL, GAS-ABSORBING AND BLEACHING PROPERTIES OF CLAYS

| SAMPLE | Mortality % <i>T. castaneum</i> exposure in hr (hr at 26°C., 65% R.H.) | | | | CCl ₄ adsorptive capacity gm./gm. of clay 25°C | % Bleaching of refined groundnut oil, 0.5 gm clay in 10 ml oil |
|-------------------------------|--|----|----|-----|---|---|
| | 4 | 8 | 16 | 24 | | |
| Fuller's earth (natural) | 0 | 0 | 0 | 0 | 0.12 | 13 |
| Fuller's earth (activated) | 0 | 0 | 0 | 100 | 0.63 | 21 |
| Bageshpura clay (natural) | 0 | 0 | 0 | 0 | 0.01 | 23 |
| Bageshpura clay (activated) | 0 | 12 | 89 | 100 | 0.21 | 27 |
| Bali clay (natural) | 0 | 0 | 10 | 0 | 0.03 | 29 |
| Bali clay (activated) | 0 | 48 | 94 | 100 | 0.32 | 37 |
| Helburi clay (natural) | 0 | 0 | 0 | 10 | 0.02 | 37 |
| Helburi clay (activated) | 0 | 43 | 92 | 100 | 0.24 | 37 |
| Silica gel (heated at 110°C.) | 0 | 40 | 65 | 91 | 0.20 | 37 |

effect on *T7* multiplication. Infected cells grown in heavy water incubated in normal media show a decreased burst size of questionable significance with *T5* and a marked increase with *T7*. When the infected cells were both grown and incubated in media containing heavy water, *T5* multiplication was normal whereas the burst size observed with *T7* was significantly increased. With each bacteriophage the latent period was significantly lengthened.

It is known that the medium contributes heavily to the synthesis of *T5* deoxyribonucleic acid⁹ while such is not the case with *T7*¹⁰. Thus it is not surprising that *T5* multiplication is affected when heavy water is present in the medium during the latent period. It is possible that the increased size of cells grown in heavy water is responsible for the increase in burst size seen with *T7*. Experiments to elucidate the nature of the observed effects are in progress.

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Galactose-sensitive Mutants of *Salmonella*

In a previous communication¹ peculiar mutants of *Salmonella* were described, which had been originally discovered and called 'mutable-type' (*M*) by Murase.² These mutants, when grown in the presence of low concentrations of galactose, show a marked lysis in ordinary media, and are converted to 'protoplasts' in hypertonic media. Moreover, they are consistently non-fermenters of galactose.

We have recently studied the location of the enzymatic block in the metabolism of galactose. The strains used were, *Salmonella enteritidis* No. 11 (wild type), 11-1-*M* (*M* mutant derived from No. 11), 11-1-*TB* and 11-1-*TW*. The last two strains were

Table 1 THE METABOLISM OF GALACTOSE BY VARIOUS MUTANT STRAINS

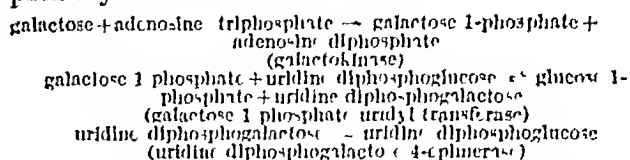
| Strain | No. 11 | 11-1- <i>M</i> | 11-1- <i>TB</i> | 11-1- <i>TW</i> |
|---|--------|----------------|-----------------|-----------------|
| Lysis by galactose* | — | + | — | — |
| Acid production from galactose† | + | + | — | — |
| Consumption of galactose (μmoles/100 mgm dry weight cells/30 min.) | > 75 | 20.5 | 6.4 | 0 |
| Activity of galactokinase‡ (μmoles/100 mgm acetone-dried cells/30 min.) | 53.5 | 21.4 | 4.3 | 0 |
| Accumulation of Gal-1-P (μmoles/100 mgm dry weight cells/30 min.) | 0 | 1.20 | 0.87 | 0 |
| Activity of transferase | + | + | Not examined | |
| Activity of epimerase | + | — | | |

* Tested in broth with 0.1% galactose.

† Tested on BTB-galactose agar.

‡ The reaction mixture contained 10 μmoles galactose, 4 μmoles adenosine triphosphate, 10 μmoles magnesium chloride and 60 μmoles sodium bicarbonate in 2.0 ml. The gas phase was 80 per cent nitrogen-20 per cent carbon dioxide.

galactose-negative, galactose-resistant mutants derived from 11-1-*M*. The results of the studies of galactose metabolism are summarized in Table 1. To measure the consumption of galactose, $5 \times 10^{-4} M$ galactose was added to the growing cells in citrate-ammonium medium. Aliquots were deproteinized by barium hydroxide followed by zinc sulphate, and the reducing sugar was determined. The slow utilization of galactose by *M* and *TB* cells is not merely due to the simple intracellular accumulation since treatment at 100°C for 2-3 min.³ before deproteinization did not alter the results. Then the enzymes on the Leloir pathway⁴ were studied.



The activity of galactokinase was determined manometrically on the acetone dried preparation of the cells induced for 30 min. by 0.1 per cent galactose in plain broth. *M* cells had plenty of galactokinase, but its activity was lower in the galactose resistant mutants. Then, it was found that a compound containing acid labile phosphate was accumulated in *M* cells grown in the presence of galactose. This compound behaved in exactly the same way as the authentic sample of galactose 1-phosphate on paper chromatography with various solvents (including that of Harrap⁵ which was found to be able to separate clearly galactose-1-phosphate from glucose-1-phosphate). When the accumulation of galactose-1-phosphate was determined as acid-labile phosphate which was not adsorbed by charcoal, it was found to be less in resistant strains than in *M* cells. These results show that (1) *M* mutants have high levels of galactokinase, but are blocked in the later step of galactose metabolism as is evident from the accumulation of galactose-1-phosphate, (2) lytic effect is correlated with the metabolism of galactose by galactokinase, because the less galactokinase a strain has, the more does it seem to be resistant to galactose.

To determine the presence of galactose 1-phosphate uridyl transferase (transferase), the induced cells were extracted by grinding with alumina and the extract was incubated with galactose-1-phosphate (0.2-0.4 μmole), uridine diphosphoglucose (0.05-0.1 μmole), tris buffer (pH 8.7), magnesium chloride, cysteine and crystalline phosphoglucosmutase. Phosphoglucosmutase was to convert the produced glucose-1-phosphate to glucose-6-phosphate. After deproteinization with 0.5N perchloric acid, the formation of glucose 6-phosphate was determined as the disappearance of acid-labile plus inorganic phosphate during the incubation. By this method, abundant transferase was demonstrated in wild-type cells. With the extract of *M* cells, the reaction proceeded rapidly at first, but it soon reached a plateau, and the total amount of the product formed was far less than the amount of galactose-1-phosphate added. Since in this assay system, uridine diphosphogalactose-4-epimerase (epimerase), this observation suggests the presence of transferase and the absence of epimerase. Furthermore, the following results confirm this interpretation. (1) If substrate amount of uridine diphosphoglucose (0.8 μmole) was used, almost complete utilization of galactose-1-phosphate was observed. (2) The extract of a mutant of *E. coli* K-12

(W 3000)*, which by itself did not show any detectable transformase activity but is reported to contain abundant epimerase[†] was able to allow the reaction to completion with the catalytic amount of uridine diphosphoglucose, if combined with the extract of *M* cells. (But the former loses its catalytic activity when treated for a few minutes at 100°C.) Thus it seems now obvious that *M* cells have a block at the epimerase level. This is in contrast to the transferase less mutants of *E. coli* which are reported to show marked bacteriostasis but not lysis in the presence of galactose[‡]. We were very recently informed by Dr H M Kalekar[§] that he also had independently demonstrated by his more specific method of assay that the metabolic block of one of our *E. coli M* mutants lies at the level of epimerase.

Since epimerase is believed to be responsible also for the biosynthesis of galactose the sugars in the cell wall hydrolyzate were analyzed by paper chromatography. It was found that wild type cells contain a large amount of galactose in addition to glucose and rhamnose, but *M* cells did not contain galactose and rhamnose at all. This is in agreement with the recent report of Kalekar and Kurahashi[¶] that their *E. coli* mutant W 3000, lacking epimerase, transferase and galactokinase does not possess galactose and rhamnose in its polysaccharides. In the light of this finding some peculiar features of *M* cells become intelligible. *M* cells form somewhat rough colonies, they have greatly altered susceptibility to phages. In the transduction using temperate phage PLT 22 and *M* mutants of *Salmonella typhimurium* LT 2 and LT 7, these various characteristics behaved all together with sensitivity to and non fermentation of galactose. These characteristics had been interpreted as the pleiotropic expression of a single gene mutation but they can now be considered as solely due to the abnormal composition of the cell wall induced by the primary defect in epimerase, and it serves to demonstrate how far reaching the effect of a single enzymatic defect could be.

The mechanism of lysis has not yet been elucidated. But considering the results[‡] which show that the synthesis of neither cell wall lipopolysaccharide nor cell wall protein is quantitatively impaired by the presence of galactose, the simple inhibition of cell wall synthesis[‡] seems rather unlikely. In the *M* mutants, of *S. typhimurium* LT 7 which cannot adsorb phage PLT 22 in contrast to wild type cells, galactose appears to induce the *de novo* formation of 'normal' phage receptors. It might be considered that the incompatibility between the newly formed 'normal' cell wall and the pre-existing 'abnormal' one might be the direct cause of lysis by galactose.

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Factors in Forest-Tree Litter Extracts affecting the Growth of Soil Micro-Organisms

It is well known that beech litter is less susceptible to decomposition than is the litter of many other species including maple. One reason for this may be the presence or absence of certain factors inhibiting or stimulating microbial growth. For example factors inhibitory to various fungi have been shown to occur in leaf exudates of certain plants¹ and in many plant extracts^{2,3}. Antibacterial factors stimulating certain mycorrhizal and saprophytic Hymenomycetes have also been observed⁴. Antibacterial factors have been demonstrated in extracts of oak and maple leaves⁵, spruce needles⁶ and in other species⁷. Autoclaving of the extract has been shown to increase the inhibition of fungi⁸ and bacteria⁹ under the experimental conditions used.

Rather different properties of inhibition and stimulation were observed in the following study in which newly fallen beech (*Fagus grandifolia*) and maple (*Acer saccharum*) leaves were extracted with cold water. The dried leaves were milled, homogenized with ten times their weight of cold water filtered and then centrifuged to remove suspended organic material. The pH was adjusted to 6.8 and half of the extract sterilized by Seitz filtration and the remainder by autoclaving. Medium consisting of equal quantities of Difco nutrient broth and leaf extract was then inoculated with each test organism (Table 1). Fungi were incubated for 20 days and growth determined by dry weight measurements. Bacteria were incubated for two days and growth estimated by plate counts. The results are shown in Table 1.

The fungi showed similar growth responses as also did the bacteria but the two groups differed from each other. Thus the fungi alone were inhibited by the filtered extract but only that prepared from beech leaves was active in this way. The bacteria however

TABLE 1. GROWTH OF FOUR MICRO-ORGANISMS IN NUTRIENT BROTH CONTAINING TREE LEAF LITTER EXTRACTS STERILIZED IN TWO WAYS

| | Control | Beech water filtered | Beech Auto- claved | Maple water filtered | Maple Auto- claved |
|--|---------|-------------------------|--------------------------|-------------------------|--------------------------|
| <i>Nitrosopora nigrescens</i> mean (25 ml.) | 4.1 | 1.1 | 24.4 | 8.2 | 16.7 |
| <i>Aspergillus niger</i> mean (25 ml.) | 4 | 1.7 | 31.4 | 41.1 | 39.7 |
| <i>Asciobolus</i> sp. No. x 10 ⁴ /ml. | 67 | 52.5 | 1 | 226 | 0 |
| <i>Pseudomonas fluorescens</i> No. x 10 ⁴ /ml. | 170 | 515 | 14 | 435 | 0 |

were inhibited strongly by both autoclaved extracts which were stimulatory to both fungi tested. The significance and mechanism of the apparently separate bacterial and fungal inhibitors must await further investigation, but it is conceivable that the fungistatic activity of the filtered beech extract may have ecological significance in the field.

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FISHERIES

Prediction of Selection Factors in a Tropical Trawl Fishery

THE discovery of a potential trawl fishery in an under-developed region may lead to the rapid expansion of the mechanized fleet and the exhaustion of the resource in a very few years, this has recently occurred in Liberia¹ and appears to be happening in Ghana². If it were possible, in the early stages of development, to introduce appropriate mesh-size regulations (together with a vessel-licensing system) the exploitation of the resources might be placed on a more rational basis, but it is characteristic of such a situation both that the research facilities are limited and that the exploited stocks comprise a variety of species, each of which will be selected differently by a particular mesh-size. Devold³ comments on such a situation, which has now arisen through the introduction of modern trawlers on the Brazilian coast.

As an interim measure, and as an alternative to legislation by intuition, the derivation of selection factors (S) from the length/girth (L/G) relationship appears to be promising. Graham⁴ comments such a derivation, but the relationship between L/G and S appears to have been little investigated. Margetts⁵ has made an indirect approach in the case of European haddock and whiting, while Cassie⁶ has made a direct comparison for the New Zealand snapper. Cassie postulated that the 50 per cent retention length (L') for snapper would be close to the length appropriate to a girth equal to the circumference ($2M$) of the mesh under consideration, for this species the calculated, or predicted, value of S was 2.35, the best experimental estimate 2.32, the mean experimental estimate for single twine cod-ends 2.35. Agreement was thus much closer than in the case of Margetts's work, which was based on much more sensitive girth measurements and calculations, but where the best estimate of S for haddock was 4.06, against the value currently accepted by the International Council for the Exploration of the Sea of 3.30.

For Cassie's postulate to be generally true it must be possible for a normally active fish seeking to escape from a trawl not to expand the diamond shape of the mesh nearly to its maximum area, an experiment in which a trawl net was anchored at the surface in a 2-3 knot tideway has shown that the force necessary to thrust a greased wooden cone through the mesh to its full expansion is surprisingly small—a sudden thrust of 2 kgm would appear to be within the powers of an active 10-12 in teleost, and expands the mesh (in this case of single cotton twine) to within 7 per cent of the maximum possible without pulling the knots.

The L/G ratios of the more important demersal fish off Sierra Leone have been investigated and it is now possible to draw up a table of predicted values of S for these fish, based on the calculation $S = L'/M$, L' being derived either from the equation $L = nG \pm k$ obtained by least squares in the case of good samples, or $L = nG$ in the case of small samples. These values are given in Table 1.

Concurrently with this investigation, covered cod-end experiments have been started using an open 28-ft trawler, these will presumably require several years for completion, but preliminary data make possible an estimate of the accuracy of the predictions for two species. In the case of gwangwa the agreement between the two values is very close

Table 1. PREDICTED SELECTION FACTORS FOR WEST AFRICAN DEMERSAL FISH, FOR A RELATIVELY FINELY MESH OF SUCH MATERIAL AS COTTON, MANILA OR NYLON

| | |
|--|------|
| Sheephead (<i>Drepane africana</i>) | 1.41 |
| Spadefish (<i>I. phippus</i> type) | 1.44 |
| Catfish (<i>Tachysurus gambensis</i>) | 1.01 |
| Snapper (<i>Pagrus ehrenbergi</i>) | 2.40 |
| Crocod (<i>Pristigaster jubelini</i>) | 2.89 |
| Shinbone (<i>Galeoides deca dactylus</i>) | 3.30 |
| Gwangwa (<i>Pseudotolithus elongatus</i>) | 3.59 |
| Lady fish (<i>Pseudotolithus senegalensis</i>) | 3.66 |
| Whiting (<i>Pseudotolithus senegalia</i>) | 3.71 |
| Spanish (<i>Polydactylus quadrifidus</i>) | 3.02 |
| Tenny (<i>Lops senegalensis</i>) | 4.22 |
| Lady fish (<i>Pseudotolithus macrognathus</i>) | 4.26 |
| Sole (<i>Cynoglossus gorceensis</i>) | 4.50 |

(Table 2) but in the case of crocod (often 'croakers', Crocod?) the experimental value of 3.45 for a small sample of 338 fish is not very close to the prediction—though even so the value of L' for the mesh used is within 5 per cent of that predicted (19.5 against 21.3 cm).

Table 2. PREDICTED AND EXPERIMENTAL RETENTION DATA FOR GWANGWA

| | | N | M | S | 0% | L' 50% | 100% |
|----------|------|------|------|------|--------|-------------|-------|
| Series A | Exp | 2738 | 0.70 | 3.47 | (13.0) | 23.25 | 27.0 |
| | Pred | | | 3.48 | 13.0 | 23.33 | 31.40 |
| Series B | Exp | 2076 | 0.70 | 3.40 | (12.0) | 23.75 | 23.0 |
| | Pred | | | 3.47 | 13.23 | 23.01 | 31.87 |

Series A, 10 hauls, series B, 16 hauls, totalling together 401 hr trawling time in the Sierra Leone estuary. N , number of fish in each series, M , mesh in cm, L' , percentage retention length in cm.

The disparity between the predicted values for gwangwa in Tables 1 and 2 arises from the fact that over the size range of fish examined the slope of L/G has a significant positive intercept—so that the value of S will vary slightly with the mesh size. Table 1 is based on mean figures for 1-, 2-, 3- and 4-in meshes and Table 2 on 6.70- and 6.79-cm meshes.

An attempt has also been made to predict the range of the selection ogive; but here the agreement between prediction and experiment in the same two species was rather poor (Table 2). A survey was made of all available published selection ogives, from which a mean value for the range (R) in terms of the ratio R/L' was obtained—0.79 for roundfish, 0.53 for flatfish. These were further broken down into R_1 (the range 0-50 per cent retention) and R_2 (50-100 per cent), a mean for roundfish was calculated— $R_1 = 0.53R$, $R_2 = 0.44R$. For gwangwa, the selection in fact proved to be much sharper for R_2 than was predicted, and was in the region of 0.26R, while the inclusion in the cod-end of many very small fish stunned by the large and prevalent scyphomedusae of these waters extended the ogive to the lower limit of the size-frequency distribution of the sample.

The great range in the values of S for these fish reflects the diversity of the commercial species and indicates the difficulty of reaching rational exploitation of such stocks, but it is hoped that it will be possible to use these predictions to determine, to some extent, the effect of mesh size in the now rapidly expanding Sierra Leone trawl fishery in which, subjectively, the size and fishing power of the fleet appears to be approaching the limit which the resources will stand.

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July 7

¹ Miller, G. C., U.S. Dept. Interior Fisheries Leaflet, 440 (1957).² Johnson, F. R., Rep. Fisheries Department, Ghana, 1957 (1958).³ Devold, F., Rep. Govt. Brazil on Fishery Biology, F.A.O. Rpt. 708 (1958).⁴ Graham, M. J. *Consil.*, 20 (1), 64 (1954).⁵ Margetts, A. R. *J. Consil.*, 20 (1), 56 (1954).⁶ Cassie, R. M., N.Z. Marine Dept. Fisheries Bulletin 11 (1955).

GENERAL EDUCATION IN A MODERN DEMOCRACY

IN his presidential address to the British Association at York on September 2 Sir James Gray pleaded strongly for a wider outlook in the teaching of science and stressed the need for a considered judgment as to the proportion of our total educational effort which should be devoted to the training of scientists and technicians—upon whom we depend for maintaining or extending our standard of living—and the proportion which should be expended on raising the intellectual standards whereby the bulk of the population forms its judgments on matters which are susceptible to personal prejudice or political propaganda. Sir James recognized the implications of Dr Trenaman's inquiry into the impact of the mass media and maintained that the key to the problem lies in the schools. The responsibility resting on secondary school teachers is not easily exaggerated, and Sir James pointed out that really inspired teachers, working with adequate but simple equipment, would achieve far more for general education than specialists in highly equipped laboratories.

In the concluding part of his address, Sir James Gray referred to the possible contribution which the British Association might make to the problem of general education so far as science is concerned, and the attention given to this question was a feature of the York meeting. Apart from this no fewer than three of the presidential addresses to Sections of the Association discussed general or particular aspects of the main problem raised by Sir James. A provocative address by Prof J Jowkes to Section F (Economics) for example, examined the question of balance between general education of the population in science and that devoted to the training of scientists and technologists. In Section L (Education), Sir James Robertson raised much the same issue in frankly discussing the purpose of our educational effort, while, addressing the Assembly of Corresponding Societies, the Countess of Albemarle discussed the question how the ordinary citizen could prepare himself or herself to live intelligently in a scientific age, and the sources of information and instruction available for that purpose.

The Countess of Albemarle suggested that there are three essential needs for the ordinary citizen: awareness of the character of the times in which he lives, some understanding of the methods of scientific research, and some readiness or determination to keep abreast of scientific development and invention. As Sir James Gray had already pointed out—and as Dr Trenaman's inquiry shows—the attempt to meet these needs must begin in the schools and there were other papers read at York which were equally concerned with the way in which this should be done. Mr J Maitland, in Section J (Psychology), considered specifically the communication of science to the layman. Mr N F Newbury dealt with the place of science in the primary school before Section L and,

before the same Section, Dr K Laybourn, in discussing the training of teachers of science and mathematics and what the schools require laid his own emphasis on the importance of quality and the decisive contribution which an outstanding or inspired teacher in love with his subject and his job could make.

It is, however, instructive to examine some of these fundamental issues debated at York in the light of the Clayton Memorial Lecture which Sir John Wolfenden delivered to the Manchester Literary and Philosophical Society in 1958. He did not attempt a definition of education, but pointed out that it is an essential part of a teacher's duty to instruct his pupils in certain areas of human knowledge and skill. This responsibility for instruction is inescapable and it is obvious that such instruction is what is in the minds of those who raised these issues at York. Sir John, however, emphasized that education is among other things, the influence of one personality on another. That has been clearly recognized in the great schools and universities of Britain. It is implicit in the comments made at York as to the importance and influence of the great and inspiring teacher.

Sir John Wolfenden in this lecture proceeded to discuss some of the implications arising from this influence of the teacher upon immature minds, and much of what he said is important not only in the present context but also in that of the proposal recently advanced for giving votes to young people at eighteen years of age. He faces frankly the difficulty of presenting truth objectively particularly in relation to judgments of value, and no less he recognizes that the immaturity of the minds of our pupils is a fundamental difficulty. Because of that immaturity, they are not capable of making up their minds for themselves when confronted with carefully balanced lists of credits and debits, and Sir John believes that of all the demands made on intelligent boys and girls nowadays, this is the one which causes the most unhappiness and strain. It is not helpful to withdraw our experience and comparative maturity from them at this point.

Nor does Sir John believe that, in fact, it is possible to do so. There is no neutrality in many such matters, and there is force in his suggestion that it may be as dishonest to pretend not to hold views which one does hold as to pretend to hold views one does not. Moreover, the significant influence on the young is what a man is and does, not what he says, and what he is and does are inseparably fused with what he believes with his convictions, principles and faith. Tolerance and an open mind are indeed essential to human thought and progress but they must be understood and practised as positive, not as negatives. It is no part of real tolerance. Sir John reminds us, to believe that all opinions are equally

valid, or of a genuinely open mind to be empty. Empty minds and closed minds are equally a reproach to the educator, and his final plea is not for preferential treatment for any one set of opinions or doctrines, but for a free, fair chance for all, accepting the risks involved where immature minds are concerned, because in this way we come nearest to being faithful to our immature pupils and to the truth itself.

Sir James Gray suggested that the value of an educational system can be judged by the extent to which it leaves people with a desire to know more about the world at large, and aware of the need—and the possibility—of satisfying this at least in part, by personal effort. Obviously, too, a constantly changing environment involves a continuous review of the general pattern of teaching, but apart from this, it is a serious indictment of specialist training in science and technology that it so often leaves the specialist not merely with no knowledge of the humanities but also with no desire to attempt to make good the loss. That of itself has not only destroyed the catholicity of intellect without which civilization cannot survive, but it has also contributed to make the scientist and the technologist the tools, first of commercial power, and later of the impersonal power of the State.

This argument is developed by R. T. Rolt in an appreciation of the width of knowledge of I. K. Brunel with which he concludes his biography of that distinguished and versatile engineer, and his argument found echoes in a recent address of Sir Solly Zuckerman on science and freedom, as well as in Sir Charles Snow's thesis of the two cultures. The divorce of the scientist and the engineer from the humanities involves a loss of proportion, and from that springs in some measure their loss of influence, while the door is opened to misunderstandings, doubts and fears which have both shaken man's confidence and weakened his control over events. Sir James Gray wisely remarked that no young scientist should be allowed to forget that new discoveries tend to arise from the borderland between different subjects, where the discipline of one is applied to another, but that alone will not suffice. It would seem to follow from Dr. Trenaman's study that this question of general education must be tackled in the schools, before specialization begins, if anything effective is to be done.

Sir James Gray's address, no less than Sir John Wolfenden's, thus leads directly to the central question which Sir James Robertson discussed. What are our schools for? It may still be a more open question than is often admitted, how much of our educational effort should be devoted to the training of professional scientists and technologists, and neither Sir James Gray nor Prof. Jewkes denied that we might need to increase the present proportion. What they did emphasize was that we should have due regard to the cost, and before we denied, in consequence, to a very much larger fraction of the community a reasonable chance of "seeing life steadily and as a whole", we should be sure, on the

basis of impartial inquiry, that the need existed and that the cost is justified.

This question, however, cannot be entirely separated from that of the general education of the community. If science is to be of direct cultural significance, it cannot, as Sir James Gray said, shut itself off from one of the main factors which have influenced man's attitude to social problems, and implicit in his address was a suggestion for further inquiry into the way in which scientists might receive this general education, possibly through the activities of the British Association itself. If this inquiry supported a wider, and perhaps more biological outlook on general education, very far-reaching re-organization of both schools and universities might be involved, but this could scarcely be undertaken without giving a considered answer to the question, what are our schools for, if not to the corresponding question about the purpose of university education. Even to urge that science can only play its full part in furthering human welfare if it is used, at a very early stage of education, as a means of encouraging a dispassionate but optimistic attitude towards all aspects of human affairs, involves at least an answer to the first question.

Sir James Robertson's survey was largely inspired by the view that we are neglecting the greater task of education for the lesser, though not unimportant, task of instruction, and it should already be clear that many of our present shortcomings arise from this fact, perhaps in part, too, from a failure to realize that what ordinary children need most of all is neither this skill nor that smattering, but just to be humanized and helped even a little way towards civilized living. It might well be urged that without this the scientist and technologist, too, are unlikely to contribute much towards meeting the real needs of mankind. If, in fact, the main effort of the secondary modern school is diverted from the general education of the ordinary child, no improvements in the extent or quality of further education are likely to repair the damage. It is abundantly clear already that the fundamental reason only a small minority of British adults continue their general education is not the lack of facilities but the defects in the education they have already received. It is in the schools and the schools alone that the basis of a sound general education can be provided, either for the ordinary citizen or for the specialist.

The whole trend of Prof. Jewkes's address supports Sir James Robertson's conclusion that until we are content to accept children as they are, we will continue to lose the chance of developing the gifts they have, in our perverse determination to make them manifest powers which in fact they do not possess. His second conclusion is endorsed by Sir James Gray's address in its aims and emphasis: our education should reflect, as it does not at present, the inescapable truth that it is for most of us relatively easy to get a job and do it decently, but tragically hard to be good human beings in our communities, our homes and our solitariness. It will not be easy to change the emphasis from vocational training to

education for life, nor perhaps even possible without a change of heart, but until it is done we can scarcely approach the problem of living with science and the effective use of the spoken or the written word and the visual image.

To set Sir James Robertson's plea that the ordinary child needs to be humanized and to be helped towards civilized living against Sir John Wolfenden's plea that it is not helpful to withdraw our experience and comparative maturity from our pupils when they are faced with judgments of value, sufficiently illustrates how much common ground exists in these two approaches and how much depends on the teacher. That remains the key problem, and especially how men and women of the right type are to be found and produced. Even if the need for Britain to produce more highly qualified scientists and technologists is fully established, the development of general education for the ordinary citizen may still remain the more urgent problem for at least two reasons. The production of scientists and technologists of the required qualities is linked with this problem of general education in the schools and the supply of appropriate teachers. Moreover, since the general citizen, as the Countess of Albemarle observed, needs increasingly to have some understanding of what science is about, because decisions in public affairs nowadays usually in some measure and at some point involve an assessment of scientific and technical data, the appropriate measures to increase the supply of teachers—and in turn of scientists and technologists—depend very largely on the existence of an informed opinion capable of understanding the action required, and capable of supporting it until it has been carried to a satisfactory conclusion.

RESEARCH IN GAS DYNAMICS

Fundamentals of Gas Dynamics

Edited by Howard W. Emmons. (High Speed Aero dynamics and Jet Propulsion, Vol. 3.) Pp xiii+749 (London: Oxford University Press, 1958) 140s. not

THE third volume in the Princeton series, 'High Speed Aerodynamics and Jet Propulsion' is concerned with the fundamentals of gas dynamics. In his preface the editor of the volume describes gas dynamics as a rapidly developing branch of physics and applied mathematics. Tsien's introductory chapter, a general development of the equations of gas dynamics but dealing principally with the fluid mechanics of a continuum, amply illustrates the importance of applied mathematics in this field of study. All possible combinations of compressible flows, adiabatic or diabatic, irrotational or rotational, steady or unsteady are considered. The last chapter on the flow of rarefied gases, by Schaanf and Chambré, defines clearly the regimes of gas dynamics, develops equations for free molecule and slip flows and presents experimental data for the slip flow and transition regimes. This chapter emphasizes that a broad knowledge of physics is required by a worker in the field of high speed aerodynamics.

Yet any engineer concerned with problems in gas dynamics will question whether Emmons's definition is complete, for while the need for a background in

mathematics and physics will be agreed, the development of any branch of fluid mechanics as complex as this one must depend upon verification of analytical work in engineering experiments. Crocco's chapter on one-dimensional flow (a 'book' of three hundred pages in itself) supplies a logical analytical development but shows an awareness of this need for experimental data. It is surprising that some of the now classical descriptions of one-dimensional compressible flows (for example, the flows in ducts with friction and heat transfer under varying pressure ratios) have not been backed by a great deal of experimental work. But Crocco has gathered together some excellent photographs of shock phenomena and presents the results of experiments that this reviewer has not seen before, particularly the work of Frössel. Some interesting experimental data obtained by Neumann and Lustwerk for the 'pseudo shock' (the complex oblique shock wave pattern with turbulent mixing, which occurs when the boundary layers are thick) are also included together with a review of the work of Shapiro and his associates on the zero-thornpressor, a device in which the stagnation pressure of a compressible fluid flow may be increased due to the abstraction of heat (by injection and evaporation of water droplets).

Hayes's chapter on shock waves and gas dynamic discontinuities and that on shock wave interaction by Polachek and Seeger are well written and logically developed. (This latter chapter contains some beautiful photographs of regular and Mach reflections and intersections and of shock refractions.) Stevor's article on condensation phenomena again interesting and readable appears somewhat out of place in a volume in this series, for much of the material deals with steam flows. Kantowitz's chapter on unsteady gas dynamics appears to be a little brief to this reader, a non-specialist in the field who found the brevity of the last article on the application of pressure waves in heat engines disappointing, especially as the quoted references on this subject are difficult to obtain. (There are numerous references elsewhere in the volume to papers produced 'internally' by laboratories. This growing practice of referring to unpublished work is to be deplored.) Emmons's own individual contribution to the book on flow discontinuities associated with combustion is a lucid piece of writing, although the difference in notation between this section and the introduction on general aspects of combustion by von Kármán is a little confusing. Sir Geoffrey Taylor, with assistance from R. S. Tankin, provides a section on the Chapman-Jouguet theory of detonation.

One surprising omission is the lack of a chapter on the flow of real gases at high temperatures (that is to say, dissociated or ionized gases), although Crocco includes articles on the flow of gases with variable specific heats and gases obeying van der Waals's equation.

Most workers in the field of gas dynamics will wish to know how this book compares with Shapiro's volumes on compressible flow published in 1953, but the comparison is a difficult one to make for Shapiro's book is largely devoted to the teaching of gas dynamics. The present volume is aimed at reviewing the state of research in gas dynamics, and will be widely used by specialist research workers in different fields.

If any criticism may be made of the new volume it is the usual criticism of a book by several authors—that of duplication of content material and differ-

the article were more chemical and technological than it is, even though there are some useful references to chemical preparation

"Non-oxide Ceramic Dielectrics" by P. Popper would seem to contain rather too much theory which is not immediately relevant. However, it is useful to have information on this interesting new subject by an author who is actively engaged in research on it

"Electrophoretic Deposition of Insulating Materials", reviewed by J. B. Birks, is a practical subject which involves much chemical 'fool'. The author succeeds in presenting the relevant theoretical background of his subjects clearly and concisely, which is useful since colloid science is generally treated in a biological context. The article gives a helpful survey of the practical applications

V DANIEL

EMBRYOLOGY

A History of Embryology

By Dr Joseph Needham. Second edition, revised with the assistance of Dr Arthur Hughes. Pp 304 + 18 plates. (Cambridge. At the University Press, 1959) 52s 6d net

THIS new edition of Dr Needham's remarkable contribution to the history of science will be widely welcomed. Its first appeal is to professional biologists, who will (or should) want to know more about the way their own science found its way out of abysmal ignorance and superstition towards greater knowledge and understanding, and historians of science will find it an indispensable source-book.

But it is important for wider reasons. It is important for the general historian, who will find in it numerous illustrations of the social relations of science. One that I found illuminating was the fact that in the seventeenth and eighteenth centuries there was a widely held conviction (abundantly justified by later events) that research into the nature of generation would throw light on orthodox theological doctrines, such as that of 'original sin', and that this "led to an economic situation of value for biological development". To-day it is devoutly to be wished that the powers that be, including public opinion in general, would extend this conviction and realize that research in biology will throw light on the central problem of man's nature and destiny.

The historian will also find many examples of the unfortunate political and social results of wrong attitudes to science and technology, for example, the contempt of antiquity for the 'base mechanic' and his arts, and the recurrent incomprehension of science and scientific method by governments and dominant classes. As Sir Charles Snow has so pithily pointed out in his recent Rede Lecture this incomprehension between the professional scientists and the representatives and products of so called humane studies can be mutual, and in Britain has led to the development of two cultures within the one nation.

It would seem that the only way to heal this split is through some reform of education, aimed at the integration of the sciences and the humanities in the cultural process, and many of us feel that for this the historico-evolutionary approach is necessary.

The evolutionary concept links man with the rest of life, mind with matter, contemporary history with archaeology, while the history of science and

its gradual invasion of new fields can be the bridge between the scientific and other elements in human history. Books like Dr Needham's are of the greatest value in helping to realize this process of our cultural re-education and re-integration.

JULIAN HUXLEY

FOURIER SERIES

Trigonometric Series

By Prof A. Zygmund. Second edition. Vol. 1 pp. xi + 383. Vol. 2 pp. vii + 354. (Cambridge. At the University Press, 1959) 84s net each volume

ZYGMUND'S authoritative treatise, which first appeared as a single volume in 1935, has been thoroughly revised and much enlarged for this second edition. The first volume contains practically everything which was in the original edition. The essential foundations on convergence and summability are dealt with in the earlier chapters, the reader needs a firm grasp of the elements of point-set theory and of Lebesgue integration. The main results are illustrated in a good chapter on special Fourier series. The rest of the first and the whole of the second volume deal with special problems and topics, much of the material in the second volume being work done during the past thirty years, showing, in particular, the influence of Littlewood and Paley. Each chapter is closely packed, and only the very indolent will ignore the additional wealth of content available in the annotated exercises.

The author marshals his material skilfully. A good example is his chapter on interpolation of linear operations, where the Riesz-Thorin interpolation theorem and the famous Riesz-Fischer, Hausdorff-Young and Riesz theorems which interpret and generalize the Parseval formula

$$\frac{1}{2\pi} \int_0^{2\pi} |f|^2 dt = \sum |c_n|^2$$

for a function f with Fourier coefficients c_n , are neatly stitched together and embroidered with Paley's remarkable theorem on Fourier coefficients and the Hardy-Littlewood theorems on re-arrangement of Fourier coefficients. His chapter on multiple Fourier series emphasizes the need for significant rather than obvious generalizations.

Even where the ground has been well ploughed, some problems remain. For example, it is now more than eighty years since du Bois-Reymond constructed a continuous function with a Fourier series diverging at one point, the extension to divergence at an everywhere dense set of points followed easily enough, but so far all such sets have been of zero measure. The question still stands. Can a continuous function have a Fourier series which diverges at all points of a set of positive measure? A similar problem was solved some thirty years ago by Kolmogorov, with a delicate argument producing an integrable function with a Fourier series diverging everywhere.

In its new form, beautifully produced by the Cambridge University Press, this book remains the standard and indispensable text for any analyst interested in Fourier series for their own fascinating sake.

T A A BROADBENT

Beiträge zur Neotropischen Fauna

Herausgegeben von Prof Dr Erich Titschack und Dr Hans Wilhelm Koepeke 1 Band, Heft 3 Zur Kenntnis der Pseudoscorpioniden Fauna des Anden gebietes Von Max Beier Pp 185-228 Kritische Untersuchungen der Newportia Arten Von Wolfgang Bücherl Pp 229-242 Ein neuer *Aethes* (Aves, Furnaridae) von der Küste und dem westlichen Andenabhang Südperus Von Maria Koepeke Pp 243-248 Beiträge zur Kenntnis der Fische Perus II Von Hans Wilhelm Koepeke Pp 249-268 (Jena Gustav Fischer Verlag, 1959) 10 95 DM

THE first two papers in the above collection which continues this important new publication are of considerable interest to students of the multitudinous neotropical invertebrate fauna. Dr Beier deals with a rich collection of pseudoscorpions from isolated regions of the Andes, especially Peru. This region appears to be the developmental centre of genera like *Stenolpium* and *Parowulius*, while in Chile the nearctic genera like *Dinocheirus* fade out. There are many endemic species here, and Dr Beier has found it necessary to make several new genera, all of which appear to be soundly based. Whether the Pseudoscorpions show replacement of species by altitude is difficult to determine: this is shown by such animals as some of the Chilopods, but unfortunately few of Beier's specimens have altitude data with them. The new genus *Teratolpium* is found at high altitudes only but conversely *Pachylolpium granulatum* Beier is found from 700 to 1,630 metres. It is to be wished that, where a choice was available the type specimen chosen should have been one from a known altitude (cf *Proparypus peruanus* Beier). Problems for future investigation may be glimpsed here and there; for example, *Lamprochernes*, a genus of world wide distribution, has a species high up in the Andes, while *Apololpium vastum* Beier has been found only on orchids. Bücherl's very important revision of the Scolopendromorph genus of Centipedes, *Newportia* places the systematics of this group on a satisfactory basis for the first time. The three subgenera *Newportoides*, *Scolopendroides* and *Newportia* had been used or not by previous authors almost according to taste or fancy. Bücherl shows quite conclusively that they apply to well marked groups of distinct geographical range. A really workable key covers all the known species and sub species and entails several changes of attribution and status. F. A. TURK

Crushing and Grinding

A Bibliography Pp ix+435 (London H.M. Stationery Office, 1958. Published for the Department of Scientific and Industrial Research.) 35s net

THIS bibliography will be invaluable to the very many industrial users of the processes of crushing and grinding and to research workers interested in comminution, particle size determination and particle classification. The bibliography proper is preceded by short authoritative reviews on fundamental aspects of crushing and grinding; problems of breakage and structure of coal; methods of particle size analysis; industrial grinding, crushing and grinding in the ceramic industry; grinding in the cement industry; crushing and grinding of minerals; grinding in the field of dyestuffs and organic chemi-

cals fire and explosion hazards in crushing and grinding operations. The sections into which the bibliography itself is divided (with the number of references in each section shown in brackets) are: fundamental aspects (450), crushing and grinding practice (354), coarse reduction (154), fine reduction (579), non mechanical methods (63), materials (744), methods of particle size and surface area determinations (186), classification (100) dust and fire hazards (141). Nearly every reference is accompanied by a useful abstract. There is a name index and a comprehensive subject index. The Department of Scientific and Industrial Research and the small committee, under the chairmanship of Mr A. S. Whitto, appointed to advise on the planning of the work, together with Mr W. H. Bickel, who undertook most of the detail of the work, are to be congratulated on this compilation. This is the second bibliography published by the Department of Scientific and Industrial Research on unit operations—the first was on industrial drying (1951), it is to be hoped that further similar bibliographies will be produced. S. G. WARD

River Pollution

1: Chemical Analysis By Dr Louis Klein Pp ix+206 (London Butterworths Scientific Publications New York Academic Press, Inc., 1959) 30s., 3 50 dollars

THIS book is an expansion and revision of two chapters which appeared in an earlier work concerned with the general aspects of river pollution. The pollution of the rivers of Britain has been widely discussed during recent years both in lay and scientific circles. While it may well be true that one photograph, particularly if it is in colour, may be worth a hundred dissolved oxygen samples in so far as securing public support or influencing a jury is concerned, the satisfactory resolution of the many problems involved can only be achieved after recourse to analytical methods.

Dr Klein deals in this text with physical and chemical methods for the analysis of waters, sewage and trade wastes. Biochemical methods are not considered. The recent recommendations of the official "Methods of Chemical Analysis as applied to Sewage and Sewage Effluents" and the "Recommended Methods for the Analysis of Trade Effluents" prepared by the Joint Committee of the Association of British Chemical Manufacturers and the Society of Analytical Chemistry are incorporated. No attempt is made to give detailed procedures but the many methods available are discussed critically and the most suitable method for a particular problem is indicated. The bibliography contains nearly 600 references to the literature. The appendix includes tables of saturation values for dissolved oxygen, conversion tables for various units of measurement, including degrees of hardness, tables of alkali conversion factors and various volumetric factors, and some typical analyses of waters and effluents.

There seem to be few errors, one, common to many text-books, is that ferrous can be used as indicator in the dichromate ferrous titration. Unless an unusually high acid concentration is used the end point is poor. The book would be of greater practical importance had it detailed the methods for the more widely should certainly ture of this

Bumblebees

By Dr John B Free and Dr. Colin G Butler With two appendices by Dr Ian H H Yarrow (The New Naturalist: a Survey of British Natural History) Pp xiv+208+25 plates (London: William Collins, Sons and Co., Ltd., 1959) 25s net.

IN their preface the editors express the hope that this book will widely encourage naturalists to take up the study of bumblebees, and it is indeed a stimulating work. Much information is given in an easily understood form, and possible answers to problems as yet unsolved are suggested. This eagerness to press forward on to untried ground does, however, occasionally lead the authors into making assumptions which are not entirely justified by the available experimental results. Certain over-simplifications also occur in places, as, for example, on p 66 in the description of an experiment by Dr Free, which was designed to test whether bumblebees entering a strange colony can be recognized by their scent alone. Reference to the original paper shows that the results were less clear-cut than stated here. Nevertheless, in assessing the overall scope and value of the book these criticisms prove to be relatively unimportant.

The development of colonies from their inception in the spring until the final hibernation of the mated young queens is described and, as in other chapters, the descriptions are illustrated by numerous original photographs. Among other topics discussed are the division of labour, collection of food, recognition of intruders in the nest, and predators and parasites. Not only are the biology and behaviour of bumblebees considered, however, for there is also an interesting chapter on their economic importance, in which their value as pollinators of crops and in plant-breeding is reviewed, various suggestions are also put forward for increasing their numbers in farming areas.

Two appendixes by the authors on methods of collecting and rearing colonies contain much useful practical information, while a further two appendixes by Dr Ian Yarrow give a simple key to the British species of *Bombus* and *Psithyrus* and details of their distribution.

M. DELIA ALLEN

Foundations of Set Theory

By Prof Abraham A Fraenkel and Prof Yehoshua Bar-Hillel. (Studies in Logic and the Foundations of Mathematics) Pp x+415 (Amsterdam: North-Holland Publishing Company, 1958) 42 guilders, 1s

Axiomatic Set Theory

By Prof. Paul Bernays With a Historical Introduction by Prof Abraham A. Fraenkel. (Studies in Logic and the Foundations of Mathematics) Pp vii+226 (Amsterdam: North-Holland Publishing Company, 1958) 45s

THESE two books are the latest in the series of Studies in Logic and the Foundations of Mathematics, produced by the North-Holland Publishing Co. The first opens with a short chapter on the paradoxes of set theory and then proceeds to the axiomatic foundations, including the axiom of choice; the axiom systems of von Neumann, and of Bernays and Gödel are discussed. There is a chapter on type-theoretical approaches, containing developments by Quine, Wang, Lorenzen and others, and an interesting section on set theories based on non-standard logics. Here, in particular, is a discussion of the rather obscure ideas of the Polish logicians,

Leśniewski and Chwistek. About seventy pages are devoted to intuitionistic conceptions of mathematics, and the bulk of the discussion concerns, of course, the ideas of Brouwer. The final chapter is concerned with metamathematics and semantics. The bibliography, extending to fifty pages, covers comprehensively the years 1947-56, and will probably become the standard for this period.

"Axiomatic Set Theory" is, apart from the introduction by Fraenkel, largely a presentation of a modified form of the material published by Bernays over the years 1937-54 in the *Journal of Symbolic Logic*. It is a formal development and is carried out in detail in its applications to analysis, including the theory of real numbers, and to cardinal arithmetic. The book is, as the author says, "designed for a reader who has some acquaintance with problems of axiomatics and with standard methods of mathematical logic".

To the 'working mathematician' these two volumes will indicate something of the great amount of effort which, in recent decades, has been expended in the field of symbolic logic and the foundations of mathematics. The situation is still very fluid, and it appears that "the third foundational crisis that mathematics is still undergoing" is far from becoming a thing of the past.

L. S. GODDARD

Elementary Statistical Physics

By Prof C Kittel Pp ix+228 (New York: John Wiley and Sons, Inc., London: Chapman and Hall, Ltd., 1958) 64s net

THIS book contains a short but concentrated treatment of a wide field of theoretical physics. Part 1 (116 pages) deals with classical and quantum statistical mechanics and its relation to thermodynamics; Part 2 (52 pages) with fluctuations, random processes in general (including the Wiener-Khinchin theorem), Brownian motion, noise and irreversible processes, and Part 3 (46 pages) with detailed balance, kinetic and transport theory. The three parts are divided into a total of 45 sections, many of which are preceded by references to standard works and recent papers.

The exposition is usually clear and as simple as the topic permits, though there is an exception on p 19 where the law of increasing entropy is discussed before the entropy of a non-equilibrium state is defined. The amount of application to particular problems is inevitably small in relation to basic theory. Assemblies of non-interacting particles only are considered, except for an example on a linear ferromagnet in the section on the density matrix and an appendix proving the virial theorem of Clausius. However, where possible, the author discusses both knotty points and recent developments, as examples may be mentioned sections on the thermodynamics of magnetization and negative temperatures, respectively. Problems are given, but some of these seem to be intended more as invitations to follow up the references than as exercises on the text. For example, after no more formal definition of a Markoff process than the statement that the two-event probability function p_2 "contains all the information we need" the student is asked to prove the Smoluchowski (Chapman-Kolmogoroff) equation.

The book may be recommended for readers who wish to find out about some of the great variety of problems and methods in modern statistical physics.

G. M. BELL

MYXOMATOSIS PRESENT POSITION AND FUTURE PROSPECTS IN GREAT BRITAIN

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SINCE the introduction of myxomatosis into Australia and its destruction of millions of rabbits, the situation there has fundamentally changed, and with a startling rapidity. The virus has become attenuated so that more rabbits survive, and still more important, natural selection has ensured that the present population of rabbits has a greater innate resistance to the disease. As a result of these two factors, myxomatosis is no longer regarded as of great value in keeping down the rabbits in Australia. Workers in that country¹ have studied the changes in the virus and in the rabbits in a most imaginative and painstaking manner, and in consequence we now have a fairly clear picture of developments there.

Course of events in Britain In Britain, the history of myxomatosis appears to be following a rather different course. This is doubtless due mainly to the fact that the effective vector here is for the most part, the rabbit flea (*Spilopsyllus cuniculi*), whereas in Australia mosquitoes are the principal vectors and *Spilopsyllus* is not present.

When the disease first spread in Britain in 1954-55 it did not sweep over the country but was gradually distributed in a patchy manner and the natural local spread was slow but effective so effective that by the end of 1955, the great majority (well over nine tenths) of the wild rabbits had been killed by the disease. Of course, pockets of susceptible rabbits escaped infection and continued to breed, as did the animals recovering from infection.

There were few reports of myxomatosis in the first months of 1956, but what may be called secondary outbreaks were soon evident and, as shown in Table 1, have since appeared in many places. Curiously enough, the only English counties having little or no secondary myxomatosis have been in the west and south west whereas the only Welsh counties over reporting secondary myxomatosis have been the five on the west coast. It was possible to say, in 1956, that there were no really heavy rabbit infestations on the mainland but during the past three years rabbits have gradually increased so that there are now considerable populations in some areas and damage to crops is more frequently reported.

Samples of myxoma virus collected in the field have been sent to Prof F Fenner at the Australian National University Canberra since October 1953 and

two of these, sent in September 1954 from Sussex, were somewhat attenuated.² The first evidence of extensive infection with attenuated virus was in Sherwood Forest, Nottingham in April 1955³ and other cases have since been found in many areas (see Table 1). The British attenuated or atypical myxoma usually produces a nodular lesion with less diffuse oedema than in typical cases. During the early stages the nodules may contain fully virulent virus but when they shrink and form scabs they contain virus of reduced virulence. By means of the gel diffusion precipitin test⁴ cases of typical and atypical myxoma may be rapidly distinguished and the stage of the infection assessed.

The connexion between the virulent and attenuated strains is at present by no means clear. In the Sherwood Forest area myxomatosis has persisted continuously since 1954 and both typical and atypical infections have been present since 1955. In the Edenbridge area of Kent, on the other hand there was no secondary outbreak of disease from 1954 until March 1958 despite the marked increase in the rabbit population, although isolated cases of infection were found. In 1958 the Edenbridge rabbits were greatly reduced by disease which was typically virulent for the first four months after which the presence of atypical infection was also demonstrated.

Changes in virulence of the virus As Fenner and Marshall have shown the attenuation of myxoma virus in Australia is a logical consequence of the relationships existing between virus host and vector. A rabbit bitten by a mosquito which carries a relatively avirulent virus will survive longer than one infected with a more virulent strain and will therefore, be able to serve longer as a reservoir of infection. Virus will thus be carried by more mosquitoes to other rabbits. In Australia natural selection thus tends to favour an attenuated strain. In fact, fully virulent viruses deliberately introduced into areas where less virulent ones are already prevalent will dominate the scene for only a short time⁵ the less virulent ones supplant them in a matter of months. Virus which is too attenuated, however, causes lesions which appear only cannot serve as a good source for virus: so the tendency is towards domination by strains of intermediate virulence.

As already mentioned attenuated myxoma virus has appeared in some areas of Britain and is on the increase, but modified strains have not, as in Australia, steadily ousted the highly lethal ones. After six years the latter seem to be at least as numerous as milder ones. This might have been predicted from the nature of the virus-flea-rabbit relationship which presents notable differences from the virus-mosquito-rabbit system in Australia. In contrast

Table 1 NUMBER OF COUNTIES IN ENGLAND AND WALES WITH OUTBREAKS OF MYXOMATOSIS

| Year | Virulent disease | Attenuated disease (No of incidents) |
|------|------------------|--------------------------------------|
| 1956 | 21 | 5 (24) |
| 1957 | 38 | 10 (42) |
| 1958 | 47 | 23 (106) |

to the Australian situation, there is likely to be some evolutionary pressure in favour of a virulent virus. Fleas on rabbits infected with such a strain will naturally leave the rabbit when it dies and spread the highly lethal virus. Where, however, a rabbit survives, the *Spilopsyllus* may have no occasion to seek a fresh host. Even if the rabbit dies after a chronic illness, there may well be only a little virus on the flea's proboscis at that stage. On a short-term basis survival of the highly lethal virus could thus be favoured. Marshall and Fenner² have made suggestions on similar lines.

This, however, can scarcely be the end of the story. For, as Theobald Smith taught, a parasite which kills all its victims will soon perish for lack of fresh hosts to infect. There will thus be a counteracting long-term tendency to perpetuate a not too virulent virus. In practice there have been several instances where, at the beginning of a myxomatosis outbreak, highly lethal virus has been recovered, whereas in samples obtained later in the outbreak attenuated virus has predominated. Rabbits with attenuated virus may be ill for a long time and the virus may persist in attenuated form by exchange of infected fleas in burrows. The resultant of opposing evolutionary tendencies may well be a mixture of highly lethal and attenuated viruses existing side by side in the same locality. Such a result could be brought about if the favoured virus were one which, as regards virulence, was genetically unstable, but what will in fact be the outcome, only time and alertness of investigators can reveal.

Changes in resistance of rabbits. In Australia, a standard virus which originally killed 90 per cent of wild rabbits was only able, after the population had been exposed to seven successive epizootics, to kill 30 per cent of currently caught young ones³. This tremendous increase in resistance seems to be of more practical importance than any change in the virus, and infection with myxomatosis has now become a minor factor in controlling Australian rabbits despite the fact that there is usually an epizootic each summer. The British results summarized above do not suggest that any such change has occurred among our rabbits. One wonders, indeed, whether this would be expected in a population of hosts with an average life-span of about a year and with outbreaks of disease at irregular intervals which may, as around Edenbridge, be as long as four years.

Discussion. The main object of this article is to try to dispel the idea that myxomatosis here is bound to behave just as it does in Australia. There is already good evidence that it is not doing so, and

possible explanations of this have been brought forward. We do not know how the virus persists between outbreaks and how it manages to re-appear after an apparent absence when rabbit numbers have materially increased. It could conceivably persist in a modified form in an immune population or in some biting arthropod, but evidence is lacking that either method is actually possible over a period of years. It could also be introduced on rabbit fleas temporarily carried on migrating birds, or on wind-dispersed, infected *Anopheles maculipennis* (= *A. atroparvus*) since these mosquitoes are known to be vectors in southern England, though of minor importance compared with fleas. Their role is believed to be rather greater in France, and if this is in fact so, myxomatosis there may have a different future from that in England. There remains the possibility of deliberate introduction by man, even though the Pests Act of 1954 made it an offence to use a rabbit infected with myxomatosis to spread disease among uninfected rabbits. Few would deny that the indiscriminate spreading of the disease is undesirable, particularly in the absence of much more knowledge about the infection and the long-term consequences of its introduction. In any event we must admit that we do not know which, if any, of the agencies discussed are adequate to account for the persistence of the disease and its re-appearance at times after a considerable absence.

The increase in rabbit damage to crops in 1959 serves as a reminder that, despite myxomatosis, the rabbit population of Britain is again rising. Much useful control has been possible by the concerted action of landholders through Rabbit Clearance Societies: there are now 370 of these, covering seven million acres of land or about 15 per cent of the agricultural area of Britain. It would be most unwise to relax such efforts. Above all, it is of tremendous importance for the future of farming in Britain that we should learn more of the natural history of myxomatosis and the factors making for changes in the virus and in the rabbits. Myxomatosis provides an unusual opportunity to study and compare the evolution of a host-parasite relationship in the contrasting environments of countries at opposite ends of the Earth.

¹ Fenner, F., and Marshall, I. D., *J. Hyg., Camb.* 55, 149 (1957).
Andrews, C. H., Muirhead-Thomson, R. C., and Stevenson, J. P.,
ibid. 54, 478 (1956).

² Hudson, J. R., Thompson, Harry V., and Mansel, W., *Nature*, 176, 783 (1955).

³ Mansel, W., and Thomas, Valerie, *J. Comp. Path.* 68, 188 (1958).

⁴ Fenner, F., Poole, W. E., Marshall, I. D., and Dyce, A. L., *J. Hyg., Camb.* 55, 192 (1957).

⁵ Marshall, I. D. and Fenner, F., *J. Hyg., Camb.* 56, 283 (1958).

⁶ Fenner, F., *Brit. Med. Bull.* 15, 240 (1959).

INTERNATIONAL COUNCIL FOR THE EXPLORATION OF THE SEA

SPECIAL INTERNATIONAL GEOPHYSICAL YEAR MEETING

AS part of the oceanographic programme for the International Geophysical Year the onus of carrying out a Polar Front Survey in the North Atlantic Ocean was placed by the Comité Spécial de l'Année Géophysique Internationale (the body established by the International Council of Scientific Unions for the planning of International Geophysical Year operations) on the International Council for the

Exploration of the Sea with the help of the International Commission for the Northwest Atlantic Fisheries. A sub-committee of the International Council for the Exploration of the Sea under the chairmanship of Dr G. Böhnecke (Federal Republic of Germany) co-ordinated the research plans of the different countries, and forty-six research and other ships of eleven nations took part in the survey. At

a meeting held under the chairmanship of Dr J B Tait (Britain) at the Council's headquarters in Copenhagen during October 1-3, 1959, 45 papers were presented dealing with the first results of the survey.

About sixty attended the meeting, and Mr A. J. Leo and Dr D. H. Cushing (Britain) acted as reporters.

Hydrography

The hydrographical papers were given in groups, according to geographical regions.

Barents Sea. The paper by Prof I. Hela (Finland) described Finnish work at the beginning of the International Geophysical Year. Various sections were worked and can be compared with those of the German research ship *Poseidon* in 1927. The temperature and salinity of the Atlantic water penetrating the Barents Sea were higher in 1957 than in 1927. An increase in salinity of 0.04 per mille on the standard values of all the basic water masses was observed. Surface temperatures and salinities were higher than the average values given in the atlas by Dr Krauss. Mr A. J. Leo showed that the volume transport of the West Spitzbergen Current was below normal taking the International Geophysical Year as a whole, and that temperatures in the south-eastern Barents Sea were subnormal. He related this state to the abnormally strong development of the Polar high pressure system and the southward displacement of the atmospheric Arctic Front. Norwegian work in the area during various seasons was described in a paper by Mr L. Midtun (Norway) which was read by title.

In the first of two papers on the chemistry of Barents Sea water, Dr S. Gripenberg (Finland) found that the alkalinity/chlorinity ratio was higher in the Norwegian coastal water than in the Atlantic water or the East Spitzbergen Current, but that this reversal applied when the boron/chlorinity ratio was considered: this implies that most of the boric acid is bound up in organic complexes. In the second paper Dr A. Völpiö (Finland) showed that different methods of analysis gave different results for the total iodine content of sea water and demonstrated how little we know about the iodine content of sea water.

Greenland and Norwegian Seas. Drs T. I. Gorshkov and E. V. Solyankin (U.S.S.R.) showed that the deposits on the sea bed, by differing in their chemical composition, particularly in their content of carbonates and of iron and manganese oxides, are indicators of the hydrographic conditions prevailing in the basins of these two seas. Dr J. N. Carruthers (Britain) pointed out the pioneer use by Otto Pettersson of this technique. In a paper read by title Dr G. N. Zaitsev *et al.* (U.S.S.R.) have computed the water and heat budget of these seas. When the various components are summed, the difference between the heat input and output amounts to only 0.4 per cent. The authors then proceed to show the relative importance of these different components in different parts of the seas: advection of heat by currents is found to be the most important. Finally, they have computed the nutrient salt budget. Dr A. P. Alokskov *et al.* (U.S.S.R.) described Russian hydrographic work in the southern part of the Norwegian Sea in 1958. In April the East Iceland Arctic Current was strong, blocking the inflow of Atlantic water to below average. In October the

inflow was intensified. The waters near the bottom in this area were found to have a salinity of 34.87-34.88 per mille and the authors assumed that they are related to the East Iceland Arctic Current and flow from west to east. It was pointed out by Mr O. Sælen (Norway) that these salinity values are lower than the standard values for Norwegian Sea bottom water. Dr J. B. Tait (Britain) pointed out that the water might have been Arctic Intermediate Water. In reply to a question, Prof J. V. Probragenski (U.S.S.R.) said that the salinities had been determined by the Knudsen titration method. At this stage Prof G. Dietrich (Federal Republic of Germany) stressed that the results collected during the Polar Front Survey should be sent to the International Council for the Exploration of the Sea as well as World Data Centres A and B. Mr Sælen described Norwegian work in the same area in 1958, in March and October: an intensification of the inflow of Atlantic water in the latter month was noted, as had been reported by the Russian workers. A special feature observed was the ascent of cold water along the continental slope off Norway. Finally Dr J. Eggvin (Norway) presented a series of temperature, salinity and current charts for the Norwegian and Greenland Seas, and showed how the Norwegian Sea bottom water is formed in the region north of the Jan Mayen Ridge in some years and not in others depending on the meteorological conditions, and how this bottom water flows southwards from the Greenland Sea along the foot of the Norwegian continental slope towards the Faroe-Iceland Ridge. It was further shown that the temperature of the bottom water of the Greenland Sea increased in temperature northwards from the main area where it is formed. This temperature increase is a result of mixing with Atlantic water. The positive difference between the temperature of the bottom water of the Arctic Ocean and that of the Greenland Sea can therefore be explained without as previously, assuming a submarine ridge (1,200-1,500 m.) between Spitzbergen and the north-eastern part of Greenland. This is of interest in view of the recent work of Dr L. Balakrishna (U.S.S.R.), who by investigations on board ice breakers has shown that the sill depth between the Greenland Sea and the Arctic Ocean exceeds 3,000 m. In discussion of this paper it was pointed out that the sinking of water to form the bottom water might set up a system of compensatory surface currents which would be of importance to the Barents Sea fisheries.

Shetland-Faroe-Iceland Region. Dr J. B. Tait and Mr J. H. A. Martin (Britain) had computed the volume transport through the Faroe-Shetland Channel over the period of the International Geophysical Year and found it to be high at the beginning and end but low at other times. Gulf of Gibraltar water seems to have been present in the oceanic water mass in June 1957 and June 1958. In June 1957 the inflow was cut into two parts by Arctic Intermediate Water which was moving southwards, and in June 1958 it was similarly divided by a southerly flow of Norwegian Sea water. Over spill of cold Norwegian Sea water was noted along the Faroe-Iceland Ridge in June 1957 and March 1958 but not at other times.

On the basis of surveys made along the Faroe-Iceland Ridge during 1957-58, Dr J. H. Stool (Britain) had come to the conclusion that overflow of very cold (0-2°C) water is rare and unimportant, but that there is continuous overflow of a slightly warmer

(2–4°C) water which is the product of mixing of water masses of Atlantic and Arctic types on the top of the ridge. This overflow has a geostrophic motion north-westwards along the southern side of the ridge, and it then turns southwards along the eastern side of the Reykjanes Ridge. The total flow over the ridge is calculated as being near the mean value of the Faroe-Shetland inflow. A discussion of this paper by Prof Dietrich showed that, on about 50 per cent of the surveys of the ridge, overflow of cold (0–2°C) water has been found. The relative importance of overflow directly across the ridge and outflow through the channel between Faroe and Faroe Bank was debated by Dr Tait, Mr F Hermann (Denmark) and Dr Carruthers.

North Atlantic Ocean Prof Dietrich described various stages in the evolution of the International Geophysical Year and considered the next stage the exploitation of the observations. He suggested the preparation of an atlas of maps and sections of the North Atlantic. Using German observations, he demonstrated the existence of six water masses on the Cape Farewell-Flemish Cap section. In particular, he examined the origin of the North Atlantic deep water in the Labrador Basin and the overflow of cold water across the Iceland-Greenland Ridge, and showed how the latter could be tracked over a great distance clinging to the lower part of the continental slope and not flowing along the very bottom of the basin. He also showed how the winter surface isotherms are a guide to the circulation of the North Atlantic in that season.

A paper was given by Dr W Krauss (Federal Republic of Germany) showing that internal waves can be set up in the deep layers of the ocean as well as in the upper layers by the action of the wind.

From dissolved oxygen/potential temperature diagrams, Dr L H N Cooper (Britain) concluded that the water column in the Bay of Biscay consists of a layered series of resident water masses resembling a pile of plates stacked one on the other. He regarded these plates as being the result of the overspill of boluses of cold water across the Faroe-Iceland Ridge. He also demonstrated a secular change in dissolved oxygen content since 1922. It was pointed out by Prof Dietrich that the stepwise structure described could also be explained by Dr Cooper's earlier turbidity current theory, and that this structure had not been as yet found in other areas where very detailed hydrographic observations had been made (for example, south-west of Iceland). The dating of the climatic fluctuation which had brought about the secular change in dissolved oxygen content was discussed by Mr Leo and Dr Cooper.

French observations in the North Atlantic and Davis Strait were described by M G Poluchon (France). Charts of the currents in the region of 50°N showed the meandering of the current as it leaves the Grand Banks area and a decrease in the meanders as the current proceeds eastwards.

Dr J Joseph (Federal Republic of Germany) described his work with a transparency meter combined with a thermocouple. The turbidity distribution depends on local production on one hand and advective processes and turbulence on the other. Connections between the turbidity sections and the temperature sections could be seen. He also showed that there is no change in turbidity at the deep scattering layer. In discussion a strong case was made for fish as being the cause of this layer.

Dr H Weidemann (Federal Republic of Germany) described work with towed electrodes (*GEK*) between Greenland and Iceland. At a fixed station south of Iceland the records collected over a period of 30 hr allowed the relation between wind and surface current to be investigated. The results gave a mean deflexion of current to the right of the wind of 27° and a current/wind ratio of 1.4–1.5 per cent. The difference between these values and Ekman's theoretical values can be explained by assuming that conditions were non-stationary.

Mr F Hermann described Danish observations in the North Atlantic in July–August 1958. West of the Reykjanes Ridge the basin was largely filled with sub-arctic mixed water, as already described by Prof Dietrich. Cold water coming over the Iceland-Greenland Ridge was again found on the bottom in the western part of the Irminger Sea. East of the Reykjanes Ridge a bottom layer with a temperature below 3°C was found, consisting of mixed water derived partly from overflow across the Faroe-Iceland Ridge, partly from Atlantic water and partly from sub-arctic water. This water circulated anti-clockwise around the basin and crossed the Reykjanes Ridge to flow north on its westward side and mix with the overflow across the Iceland-Greenland Ridge. In the Davis Strait water which had overflowed the Greenland-Baffin Island Ridge but which does not contribute to the North Atlantic circulation as a whole was detected.

Dr R A Cox (Britain) gave an account of the work of *R R S Discovery II*. A section showing the distribution of silicate along lat 24°N had three outstanding features: the depletion of silicate but not of phosphate at the surface in the Sargasso Sea, the high silicate content of the bottom water of Antarctic origin west of the mid-Atlantic Ridge, and the very irregular bottom topography. Work with Swallow's neutrally buoyant floats west of Portugal showed how even in the deep ocean there are great variations in current speed and direction. The outflow of Mediterranean water from the Straits of Gibraltar had also been tracked by these floats, and it was shown that a westward movement of 12 nautical miles/day could exist close to the Spanish coast, but that farther south there were large eddies. Dr Cooper pointed out that the silicate distribution along lat 24°N showed that Antarctic bottom water must make a contribution to the bottom waters east of the mid-Atlantic Ridge, and Prof T. Braarud (Norway) did not think that the silicate deficiency prevented phytoplankton production in the Sargasso Sea. The phosphate budget of the Mediterranean Sea was discussed by several speakers. Mr Salen then described Norwegian work carried out in collaboration with *R R S Discovery II* west of Portugal. Current measurements from an anchored ship allowed the tidal streams to be analysed, they were present to the bottom (760 m) and showed no decrease in velocity with depth, but there were indications of some differences in the direction of rotation. The residual current, however, decreased with depth.

Prof N Menendez (Spain) gave an account of temperature and salinity conditions along the meridian of Tarifa in August 1958. Sections were worked at different states of the tide and the distributions found could only be explained in terms of changing mixing conditions depending on the strength of the tidal streams.

Mr L V Worthington and Mr W G Motcalf (U.S.A.) examined the salinity/potential temperature

relationship in the North Atlantic deep water using the very precise salinity data that have now become available with the development of conductimetric techniques. A salinity/potential temperature curve for the western North Atlantic below the 4°C potential isotherm has been established and its shape accounted for in terms of water masses. Departures from this curve in different parts of the Atlantic can be used as indicators of water movement. The outstanding features shown by this form of analysis were the formation of the newest Atlantic deep water in the Labrador Basin, the part played by the South East Newfoundland Ridge in preventing the Antarctic bottom water from reaching the Labrador Basin, the water of the Norwegian Sea origin on the eastern slope of the mid Atlantic Ridge, the outflow and spreading of Mediterranean water, and the fact that the western basin of the South Atlantic is the source of the deep cold water found in the rest of the Atlantic, communication to the eastern basin being through the Romanche Trench.

A paper by Mr J R Lumby (U.S.A.) read by Dr Tait showed that there were large differences in the dissolved oxygen values at comparable stations worked by American, British and Russian ships during the International Geophysical Year. Mr Worthington said that such differences could depend to some extent on the type of water bottle used, and on the method of standardization of the sodium thiosulphate solution used for titrating the samples.

Baltic and North Seas. In a paper on the southern Baltic Sea, Dr A Majowski (Poland) showed that the inflow of oceanic water had decreased since 1951-52 and that at the end of 1958, the salinity in the Baltic basins had reached its lowest level since 1952. The year 1958 had been a cold one so far as the Baltic was concerned. Similarly in a paper on the North Sea by Dr J Elarski (Poland), read by title, the winter and spring of 1958 were shown to have been cold, but by the autumn of 1958 there were positive anomalies of temperature. Dr V V Betin and Prof J V Preobrazhskii (U.S.S.R.) submitted a paper which was read by title on ice research in the Baltic during the International Geophysical Year. Aircraft were used to make synoptic surveys of ice conditions. The curves of accumulated temperature, ice extension and ice accretion so produced were found to be related.

Biology

Prof E Steemann Nielsen (Denmark) presided over the biological session.

Productivity. Three papers were presented. The first was by Mr Grim Borgø (Norway) on the productivity of the Norwegian Sea using, besides carbon 14 measurements, an estimate of productive capacity derived from measurements of transparency. A continuously recording transparency meter was described. It was shown that in 1958 the quantity of production as measured by 'productive capacity' was different from that in 1954. In reply to a question as to whether there was a correlation between productive capacity and standing stock, Mr Borgø replied that there was, but that the relationship was different in different water masses. Prof Braarud commented on the marked changes noticed from year to year and their apparent relation to hydrographic processes.

Mr Vagn Hanson and Prof E Steemann Nielsen described carbon 14 measurements and chlorophyll measurements in the North Atlantic and in the Greenland Sea. Mr Hanson showed that from Cape Farwell to Ireland greater counts of carbon 14 were obtained towards Greenland and above the Reykjanes Ridge. This was associated with greater quantities of chlorophyll. Prof Steemann Nielsen demonstrated the relationship between carbon 14 counts and quantities of chlorophyll *a* which was biased by the possible presence of dead chlorophyll. Mr G Murphy (U.S.A.) asked whether transparency might not be a better method of measuring productivity if the constants in the equation were known. Prof Steemann Nielsen replied that this would be a good method in oceanic waters but in coastal waters the quantity of inorganic material was high. Dr M Gillbricht (Federal Republic of Germany) pointed out that only one third of the turbidity in the Irminger Sea was due to plankton. Mr Borgø said that the quantity of inorganic particles ordinarily was constant and so the variations due to production differences could be estimated.

Biophysics and Biochemistry. Dr H. Schaefer (Federal Republic of Germany) described the distribution of amino acids in redfish (*Sebastes*) and certain other fish for a number of stations at sea. It was shown that the variation in relative composition of certain amino acids was much greater than that which might have been expected from studies in freshwater fish. Mr Murphy noted that a similar result had appeared in the work on the Californian sardine.

Plankton. Dr A. T. Wiborg (Norway) described the distribution of zooplankton in the Norwegian Sea. He noticed that the distribution of respiration on the echo sounders at full gain corresponded fairly well with the distribution of euphausiids and fish fry. The distribution of copepodite stages bore some relation to hydrographical conditions. In response to a question, Dr Wiborg said that smaller fish have smaller eggs and spawn later.

Drs E A Pavstikov and L N Grutsov (U.S.S.R.) presented a paper on the distribution of plankton in the Norwegian Sea. This distribution corresponded reasonably well with that presented by Dr Wiborg.

Dr J H Fraser (Britain) described indicator species in the Faroe-Iceland Ridge region and from the presence or absence of certain long lived animals concluded that the International Geophysical Year was not a normal year. Mr Loo pointed out that during the first eight months of 1958 the Polar Front lay well to the south, presumably holding back the northward flow of Atlantic water.

Dr Gillbricht gave a detailed account of the distribution of phytoplankton, zooplankton and organic particles on a section between Newfoundland and the Azores. Counts were made from small water samples of 0.3 ml for phytoplankton and of 5 ml for zooplankton. By converting all quantities to total carbon and comparing these with phytoplankton, he was able to distinguish three water masses. Prof Steemann Nielsen asked whether the organic particles were artefacts, because if the same technique is used in Danish waters many organic particles were derived from the destruction of phytoplankton. Dr H. Einarsson (Iceland) noticed that the quantity of *C. closterium* collected was fairly constant in the T. *closterium* was a fairly constant indicator that

collected with a 5-ml water sample in the same area

Mr J Corlett (Britain) described the zooplankton collected at weather stations *I* and *J* and showed that the total quantities were greater in 1958 than in 1957. Mr Hanson noticed that *Eudae nordmanni* had also been found in the Norwegian Sea. Dr Fraser said that *Thalia democratica* found by the Plankton Expedition in 1888 off west Scottish coasts appeared for the first time off west Scottish coasts in 1958.

Dr W Höhnke (Federal Republic of Germany) presented an interesting paper on the quantity and types of fungi in the sea and on the sea bed. The majority of samples taken showed development of hyphae.

Fisheries Dr Eggvin presented a paper by Mr L Midttun on echo surveys in the Barents Sea. In

general, there was a relationship between the distribution of echo-traces and isotherms in the Barents Sea.

Conclusions There appeared to be two main conclusions from the biological papers.

(1) The International Geophysical Year differed in two respects from some other years, in indicator species and in quantity of living material.

(2) Three advances in productivity studies were revealed: (a) the use of transparency as an index of productivity under certain limited conditions, (b) the fairly close relationship between standing stock (as chlorophyll) and productivity (as carbon-14 count), (c) the use of very small samples of phytoplankton (0.3 ml) and zooplankton (5 ml) to give sensible estimates of carbon in living material.

A J LEE

D H CUSHING

EFFECTS OF FOREST AREAS ON WATER RESOURCES, AND THE TECHNIQUE OF LYSIMETRY

BETWEEN September 8 and 13, two symposia were held in Germany by the International Association of Scientific Hydrology, at Hannover-Münden, where the Forestry School of the University of Göttingen is established.

One symposium concerned the influence of wooded areas on the elements of the water balance. Thirty-five papers were presented, ten from the U.S.S.R., eight from the United States, four from Great Britain, two each from Finland and Poland and one each from the Belgian Congo, Czechoslovakia, Denmark, French Africa, Germany, Holland, Hungary, South Africa and Switzerland.

The other symposium dealt with the technique of lysimetry and the causes of error in results obtained. There were seventeen papers, four from the United States, three from Holland, two each from the Belgian Congo, Germany and the U.S.S.R., and one each from Austria, France, Hungary and Great Britain.

The papers were made available in printed form at the meeting and have since been placed on sale by the Association*. Most of them are written in English, and the few others in French or German.

The symposia were attended by more than a hundred hydrologists, from other countries as well as from those which contributed papers. There was naturally a strong German representation, while both the United States and Great Britain had important teams. It was regretted that, while the U.S.S.R. had sent several valuable papers, their authors were not present to introduce them.

Below is given an appreciation of each of the two symposia and of a two-day visit paid afterwards to German field-stations concerned with one or other of the two subjects that had been discussed.

It is expected that the discussions of the papers will be reported briefly in the quarterly issues of the Association's *Bulletin*, the price of which is 150 Belgian francs only.

* Publication No. 49 (Vol. 1. Water and Woodlands) Pp. 340, 300 Belgian francs. Publication No. 49 (Vol. 2. Lysimeters) Pp. 109, 150 Belgian francs. Obtainable from Mr Arthur F. Bird, 66 Chandos Place, London, W.C.2, or the Secretary of the International Association of Scientific Hydrology, Prof. L. J. Tison, 61 Rue des Ronces, Gentbrugge, Belgium.

Water and Woodlands

In many countries, increasing concern with the provision and maintenance of adequate water supplies in the face of continuously increasing demands has stimulated considerable interest in the scientific management of this most vital of our natural resources. With fuller appreciation of the importance of form of land use in catchment areas, much attention has naturally been directed to the role of a forest cover. Compared with other countries such as the United States and Germany, Britain is a rather late entrant into this field, but within recent years, the problem has come very much to the fore and there can be no doubt, especially in view of the recent drought, that we shall have to devote very much more attention to this important issue. As elsewhere, differences of opinion exist as to whether, from the hydrological point of view, our catchments are better under forest than, say, under pasture. The answer is by no means as clear-cut as some would make out; the hydrological relationships involved are most complicated and objective quantitative assessments beset with considerable practical difficulties. It was therefore most timely that under the auspices of the International Association of Scientific Hydrology much of the experience and present knowledge in this field could be surveyed and discussed.

Almost half the contributions were concerned with investigations on the catchment scale. In principle, those involve the measurement of precipitation and run-off (both surface and subsoil), normally by stream gauging, despite the substantial cost of installation and maintenance, and, very often, difficulties in ensuring absence of leaks and a reasonable standard of precision, this approach is still essential for the provision of the basic hydrological data appropriate to the problem as a whole. As an alternative to the 'straightforward' comparison, say, between forested and non-forested catchments, Idson (U.S.S.R.) preferred continuous measurements on an area under the influence of a varying forest cover. Because of the well-known difficulties in ensuring comparability between catchments, this

latter approach would generally seem to be the more reliable one, the regression techniques used by Idson and by Anderson and Hobba (U.S.A.), in which run off is related to the various meteorological, soil or land use factors which influence run-off, offer an approach which allows for a more complete interpretation of the complex relationships involved.

In those countries where snow forms an important source of water there was general agreement as to the beneficial influence of a forest cover, the data of Anderson and Hobba (U.S.A.), Goodell (U.S.A.), Martinelli (U.S.A.) and Sozykin (U.S.S.R.) clearly showed that through accumulation and the shelter provided, the forest retards thawing, reduces the danger of spring floods and prolongs the supply of melt water. The difficulties of measuring snowfall and the need for further investigation were made clear in the papers of Martinelli (U.S.A.) and Sepänen (Finland).

General recognition was also given to the higher permeability and greater storage capacities of soils developed under forest, leading to reduced surface run-off, less erosion and a more prolonged yield of water during drought. Anderson and Hobba (U.S.A.), Valek (Czechoslovakia) and Banky (Hungary), among others, clearly demonstrated the regulatory effect of the forest on stream flow. Rodier (French West Africa) showed that flood peaks were 8-12 times lower from forest than from savannah, and the importance of this effect was recognized by Wicht in his published recommendations for the management of catchment areas in South Africa.

So far as absolute quantities were concerned most contributors were prepared to accept a somewhat lower yield from a forested area as compared with areas under other vegetative covers. Megunus (U.S.A.) provided one of the more extreme examples from the classical Coweeta experiments in North Carolina, where clear cutting of mountain hardwood forest increased the annual yield by 11-17 in and cutting of the shrubby understory by 2 in. To conserve water in the south western United States, Horton recommended the clearance of phreatophytes (vegetation with permanent access to ground water) along streams and rivers. While such losses from forest stands were generally attributed to higher levels of transpiration, usually because of deeper rooting and access to water during dry periods, some would attempt to explain at least some of the losses to interception of precipitation by the foliage. Thus, Eidmann (Germany) stated that because it intercepts appreciably less rainfall a beech forest conserves more water than a spruce forest. The implied assumption that intercepted water means a corresponding loss to the soil was contested by Leyton and Carlisle (Great Britain), who produced experimental evidence indicating, as might be expected, a marked fall in transpiration following wetting of the foliage, attention was also directed to the possibility of rather large errors in the estimation of through fall in a stand using a limited number of gauges, and the increase in accuracy obtainable when these were replaced by troughs with larger collecting areas. The papers of Bochkov and certain other Russian contributors provided an interesting contrast to the generally prevailing opinion that a forest cover means a lower yield of water. These authors argued that, because of deep ground water movement in forest soils, the gauging of small streams draining small catchments may under-estimate the yield and that over large areas, in certain cases at least, yield from the forest

may be even higher than that from open land. Sokolevsky (U.S.S.R.) also claimed that an increased water loss from forest by transpiration may be balanced by reduced evaporation from the soil. It is possible, therefore that even in the case of water yield, final judgment on the effect of a forest cover may have to be postponed, from the point of view of energy relations, at least one would not expect large differences in the loss of water from different types of vegetative cover.

A number of contributors described other means of investigating quantitatively the hydrological relations of a site. Visser (Holland) explained his soil moisture flow approach which provides an estimate of the water balance from measurements of rainfall potential evaporation and the ground water level in the soil and in ditches. Lebedev (U.S.S.R.) also provided an interesting analysis of ground water dynamics under forest and grass covers. From measurements of water loss from detached shoots of Scots pine Rutter (Great Britain) gave evidence of transpiration values apparently exceeding Penman's estimate of E_T (potential evaporation from grass); this, combined with his observations that the trees continued transpiring even down to a soil moisture deficit of 7 in or more, introduces still further problems in our interpretation of forest hydrological relationships. As yet another approach to the estimation of water losses from forest stands, Leyton (Great Britain) discussed the possibility of measuring the volume rate of sap flow in tree stems by the heat pulse method originally introduced by Huber. It was regretted that, apart from a few words in discussion by Baumgartner (Germany) there was no opportunity to learn of the present status regarding the energy balance approach.

In summarizing one's general reaction to the papers reported above and to the subsequent discussions one cannot but be impressed by the magnitude of the efforts made to gain a better understanding of the hydrological relationships of the forest. At the same time it is evident that much still remains to be done. So many aspects have to be considered and so many factors are involved that it is usually not possible to extrapolate findings from one area to another, in this respect the use of regression analysis to define certain underlying relationships has a very promising future. It is also clear that most countries do not look at the forest simply as a potential drain on water supplies, to be avoided wherever possible. As H. C. Storey, director of the U.S. Forest Service Division of Watershed Management Research, pointed out, the emphasis must be on the multiple use of the forest. Lambor (Poland) echoed the same theme in his recommendations for a water economy plan based on the proper appreciation of the comprehensive role of a forest cover.

Following the symposium, an excursion was made to various forest catchment experiments in the area. Eidmann (Düsseldorf) demonstrated two of his seven stream-gauge installations set up in small catchments to investigate the influence of various types of forest cover and of forest practice, primarily on water yield, at Lahnhof, beech and spruce forest are being compared and at Helgersdorf, coppice and high forest. The Ruhrtalesperrenverein, the organization largely responsible for supplying water to the Ruhr industries, has nine similar installations (two of which, on the Runkhauserbach (90 per cent forest) and the Königswasser (87 per cent arable) were also inspected.

Coming from a country with similar water problems, but without a single catchment experiment designed specifically to investigate forest influences, one is greatly impressed by the enthusiasm with which these problems are being tackled in Germany. It is not difficult to criticize many of these installations, precipitation measurements, stream-gauge design, the possibility of leaks and questionable comparability of catchments, all raise problems which could readily intimidate the ultra-cautious, particularly in view of the costs involved. Nevertheless, with the example set by the Americans, Germans and other nationals, and with access to their knowledge and experience, can we in Britain afford not to set up similar experiments of our own? L LEXTON

Lysimeters

A lysimeter is an apparatus used for measuring the quantity or quality of water which has percolated through a container which is filled with soil or similar material. It is easy to see that, within such a definition, lysimeters can be used for such a variety of specific purposes that each installation must be considered on its own merits, an ever-present danger is to interpret what is measured by means of the lysimeter as being representative of any conditions other than those obtaining in the lysimeter itself.

Lysimeters are commonly installed to throw light on what happens in the field, where many different factors affect the amount of percolated water. The position is essentially similar to that encountered in measuring temperature, rainfall and other meteorological factors, where, however, arbitrary standards of measurement have been accepted for purposes of making comparisons between values obtained at different sites. So far, standard conditions have not been accepted for lysimeter installations and readings, and indeed comparatively few suggestions have been put forward for standardization of observations.

It is thus not surprising that several of the papers read at the symposium described lysimeters which could throw some light on what happened, with the passage of time, only in particular circumstances. Various ingenious and, in some cases, expensive installations have been set up, in which care has been taken to avoid such things as disturbance of the natural soil profile, or of the homogeneity of the vegetation cover. But in almost none were there lacking unmeasured variables which, even though in some cases a correlation with adjoining field conditions could satisfactorily be established, allowed of any trustworthy comparison between one site and another.

W C Visser, of the Netherlands, was one of those who read papers pointing out that conditions in a lysimeter are essentially artificial, and that the factors introduced by this artificiality need to be measured or eliminated. Visser particularly recommended water-flow potential measurements in the field to 'calibrate' the lysimeter measurements, this involves measuring ground-water depth, tension in the capillary zone, tensions in the plants, and vapour pressures in the air. K Ubell, of Hungary, placed emphasis on the need to have constant records of the temperature gradients in the field and in the lysimeter. Harrold and Dreihelbis, in describing some of the work at the well-known installations at Coshocton, Ohio, showed themselves vividly aware of difficulties, which have failed to be understood by some who have quoted the Coshocton results too uncritically.

Lysimeters can broadly be divided into those measuring volume and those measuring weight. There is much to be said for the latter, because not only do they help to overcome the problem of changes in the amount of water stored in the lysimeter, but they also enable changes to be recorded as continuously as is desired, lysimeters working on volumes of outflow water necessarily have by contrast a much more considerable time-lag. Several speakers, however, pointed out that weighing lysimeters were not the complete answer which some had incautiously considered them to be, for example, one is not sure whether what is being weighed at one season is strictly comparable to that being weighed at another time of the year.

E J Winter (Great Britain) read a joint paper by P J Salter, G Stanhill and himself describing the installations at the National Vegetable Research Station in Warwickshire. Besides directing attention to some interesting and significant results which need further investigation, he stressed that much satisfactory and adequate practical advice can now be given to growers, even though more research is needed to elucidate the mechanisms of, and variations in, the water balance.

G F Makkink, in describing the various installations in the Netherlands, made the following useful summary remark: "It is considered the final aim of lysimeter research to gain an insight into the water balance of any natural soil-profile as a function of climate, vegetation and movement of the ground water. This aim widely surpasses the limited scope of the lysimeter observation of the separate institutions who own them." The recognition of this has led to appreciable progress in the Netherlands in co-ordinating results.

Several speakers, particularly G L Dupriez (Belgian Congo) and F H W Green (Great Britain), emphasized the value of first obtaining observations of potential evapo-transpiration, under 'standard' conditions, at a network of stations. Cheap oil-drum lysimeters were found to be quite adequate for this purpose, if both sited and handled under comparable conditions. Green pointed out that, by simple subtraction, one could get reasonably reliable values of the seasonal differences in 'water deficit' and 'water surplus' from station to station, even where the absolute values of potential evapo-transpiration and of rainfall were open to doubt. In this connexion, several speakers emphasized the difference between the rainfall measured in rain-gauges at the standard height and that falling on the ground. In both Britain and Germany this seemed to be of the order of rather more than 5 per cent, ground-level gauges are therefore installed at most German lysimeter stations.

One of two week-end excursions at the end of the symposium was devoted primarily to visiting lysimeter installations. The first of these visited was in the Senne heathlands, near Birolefeld, and was operated in connexion with the water undertaking of that town. It consisted of four weighing lysimeters, one metre square cross section, filled (in three cases) with 'monolith' blocks from three different soil profiles found in the area (the fourth was a 'disturbed' block from one of the areas). None of these lysimeters was irrigated, so that, particularly in a dry year like 1959, the lysimeters could supply facts but not explanations.

The second place visited was to an ingenious forest installation at Bossendorf, near Haltern, in Westphalia. Here, in addition to a more orthodox

lysimeter in an adjoining arable field, were two batteries of four lysimeters each, one under a stand of conifers and one under a stand of broad leaved trees. These had been made by pressing large rain gauge-shaped lysimeters upwards into the soil under the trees, from a horizontal gallery, painstakingly excavated to avoid disturbance of the natural conditions. The aim was limited to measuring differences in rates of recharge of soil water but they have not been operating long enough for the results to be assessed.

The third visit was to the installation of the Dortmund Waterworks at Geisbocke on the Ruhr.

Here there are batteries of (a) volume lysimeters, and (b) weighing lysimeters, filled with different materials and with different vegetation covers. Although undoubtedly useful information is obtained, the results from type (a) might be queried in view of the very large amount of bare concrete surrounding the tanks while in both types (a) and (b) reasonable homogeneity with the surrounding vegetation was achieved only in certain of the tanks. In fact, the series of records from each of these lysimeters as at some other installations, could be considered only separately, and not safely compared with those from any of the others.

F W GREEN

OBITUARIES

Prof H J. Backer

HILMAR JOHANNES BACKER was born at Dordrecht on January 13 1882, and died at Glimmen, near Groningen, on April 29, 1959. He was a pupil at the Gymnasium in Dordrecht and studied at the University of Leyden under Francimont on chemistry and H. A. Lorentz in physics. His doctoral thesis was entitled "De Nitraminen en hunne Electro-chemische Reductie". He also worked with Elbs at Giessen on the technique of electrochemical reduction and later in the Davy Faraday Laboratories at the Royal Institution in London. After two to three years on the staff at Leyden and a similar period in industry and in Government service, he was called to the chair of organic chemistry at Groningen in 1916 as successor to J. F. Eykman. His colleague, Dr J. Strating, said that Backer soon showed his capacity for hard work, for concentration and for utilizing every free moment, and yet it seemed that the passage of years only increased his broad humanity.

A survey of his researches (1905-55) reveals an increasing occupation with compounds containing the $-SO_2-$ group. This can be correlated with the early work of Francimont on α -sulphopropionic acid which Backer and Francimont resolved in 1914 by means of strychnine. Backer then prepared and resolved α -chloro and α -bromo sulphoacetic acids, α -seleninopropionic acid, α -sulphobutyric acid, several α -arsenocarboxylic acids and also chlorobromoacetic acid.

About 1930 he began a study with Strating of the unsaturated cyclic sulphones formed from sulphur dioxide and butadienes. The close relation of these compounds to the thiophenes led to a study of the oxidation of thiophen homologues in the hope of obtaining the corresponding sulphones. Thiophen itself, on oxidation, gives a 'sesquioxido' presumably formed by 1,4-addition between the unstable sulfoxide and sulphono of thiophen. It was found that certain dialkyl and diphenyl thiophenes gave sulphones on oxidation. Tetraphenylthiophen had long been known to do so. This was attributed to the presence of the substituents which increased the electron availability on the sulphur atom. In some cases a sesquioxido was formed. On the other hand, electron attracting groups in the benzene nucleus of 3,4-diphenylthiophen inhibited sulphone formation.

In 1952 Backer began to study imines of the type $(R SO_2)_2 C=C=NR$, which are very reactive. Three

of these have recently been submitted to X-ray analysis by Wheatley, Bullough and Daly in Leeds with very interesting results.

At the beginning of the occupation of the Netherlands in 1940, Backer gave much help and advice to his students whose whole world had suddenly fallen to pieces. He kept in touch with all those who were forcibly deported to Germany sent them parcels and encouraged and advised their parents. When I visited Backer in 1947 he referred only briefly to his imprisonment in 1945 and said nothing of the physical violence which he endured during interrogation. The other occupant of his cell was shot. The liberation of Groningen probably saved Backer from the same fate.

Later on, two of my research students visited Groningen at Backer's invitation, lived in his house for some weeks and worked in his Department. Dr A. Ash wrote: "It was his habit to have students lodging with him and he liked nothing better than for students to call in the evening for a short talk, help or advice were gladly given. He interested himself also in their social life. He methodically inquired of his students progress every morning and imparted an impressive practical technique particularly rich in devices for facilitating manipulation of small quantities." Dr A. G. Lowther has said:

"One's immediate impression on meeting him was that here was a man who demanded one's respect and affection. This was not only a first impression—it was there among his students—they had a real affection almost love, for Prof Backer. He never appeared to be hurried, was most courteous and had a quiet, but real, sense of humour. I never heard one word of criticism of him. There was a serenity about him and his house."

Dr Strating wrote: "Nothing could prevent him from helping a friend or a student who was in need, and thus, no doubt led to his arrest." Backer was a knight of the Order of the Netherlands Lion, a member of the Royal Academy of Sciences in Amsterdam, a correspondent of the Paris Academy of Sciences and an honorary member of the Solvay Institute in Brussels. He received honorary doctorates from the Universities of Ghent and Lille.

When those who knew him recall Backer's achievements as a man and as a chemist, his great capacity for friendship and for hard work, his fearlessness and his quiet mind, they feel that he went far towards solving happily the eternal problem *si jeunesse savait si vieillesse pouvait*.

FREDERICK CHALLENGER

Prof E. S. Salmon

AFTER a long illness, Prof Ernest Stanley Salmon died on October 12 at the age of eighty-eight. Anyone unfamiliar with mycology might be pardoned for thinking that his reputation rested on the breeding of new varieties of the hop (*Humulus lupulus* L.). Yet when he came to Wye College (University of London) in 1906, he had already established himself as the authority on an important group of fungi. Researches at the Jodrell Laboratory, Wye, had led to the publication, in 1900, of "A monograph of the Erysiphaceae", a work which remains fundamental for systematic mycology and which was reproduced as microcards only a few months ago. After further study in the laboratory of Prof Marshall Ward at Cambridge, he demonstrated the very highly developed specialization of parasitism in the same group, accounts of this may be found in the *Transactions of the Royal Society*, 1904 and 1905.

Salmon was appointed to Wye College to study diseases of plants and so was probably the first professional plant pathologist in Britain. There were then few helpful text-books, but it was not long before he had combined laboratory work and field experiments to good purpose. His first papers, which may even now be read with profit, describe in some detail a selection of the diseases of crop plants, the main emphasis being on apple scab (*Venturia inaequalis* (Cooke) Wint.) and other pathogens of fruit. Bordeaux mixture and lime sulphur, fungicides which are still in use, were introduced to Kentish orchards, while he conducted a vigorous campaign in the Press and elsewhere which led to the passing of the Destructive Insects and Pests Act in 1907.

He was elected president of the British Mycological Society in 1911, appointed reader in economic mycology in the University of London in 1912, professor of mycology in 1925 and emeritus professor in 1939. He was made Fellow of Wye College in 1948.

When, soon after the First World War, the specialist advisory service in Britain began, he was appointed advisory mycologist of the Wye Province. Until he relinquished this appointment in 1937, he led a series of investigations on diverse plant diseases. Particularly noteworthy are the contributions on fruit and hops with which are associated his colleagues, Drs H. Wormald and W. M. Ware.

Salmon arranged a programme of hop breeding in 1907 and followed this without a break until his last illness. From the beginning, one of his main aims was to produce varieties with exceptionally high preservative values, such varieties would enable the British grower to compete with imported American hops. In order to have at command a wide range of diverse types, he assembled male and female plants from different parts of the world, this unique collection, together with selected progeny, for long occupied about an acre of ground at Wye College. Of the many thousands of seedlings raised, his earliest success was the English-grown American, Brewer's Gold. This was F1 from an English male hop and a wild hop from Morden, Manitoba. Paradoxically, the variety has been more widely grown in Canada and the United States than in Britain. The varieties Bullion and Northern Brewer which have become so popular with the British hop industry during the past decade are F1 and F3 seedlings, respectively, of parents from the same sources. Other seedlings of his raising proved to be tolerant to hop wilt (*Verti-*

illum albo-atrum Reinke and Berth.) and these have been of great value for planting in infected soil.

In recognition of his work on hops he received in 1955 the Horace Brown Medal, the highest honour which the Institute of Brewing can bestow.

After the manner of the pioneer, Salmon was a strong individualist and, in his later years at least, showed little enthusiasm for gatherings, whether scientific or social. He found relaxation in literature and in his small garden of rare plants.

H. H. GLASSCOCK

Prof J. Zenneck

PROF JONATHAN ZENNECK, one of the earliest pioneers of radio science, died in Munich in April, a few days before his eighty-eighth birthday. Prof Zenneck was born in 1871 in Württemberg, Germany, and studied mathematics and natural science at Tübingen, where he obtained his doctorate in 1894. In the following year he became an assistant in the Physical Institute in Strasbourg, he moved to Dantzig in 1905 to become assistant professor, and later (1911) professor of physics in the Institute of Technology. His academic career was continued by his appointment in 1913 to the chair of physics at the Technical High School of Munich, where he remained until his retirement.

Most of the basic contributions of Prof Zenneck were made in the days when spark transmitters were used for wireless telegraphy, concurrently with the development of high-frequency machines and arc generators to produce undamped oscillations for radio-telephony. Among the earliest of his achievements was the establishment of the first radio-link for navigational purposes between Cuxhaven and Heligoland in 1899-1900. His basic experimental and theoretical contributions to wave propagation were of great importance in the early development of wireless communications. He expounded the first theory on wave propagation along the Earth (Zenneck wave) which explained the effect of the ground constants on polarization and absorption of the waves. Also well known are his basic contributions to ionospheric research, which he initiated in Germany; and he was the founder of the first German ionospheric research station, Herzogstand, in Kochel, Bavaria, which was in operation until 1945.

Dr Zenneck's interests were not limited to radio. He also contributed to other areas in the general field of applied physics such as acoustics and gas discharges. He was the author of the first German text-book on wireless telegraphy, "Electromagnetic Oscillations and Wireless Telegraphy", published in 1906, which was the classic work in this field for many years. He was also the editor of the *Hochfrequenztechnik und Elektroakustik*, the leading journal of the time during the early days of radio.

His second book, entitled "Wireless Telegraphy", was published in Germany in 1908, and a second edition appeared four years later. It was translated into English in 1915 by A. E. Seelig, and published in London and New York, forming one of the most useful text-books available to students at that time on the generation, propagation and detection of electromagnetic waves in the radio part of the spectrum.

He received many honours and medals from academic and professional societies, including an honorary doctor's degree from the Institute of Tech-

nology at Dresden. He was made a fellow of the Institute of Radio Engineers (N.Y.) in 1915, received its medal of honour in 1928 and was a member of the board of directors and vice president in 1933. He was honorary president of the German National Committee of the International Scientific Radio

Union, and was elected vice president of that Committee in 1938. All those who had the pleasure of meeting Prof. Zenneck at international conferences will remember his charming personality and his modest simplicity, combined with wit and quickness of repartee.

R. L. SMITH ROSE

NEWS and VIEWS

Nobel Prize for Physics for 1959

Dr Emilio Segre and Dr Owen Chamberlain

Dr Segre and Dr Chamberlain who have been awarded the Nobel Prize for Physics for 1959 have collaborated in research in high-energy physics for a number of years at the Lawrence Radiation Laboratory of the University of California at Berkeley. Dr Segre was born in Italy in 1905 and was a member of Fermi's remarkable nuclear research school in Rome. He emigrated to the United States before the War. Dr Chamberlain is thirty nine and, like Dr Segre, is a distinguished experimentalist. Their collaboration at Berkeley has been associated with the great accelerators which have been built there over the years. They were the leading members of a team engaged in experiments on nucleon-nucleon interaction with the help of the 184-in. synchrocyclotron, and in particular made a detailed study of polarization phenomena in high-energy scattering. The work which has now been honoured by the Nobel award has, however, been their discovery in 1955 of the antiproton in experiments with the 6 GeV proton synchrotron the bevatron. The existence of the antiproton had been confidently postulated for many years: the discovery of the positron in 1932 and its interpretation on the Dirac theory, also implied the existence of other anti-particles including a negatively charged proton. Antiprotons stubbornly eluded discovery in the very high energy (but very low intensity) bombardments of cosmic radiation, and one reason for building the bevatron was to have an intense beam of sufficiently energetic protons to create proton-antiproton pairs in the laboratory.

The actual discovery, however, involved a long series of painstaking experiments with very elaborate detection equipment which had to be specially developed. The development of effective techniques for beam separation and detection for use with machines of very great energy is a field of research in itself. The antiprotons produced when a beam of high-energy protons falls upon a target in a machine like the bevatron are very greatly outnumbered by other charged particles produced with very broad momentum spectra in the relativistic region. These background particles would cause impossible confusion in the detection apparatus if they were not systematically eliminated. Their elimination in the experiments of Segre and Chamberlain was a major programme in experimental physics. The final apparatus used was elaborate and refined. Charge and momentum separation of antiprotons from the mixed beam of particles was achieved by magnetic deflexion and focusing in separate lenses, and velocity selection was aided by time-of-flight and Cerenkov radiation techniques. When some forty events had been accumulated which corresponded within acceptable margins of error with the properties of the antiproton, it could be said that the antiproton had been discovered. As is usual in high-energy research

with large machines, team work by large numbers of physicists and engineers was involved: the award of the Nobel prize to Segre and Chamberlain underlines the fact that the brilliant individual worker is still needed to inspire and direct the work.

Royal Society Medals for 1959

The following awards of medals have been made by the President and the Council of the Royal Society. *Copley Medal* to Sir Macfarlane Burnet, director of the Walter and Eliza Hall Institute, Melbourne, Australia, for his distinguished contributions to knowledge of viruses and of immunology. *Davy Medal* to Prof. R. B. Woodward, of the Department of Chemistry, Harvard University, Cambridge, Massachusetts, for his distinguished researches in organic chemistry and particularly for his contributions to the structure and synthesis of natural products. *Hughes Medal* to Dr. A. B. Pippard, reader in physics in the University of Cambridge, for his distinguished contributions in the field of low temperature physics.

Genetics at Cambridge Prof. J. M. Thoday

A GRADUATE of the University College of North Wales, Bangor, Dr. J. M. Thoday, who has recently been appointed to the Arthur Balfour chair of genetics in Cambridge, began his research career in the Botany School, Cambridge, under the guidance of Dr. (now Prof.) D. G. Catcheside. These early studies of the action of ionizing radiations on chromosome structure were interrupted by war service in the Royal Air Force to be resumed after the War at the Mount Vernon Hospital and Radium Institute, where, in collaboration with Dr. J. Read, Thoday demonstrated the effect of oxygen tension on the frequencies of chromosome changes following irradiation. During 1947 he moved to Sheffield to take up an appointment as lecturer in cytogenetics, becoming senior lecturer in charge of the newly founded Department of Genetics there in 1954. In Sheffield his research moved towards the field of population genetics, particularly in relation to the genetical control of stability in development and to the action of disruptive selection. His experiments with *Drosophila* have been especially rewarding in the light they have thrown on the power of disruptive selection to conserve variability and to build up polymorphisms within populations. They are showing us for the first time under controlled conditions how polymorphisms can come into being and how their genetical structure reflects the selection which has brought them about. Prof. Thoday's breadth of experience and originality of approach augur well for the future of genetics in Cambridge.

Genetics at Sheffield

Dr J. A. Roper

Dr. J. A. ROPER returns to his own University (Sheffield) as the first holder of the new chair of

enetics Dr Roper graduated in chemistry at Sheffield in 1945, and was trained in bacterial biochemistry under Krebs and McIlwain. He joined the Genetics Department at Glasgow in 1948 and played a very important part in the development of that school of genetics. For his ability as a teacher, and his engaging personality, he is well liked by the students. At Glasgow he introduced, with great success, group discussion methods. Dr Roper was Rockefeller Fellow in 1953 at the California Institute of Technology, and has lectured at various times at a number of American and European universities. He is secretary of the Genetical Society.

Dr Roper's training in chemistry and microbial biochemistry was a good foundation for the research in microbial genetics on which he embarked at Glasgow. He played a major part there in a team working on the genetics of *Aspergillus nidulans*. A most decisive contribution was the first deliberate search for, and his demonstration of, what could be called the 'splitting of the gene' (*Nature*, 166, 956, 1950). Soon after he designed a way of synthesizing heterozygous diploid strains in filamentous fungi. This was the first step which made possible the discovery of the 'parasexual' cycle and the development of genetic analysis *via* mitotic segregation. In the last three years Dr Roper has become interested in investigating extra-nuclear inheritance in *Aspergillus*. Dr Roper's ability in teaching and research will be given full opportunities in this new chair, born in a most favourable environment.

The Animal Health Trust

H.M. THE QUEEN has graciously consented to become patron of the Animal Health Trust. The Trust was founded by Dr W. R. Wooldridge in 1942 for the purpose of improving the general health standards of all types of domesticated animals, and it approaches the task in two ways. First, by means of scientific investigation of the many disease problems of such animals, secondly, by stimulating the flow of trained personnel into the ranks of the veterinary profession through financial grants to needy students and by furthering the higher education and specialization of veterinary graduates. Four research centres have been established by the Trust for the study of disease in horses, dogs, poultry and farm animals, respectively, the latest of which—the Farm Livestock Research Centre at Stock, Essex—was opened by H.R.H. Prince Philip in December 1957 (see *Nature*, 181, 76, 1958). A new surgical unit to mark the patronage of the Queen is to be built at the Equine Research Station, Newmarket, at a cost of about £30,000.

The Office of the Lord Privy Seal

WITH the appointment of Lord Hailsham as the Minister with general responsibility for science and technology, including atomic energy, the Atomic Energy Office and the Lord President's Office will be combined. The new Office will be in the charge of Mr F. F. Turnbull, whose appointment as deputy secretary, to succeed Sir Friston How in charge of the Atomic Energy Office, was announced some months ago. It will be organized in two Divisions: (1) a General Division, under Mr R. N. Quirk, under-secretary, corresponding to the previous Lord President's Office, and (2) an Atomic Energy Division, under Mr M. I. Michaels, under secretary, corresponding to the previous Atomic Energy Office.

Parliamentary Responsibility for Science and Technology

THE Prime Minister made a statement in the House of Commons on October 30 regarding the responsibilities of the Lord Privy Seal and the Minister for Science, stating that other Ministers would remain responsible for the scientific establishments within their own Departments, but that the Minister for Science was to be responsible for broad questions of scientific policy outside the sphere of defence, and was advised by the Advisory Council on Scientific Policy on general questions which relate to the whole field of civil science. On November 3, Mr Macmillan indicated that the arrangements for answering questions in the House of Commons which fall within the responsibility of the Minister for Science would be as follows: questions about the Medical Research Council and radiobiological hazards, the Minister of Health; Agricultural Research Council and Nature Conservancy, the Minister of Agriculture; nuclear energy, the Department of Scientific and Industrial Research and general scientific matters, the Minister of Education; space research, the Minister of Aviation. Where questions about the development of nuclear energy relate to matters for which some other Minister is responsible, that Minister would answer them. For example, questions about nuclear-powered merchant shipping would normally be answered by the Minister of Transport, and about nuclear power stations by the Minister of Power. Mr Macmillan had earlier defended the exclusion of the new Minister of Power from the Cabinet, but neither that arrangement nor those for answering questions for the Minister of Science in the House of Commons were well received.

Scientific Developments in Britain

REPLYING to a question in the House of Commons on November 2, Mr J. B. Godber, as representing the Lord Privy Seal, said that a small temporary station is to be established near Cambridge to expand the work already being done at the Low Temperature Research Station and elsewhere, and he hoped it would be in operation by the end of next year. Meanwhile, the Agricultural Research Council is considering the wider issues raised by the proposal to establish a permanent centre for meat research. In a written answer on November 5, the Minister of Education, Sir David Eccles, as representing the Minister for Science, stated that the new Hydrodynamics Laboratory of the National Physical Laboratory had cost about £2 million, and its staff was nearly 70, including 10 scientific officers. The Laboratory would provide up-to-date facilities for testing ship designs, particularly in reproducing more realistic sea conditions, and research would be conducted to extend basic knowledge of the resistance, propulsion and sea going qualities of ships, while new ship designs would be tested for industry.

In a written reply to a further question on November 5, Sir David Eccles said that commissioning trials of the fast reactor at Dounreay had proved more difficult than expected, due to chemical engineering problems, but enriched uranium is now being loaded and the reactor is expected to become critical within the next few weeks. This reactor, he said, is an experiment in the development of fast breeder systems, and successful exploitation will depend upon the operating results. The development of the fast reactor will occupy the resources of the Dounreay

establishment for many years. The Admiralty submarine reactor development programme at Donrae is now getting under way and firms in the north of Scotland with the necessary scientific and technical experience would be given the opportunity of tendering for any development work which could be let out to industry.

Inauguration of Merlin

WHEN H.R.H. the Duke of Edinburgh formally inaugurated *Merlin* the nuclear research reactor built by Associated Electrical Industries Ltd. (see *Nature* September 5 p. 11) at Aldermaston on November 8 in an underwater closed-circuit television camera specially designed by E.M.I. Electronics Ltd. made possible the observation of activity inside the reactor. This camera, which is 30 in. long, $3\frac{1}{2}$ in. in diameter and enclosed in a pure aluminum water tight housing, is a permanent part of the equipment of *Merlin*. In addition, a standard E.M.I. camera has been mounted above the reactor on the second floor of the reactor hall. This provides a continuous view all around *Merlin* and ensures that no unauthorized staff are near the reactor when it is in use. Two 14-in. receivers, one for each camera, have been rack mounted in the control room on the ground floor and another receiver has been installed on the second floor for observation inside the reactor. A 17 in. console receiver, capable of selecting a picture from either camera, has been installed in the reactor conference room. Three more E.M.I. cameras and seven more receivers were used at the opening ceremony to give the audience an uninterrupted view of the proceedings from the moment the Duke of Edinburgh entered the reactor hall on the ground floor, while he was inspecting the top of *Merlin* from the second floor, and upon his return to the ground floor to start the reactor and unveil a commemorative plaque.

Joint British Committee for Vacuum Science and Technology

FOLLOWING the Institute of Physics' London Conference on high vacuum held in April last various suggestions were made for arranging regular meetings in Britain on vacuum science and technology, and for British participation in international conferences in this field. As a result of informal discussions a Joint British Committee for Vacuum Science and Technology has now been formed. The Committee consists of representatives from each of the following bodies: Institute of Biology, Institution of Chemical Engineers, Royal Institute of Chemistry, Institution of Electrical Engineers, Iron and Steel Institute, Institution of Mechanical Engineers, Institute of Metals, Institute of Petroleum, Physical Society and Institute of Physics. Its objects are (a) to co-ordinate and help to initiate meetings in the whole field of vacuum science and technology arranged by constituent bodies, and (b) to act in the collective interest of the constituent bodies by maintaining liaison with the International Organization for Vacuum Science and Technology and with national vacuum societies, and otherwise. The Institute of Physics has agreed to provide the secretariat for the joint committee; communications should be addressed to the Secretary of the Joint British Committee at 47 Belgrave Square, London, S.W. 1.

Scientific Policy in South Africa

THE first and second annual reports of the Advisory Council on Scientific Policy of the Union of South

Africa cover the periods December 1956–December 31 1957 (pp. 5) and January 1–December 31 1958 (pp. 7), respectively (Pretoria: Advisory Council on Scientific Policy, 1958 and 1959). The Council which has nine members, including Prof. H. O. Mönnig as chairman, was appointed late in 1956 to enquire into and report on all matters referred to the Council by the Minister of Economic Affairs. It is required to acquaint itself with scientific developments and policy in other countries and to advise the Minister concerning any action necessary in South Africa to take note of all international scientific conferences and make recommendations regarding representatives, and to investigate cases of overlapping of research and other activities referred to the Council by the Minister and make recommendations as to responsibility for the work.

In its first report the Advisory Council, attributing the shortage of scientists and technologists fundamentally to weaknesses in secondary education, recommended that the Government should increase both funds and facilities available for training scientists at the universities, as well as actively promote the training of technologists and improve the salaries and conditions of employment of scientists. A survey of the country's requirements for scientists and technologists by the Research Bureau of the Department of Education, Arts and Science was also recommended, and the Council's consideration of the condition and organization of research issued in a recommendation for the appointment by the Government of a commission to investigate the organization of agricultural research and the establishment of an independent Agricultural Research Council. The Advisory Council does not consider its responsibility regarding attendance at international conferences can be satisfactorily discharged under the present arrangements or that the set up permits adequate access in general to Cabinet level.

In its second report the Advisory Council recommends the compilation and maintenance by the National Bureau for Educational Research of a National Register of Scientists and Technologists. Some consideration was given to the relation between the Council for Scientific and Industrial Research and the universities, and at the request of the South African Chemical Manufacturers' Union the Council considered the desirability of Government support for research on the processing of agricultural products, but concluded that the proposal was undesirable and that developments in this field should be left with the Council for Scientific and Industrial Research. An inquiry into overlapping of State-aided research requested by the Treasury led to the recommendation that the Government Metallurgical Laboratory should become an institute of the Council for Scientific and Industrial Research. A Cabinet Committee has been appointed to investigate the shortage of man power in science and means of reducing this shortage, and a commission is investigating the desirability of an independent Agricultural Research Council, but otherwise no action appears to have been taken on the recommendations suggested in the first report.

Inland Telegraph Service

THE Committee appointed during December 1957 under the chairmanship of Sir Leonard Sinclair to advise the Postmaster General on the future plans of the inland public telegraph service as part of the

communication facilities of the United Kingdom", does not consider that, subject to keeping under review the extended use of the telephone for sending telegrams over the shorter distances, further integration of telegraphs with telephones, as recommended by the Bridgeman Committee of 1932, would be justified at present, though there may be scope for further integration with the telephone service or possibly with the telex service later. The number of telegrams has steadily declined from 53.3 millions in 1947-48 to 18.7 millions in 1956-57 and an estimated 16.9 millions in 1957-58, and the loss per telegram has risen from 14.2d to 40.3d in 1956-57 and 48.2d in 1957-58. This is mainly due to the relatively small gap in the communications facilities of the United Kingdom filled by the service and this gap is being reduced in size by other Post Office services. Foreign administrators face a similar problem and the traffic is expected to continue to decline. Although the service is only of marginal importance to business establishments and only occasionally used by the public for social purposes, in its report the Committee recommends retention of the service to handle a proportion of overseas and emergency telegrams and for other reasons (Report of the Advisory Committee on the Inland Telegraph Service, 1958 Pp iii+11 London: H.M. Stationery Office, 1958 1s net). Increase of the tariff is recommended and the new structure should be one of a basic charge plus a charge for every word. The Post Office, it is suggested, should consider the elimination or reduction of the deficits due to Press traffic and telegrams to the Irish Republic and should arrange to charge the British Transport Commission with the cost of Railway Pass telegrams.

Meldola Award

It is announced that the next award of the Meldola Medal will be made early in 1960 to the chemist who, being a British subject and under thirty years of age at December 31, 1959, shows the most promise as indicated by his or her published chemical work brought to the notice of the Council of the Royal Institute of Chemistry before December 31. The merits of the work may be brought to the notice of the Council, either by persons who desire to recommend the candidate or by the candidate himself, by letter addressed to the President, Royal Institute of Chemistry, 30 Russell Square, London, W.C.1, from whom further information can be obtained.

Royal Society of Edinburgh: Officers for 1959-60

At the annual statutory meeting of the Royal Society of Edinburgh the following officers and members of Council were elected: *President* Prof E. L. Hirst, Department of Chemistry, University of Edinburgh. *Vice-Presidents* Dr D. P. Guthbertson, Mr A. W. Young, Prof T. Neville George, Prof J. R. Matthews, Dr T. R. Bolam, Dr Douglas Guthrie. *General Secretary* Prof Norman Feather, Department of Natural Philosophy, University of Edinburgh. *Secretaries to Ordinary Meetings* Dr A. W. Greenwood and Dr Mowbray Ritchie. *Treasurer* Dr J. R. Peddie. *Curator* Dr R. Schlapp. *Councillors* Prof A. M. MacBeath, Prof R. A. Rankin, Prof A. E. Ritchie, Prof V. C. Wynne-Edwards, Prof E. G. Cullwick, Prof G. Pontecorvo, Prof M. M. Swann, Prof H. A. Bruck, Prof T. S. Westoll, Dr H. R. Fletcher, Prof G. L. Montgomery, Prof W. L. Weipers.

Announcements

THE Minister for Transport and Power for the Republic of Ireland has appointed Mr J. Connor, of the Department of Transport and Power, to be chairman of the National Committee for Geodesy and Geophysics in succession to Mr A. Ó Coinneam.

Mr R. LEVIN has been appointed development planning executive at Aspro-Nicholas, Ltd., of Slough, Bucks. Mr Levin was formerly chief pharmacist, Research and Development Division, and lately manager of the Technical Information Department of the Distillers Co. (Biochemicals), Ltd. He is the author of "The Pharmacy of Silicones and their Uses in Medicine".

FOLLOWING the resignation of Dr C. E. Dalgliesh as secretary of the Biochemical Society, Dr P. N. Campbell, Courtauld Institute of Biochemistry, Middlesex Hospital, London, becomes secretary to the Committee, and Dr W. J. Whelan, Lister Institute, Chelsea Bridge Road, London S.W.1, has been appointed meetings secretary.

THE National Collection of Industrial Bacteria has been transferred from the National Chemical Laboratory to the Torry Research Station (Department of Scientific and Industrial Research). All future inquiries and correspondence concerning the Collection should be addressed to the Curator, National Collection of Industrial Bacteria, Torry Research Station, Aberdeen.

A symposium on haematology has been organized by the University of Cambridge Post-Graduate Medical School, and will be held during December 7-9. Further information can be obtained from the Secretary, Medical School, Tennis Court Road, Cambridge.

THE U.S. Office of Naval Research has announced that the second Conference on Semiconductor Surfaces will be held at the U.S. Naval Ordnance Laboratory, White Oak, during December 3-4. Further information can be obtained from the chairman of the Steering Committee, Dr J. N. Zemel, U.S. Naval Ordnance Laboratory, White Oak, Silver Spring, Md.

THE Indian Society of Theoretical and Applied Mechanics has announced the Fifth Congress on Theoretical and Applied Mechanics, to be held at the University of Roorkee during December 23-26. Further information can be obtained from the Secretary-Treasurer, Indian Society of Theoretical and Applied Mechanics, Institute of Technology, Kharagpur, India.

THE autumn general meeting of the British Iron and Steel Institute will be held in London during December 2-3. The sessions, some of which will run simultaneously, will be held in the Great Hall, Caxton Hall, S.W.1, and in the Hoare Memorial Hall, Church House, S.W.1. Further information can be obtained from Mr K. Headlam-Morley, Iron and Steel Institute, 4 Grosvenor Gardens, London, S.W.1. All applications must be returned by November 27.

ERRATUM In the article entitled "Transmission of a Virus to Strawberry Plants by a Nematode (*Xiphinema* sp.)" in *Nature* of September 26, p. 962, line 5 in par. 2 should not have been inserted. The phrase should read "the causal virus of yellow crinkle and of mosaic was transmitted by mechanical inoculation from plants of a number of strawberry varieties, including . . .".

INTERNATIONAL UNION OF PURE AND APPLIED CHEMISTRY

COMMISSION ON GEOCHEMISTRY

THE Commission on Geochemistry of the International Union of Pure and Applied Chemistry held a meeting in Munich during August 26-27, during the twentieth Conference of the Union. Attending the meeting were the following members of the Commission: Prof T F W Barth (*president*), Dr F M Vokes (*acting secretary*), Prof C W Corrins, Prof C W Corrins, Prof S I Tomkoleff, Prof L R Wager, Prof F E Wickman and three observers of the Commission: Prof A P Vinogradov, Prof K. Sugawara and Prof E Ingerson.

The Commission discussed at length its future objects and aims, particularly with regard to the work of its sub-committees. The chairmen of the three existing sub-committees reported on their activities, these comprise the subcommittee on abstracting translation and information; the subcommittee on the chemistry of the oceans and the subcommittee on rock analyses. It was decided to broaden the scope and work of the Commission by forming sub-committees on "the organic compounds in the crust of the Earth" and "the beginning of the biosphere".

It was also considered highly desirable that some form of code should be compiled which could be used to indicate the exact analytical methods which had been employed in mineral and rock analyses reported in publications. It was decided to seek the co-operation of the Sections of Inorganic and Analytical Chemistry of the Union to further this end. The question of education and training for geochemistry was also discussed at some length. In particular, it was agreed that the education committee of the Geochemistry Society should be encouraged to produce a definitive report on this subject as a basis for further discussion.

The subject of future symposia on geochemistry came in for a considerable amount of discussion. It was decided to offer the Commission's co-operation in respect of the proposed symposium of the International Union of Geodesy and Geophysics to be held in Helsinki in July 1960 and that of the Geochemical Society to be held in Copenhagen in August 1960. For the Copenhagen symposium it was suggested that the Commission should be responsible for organizing a section of the geochemistry of sedimentary carbonate rocks.

Prof A. P. Vinogradov of the Vernadsky Institute of Moscow gave the members present a short summary of the current geochemical work being carried out at the Institute. He also mentioned that discussions were taking place regarding the formation of a Russian geochemical society which he hoped would in time be able fully to co-operate with similar bodies outside Russia. Prof K. Sugawara also gave a short account of the position and activities of the Japanese Geochemical Society.

Election of Members. In order to replace those members due to retire at the end of the present year, the following were elected members of the Commission: Prof L H Ahrens, Prof E Ingerson, Prof K. Sugawara and Prof A. P. Vinogradov. The officers elected for the session beginning 1960 were: *President*, Prof C W Corrins (Göttingen); *Vice President*, Prof A. P. Vinogradov (Moscow); and *Secretary*, Prof E Ingerson (Austin Texas). In addition it was decided to invite seven new observers to serve with the Commission. The president-elect, Prof Corrins, proposed a vote of thanks to the retiring president Prof Barth, for his work for the Commission during his term of office and this was carried with acclamation.

SCIENCE AND PHILOSOPHY

THE fourth annual conference of the British Society for the Philosophy of Science was held during September 25-27 at Newnham College, Cambridge and was attended by about eighty members and guests. Dr M B Hesse was conference secretary.

Four symposia were held: 'Scientific Research and the Philosophy of Science', 'Biology and Physics', 'Classification: Concept formation and Language', and 'Knowing and Being'.

At the first session with Dr J O Wisdom in the chair, it was argued whether 'philosophy of science' can be held to refer to any activity not properly subsumed under 'scientific research', and, if it can, whether that activity is relevant to research. Prof H Dingle mentioned various questions of value and purpose as well as of method papers on which were unlikely to be accepted for publication in journals concerned with particular sciences. Prof H O Longuet-Higgins, on the other hand, argued that, of the product of philosophers of science, part was science, part was philosophy, and the remainder was

of no use to man or scientist. This aroused some consternation, as members consulted their own credentials and invoked those of others but in due course a consensus emerged that scientists have to think critically about their thinking, and the comparative study of modes of scientific thought may help them to do so.

In the second session, Prof J H. Woodger described an abstractive hierarchy of terms characterized by a one-many relation, and its use as a conceptual framework in biology. With some hierarchies of cells, every cell is a distinct life, with others, only the first cell in each hierarchy elaboration occurring on subsequent levels. Morphology was the study of the arrangement and differentiation of parts; physiology was the study of the existential dependence of parts. Genetics was concerned with the process in which the first member of a hierarchy results from the conjunction of two members of other hierarchies. Dr E M Hutten not only pointed out this framework the sequence exhibited.

decay each new atom produced was similarly time-extended, stemmed from a parent atom, and consisted of existentially dependent parts, but it was not dependent on its environment analogously to a cell. In elementary-particle theory, explanation might amount to little more than classification, or an enumeration of possibilities, and might have little more predictive power than comparable biological models with their over determination and multiple-causation. The chairman, Prof C F A Pantin, referred to the occurrence, in biology, of morphological models that can be interpreted at more than one level in an organizational hierarchy. In discussion it was suggested that the predictive power of a theory might not always be manifest at the time of its original formulation, it might have to await development of deduction. There was much interest in the relative importance of the past history of an entity in biology and in physics. Historical existential dependence appears to be a function of complexity.

In the third session, with Mr G Buchdahl in the chair, Miss M Masterman and Mr R M Needham presented the strategy, and some of the tactics, of a method of analysing language by assimilating it to a library classification system in which concepts are arranged on a finite lattice ordered by a single, weak, 'concordance' (inclusion) relation. They further suggested that the formation of scientific concepts is a development of language according to this model. There was some discussion as to whether the method is a technology for mechanical translation, or a science, or a philosophy of language, and it was suggested that it could be viewed as a scientific model of language, containing the partly uninterpreted concept 'inclusion', and capable of being tested by experiments on translation and on analogy-finding.

In the fourth session, under the chairmanship of Dr W H Thorpe, Prof M Polanyi presented a

way of talking about the primary process of knowing by perception, the pre-articulate act of knowing, which partakes of the uniqueness of the individual percipient, the unspecifiable personal knowledge from which any specifiable, potentially public, knowledge is derived by a process of abstraction. Complex entities were commonly perceived and recognized as wholes before particulars had been identified, the process of discovery, in fact, might be regarded as an alternation of analysis, recognizing particulars, and integration, recognizing the relations of parts to the whole. Prof R B Braithwaite suggested that too narrow a view might be taken of specifiability, and that some levels of subjective experience, however vague, could be conveyed by language—for example, 'Oblomov' conveys the experience of laziness, beyond that, he differed from Prof Polanyi in his use of the term 'knowledge' for what was unspecifiable. In the subsequent discussion there was some reluctance to focus on this rather undemocratic mode of tacit awareness, and a preference for talking about what can be made public, with the implication that the progressive refinement of scientific language tends to eliminate the unspecifiable.

In conclusion, it is perhaps worth directing attention to the unusualness of a scientific conference at which speakers are not armed with specified and verifiable data but attend primarily to make as explicit as possible how they think, and to receive criticism of the process thereby revealed, especially from those who are not working in the same field. The coherence of this universe of discourse was illustrated by the frequency of reference from one discussion to another, the *esprit d'escalier* from one session often finding its outlet in a later one, its range, by the frequency of spontaneous quotation, not only from Shakespeare and Wordsworth but also from Swinburne (and early Swinburne, at that).
G E DENYER

FOURTEENTH ANNUAL CALORIMETRY CONFERENCE

THE fourteenth annual Calorimetry Conference, held at Yale University in the Sterling Chemistry Laboratory during September 10–12, was attended by more than one hundred scientists from the United States, Canada and Europe. Under the chairmanship of Dr David White (Ohio State University) thirty papers were read and discussed. These included heat capacity measurements at temperatures as low as 0.1° K and as high as 1,400° K, precision reaction and bomb calorimetry, solution calorimetry, and determinations of stored energy in solids.

Most of the papers were concerned with recent developments in calorimetry. However, as calorimetric techniques are extended to more extreme conditions, the problems that led to the founding of the Conference remain under new guises. The need for better temperature measuring devices was emphasized in seven papers that reported on research at temperatures below 11° K. No device comparable to the platinum resistance thermometer, now in general use for measurements above 11° K, is yet available for the very low temperatures at which some of the most important calorimetric

research is now being done. However, the reports on a device that may extend precision thermometry to at least 1° K., namely, the germanium resistance thermometer developed in the Bell Telephone Laboratories, were received enthusiastically. Twelve of these thermometers had been provided for a calorimetry conference test programme involving eleven different laboratories. Three papers at the Yale conference described the first results of the investigations, which were so promising that the Conference plans to seek a manufacturer of additional units for a more extensive testing programme.

Special addresses were given by Profs George S Parks (Stanford University) and Lars Onsager (Yale University). At the annual banquet, Parks delivered the Hugh M Huffman Memorial Lecture, "Some Remarks on the Thermodynamic Properties of Organic Compounds". Parks and one of his first graduate students, the late Dr Huffman, started the first systematic calorimetric studies of organic compounds at Stanford more than thirty years ago. Enlivening his remarks with many personal anecdotes, Parks traced the history of thermodynamic research on organic substances and the role improvement

of calorimetric methods has taken in the remarkable progress made in the past three decades. Prof Onsager gave the principal lecture of the technical sessions on "Co-operative Phenomena", a field in which he has developed much of the basic theory. Many papers at each Calorimetry Conference describe experimental studies of co-operative phenomena, and Onsager outlined the approaches one may take in seeking a theoretical understanding of such effects. Admitting that three-dimensional treatments of critical phenomena by statistical mechanics seem hopelessly complex, he dwelt mostly on more simplified treatments that give results.

In addition to the objective of promoting better calorimetric research, the Conference also is concerned with publication policies relating to calorimetric and thermodynamic articles. A "Resolution regarding Published Calorimetric Data" adopted by the eighth Conference in 1953 has proved to be valuable to editors and authors alike in establishing consistent policies based on the opinions of experts in the field. Because calorimetric research has expanded into many areas not covered by the 1953 resolution, the fourteenth Conference established a committee headed by J. P. McCullough to consider revising and extending the earlier recommendations. Drs. Edgar F.

Westrum jun. (University of Michigan) and Stig Sunner (University of Lund, Sweden) presented a proposal of the Commission on Thermodynamics of the International Union of Pure and Applied Chemistry for a joint meeting in 1961 of the Calorimetry Conference and the Subcommissions on Experimental Thermochemistry and Experimental Thermodynamics. The Conference unanimously approved the proposal for a joint meeting to be held either before or after the biennial meeting of the Union that year in Montreal, Canada. Plans will begin immediately for what should be one of the most important conferences ever held in the field of calorimetry.

At the annual election the following members were appointed to Conference offices: *Chairman*, Dr. J. P. McCullough (Petroleum Thermodynamics Laboratory, Bureau of Mines); *Chairman Elect*, Dr. D. W. Osborne (Argonne National Laboratory); *Directors*, 1959-62, Dr. N. E. Phillips (University of California, Berkeley) and Dr. J. M. Sturtevant (Yale University). Other officers include *Secretary-Treasurer*, Dr. C. E. Masser (Tufts University) and *Directors*, Dr. David White, Dr. D. H. Andrews (Johns Hopkins University), Dr. J. E. Kunzler (Bell Telephone Laboratories), and Dr. J. A. Morrison (National Research Council Ottawa).

SECOND AUSTRALIAN SPECTROSCOPY CONFERENCE

THE second Australian Spectroscopy Conference, convened by Dr. A. L. G. Rees (Division of Chemical Physics, Commonwealth Scientific and Industrial Research Organization) and held in the Chemistry Department of the University of Melbourne during June 1-3, was opened by Prof. J. S. Anderson, who welcomed the 110 participants and the four exhibitors of commercial spectroscopic equipment. The first session of the conference was devoted to ultra-violet spectra and began with a review by Prof. N. S. Bayles (Chemistry Department, University of Western Australia) of recent theoretical work on solvent effects. He directed attention to the calculations of Polansky on the interaction between two H atoms which predict a red shift in the atomic spectrum beyond a critical distance and a blue shift at closer distances to the calculations by Longuet-Higgins and Pople of the red shift in the spectra of non-polar solutes in non-polar solvents arising from dispersive forces and to McRae's formulations of the case of polar solute and polar solvent. The McRae formula predicts a frequency shift between absorption and fluorescence arising from the change of dipole moment between the ground and excited states, thus providing a method for measuring the dipole moments of excited states for comparison with calculated values.

One set of contributed papers in this section dealt with the spectra of aromatic hydrocarbons. Drs. G. R. Hunt and I. G. Rosa (Physical Chemistry Department, University of Sydney) discussed a vibrational analysis of the 7000 Å and 3500 Å absorption systems of azulene which appears to confirm the predictions of Pariser and of Moffitt concerning the nature of the excited states. Dr. L. E. Lyons and Mr. G. C. Morris (Physical Chemistry Department, University of Sydney) presented results on the absorption of anthracene vapour (38,000 to

60,000 cm⁻¹). They confirmed the second π - π transition as allowed and also observed four members of a Rydberg series converging to an ionization potential of 8.81 eV. Dr. N. S. Ham (Division of Chemical Physics, Commonwealth Scientific and Industrial Research Organization) reported some calculations by the free-electron model, with electronic interaction of the spectrum of the perinaphthyl cation C₁₀H₇⁺, which agree well with the reported spectrum and also predict an unreported absorption band at about 6000 Å.

Studies by Dr. I. G. Rosa and E. J. Wells (Physical Chemistry Department, University of Sydney) on the interesting tetrahedral molecules OsO₄ and RuO₄, failed to reproduce the extensive fine structure reported in the room temperature spectra by Langseth and Quiler in 1934. The authors gave a vibrational analysis of their spectra and used the energy level scheme of Ballhausen and Liehr to assign the two allowed transitions. A theoretical paper by Dr. E. G. McRae (Division of Chemical Physics, Commonwealth Scientific and Industrial Research Organization) was concerned with electronically excited states of aggregated identical molecules, the intra-molecular vibrations were explicitly included. Two limiting cases were recognized, depending on whether the interaction energy was large or small with respect to the vibrational energy. An interpretation of the J band of N,N-diethyl pseudo cyanine was offered on the basis of this theory.

Dr. H. A. McKenzio (Division of Food Preservation and Transport, Commonwealth Scientific and Industrial Research Organization) spoke on the difference spectra in acid solutions and in urea solutions of bovine serum albumin, ovalbumin and conalbumin.

Dr. L. E. Lyons (Physical Chemistry Department, University of Sydney) in state spectroscopy.

observed in ionic solids and semi-conductors. Such effects include structure in the absorption edge of the conduction band, hydrogen-like absorption series due to excitons, the high intensity of the conduction band absorption of germanium due to the low effective mass of the electrons, intervalence band transitions in germanium, and the magnetic splitting of the conduction-levels in InSb. The use of cyclotron resonance in determining the presence of excitons and in evaluating effective masses was also noted. Crystal field effects in the spectra of inorganic complexes and the Davydov splitting in molecular crystals were also discussed.

Dr J A Friend (Chemistry Department, University of Tasmania) and Dr Lyons have identified two transitions in the crystal spectrum of sodium nitrate, an allowed one at 2000 Å and a weak $n \rightarrow \pi^*$ transition at 2870 Å. Dr J Ferguson (Division of Chemical Physics, Commonwealth Scientific and Industrial Research Organization) has analysed the polarized spectra of microcrystals of some cobalt (II) tetrahedral and octahedral complexes. The absorption spectra of the tetrahedral complexes of the type CoPy_2X_2 are modified by intermolecular interaction in the crystal while the octahedral complexes can be interpreted by simple crystal field theory. Mr J E A Alderson (Physics Department, University of Western Australia) discussed the luminescence spectra of thallium-doped potassium iodide in the spectrum range 600 Å to 2500 Å recorded on a normal incidence grating spectrometer with a photomultiplier as detector. Dr L E Lyons, Dr J R Walsh and Mr J W White (Physical Chemistry Department, University of Sydney) presented the polarized visible spectrum of single crystals of phthalocyanine. An attempt was made to calculate the crystal spectrum using the Davydov theory, but the error in estimating the dipole vector is too large to allow an unambiguous assignment of the crystal levels.

Two papers on vacuum spectroscopic technique were presented. One by Mr R S Crisp (Physics Department, University of Western Australia) described a grazing incidence, photon-counting grating spectrometer, working in the range 40–1000 Å. It has been found that the soft X-ray band emission spectra obtained with this instrument change with the material of the grating (aluminum to glass), with time, and with the order in which the grating is used. These effects have no explanation at the moment. J V Sullivan (Division of Chemical Physics, Commonwealth Scientific and Industrial Research Organization) described a double-beam photoelectric 1 m grating spectrometer, which has been tested down to 1500 Å. The monochromator employs a concave grating in a new type of mounting in which deviations from the Rowland circle lead to no detectable loss in resolution. The double-beam system involves grazing incidence reflexion to split the exit beam and two electronically coupled photo-multipliers to record the spectra. Examples of spectra recorded over the range 1500–6000 Å were presented.

The second day of the conference began with a review of some of the infra-red, Raman and microwave work of 1958 by Prof A N Hambly (Canberra University College). Topics discussed included accurate determination of molecular geometries from gaseous Raman and microwave spectra, information on torsional modes barrier heights, barrier tunnelling and rotational isomerism from spectra in the caesium iodide and microwave regions, pressure induced

transitions in gases. Perturbation effects and solvent effects need further study, for the reviewer pointed out that despite considerable work on the subject, the intensities of infra-red bands in polar solvents still do not accord with the theories.

In a research paper Prof Hambly and J G Allpress (Chemistry Department, University of Melbourne) showed that infra-red spectra can be used to follow some solid state reactions. They illustrated their remarks by showing spectra of the products of reaction between U_3O_8 and alkali or alkaline-earth halides. They could detect differences that were not discernible in X-ray powder patterns.

Dr E Spinner (Australian National University, Canberra) discussed the vibration spectra and structure of the hydrochlorides of urea, thiourea and acetamide. Infra-red and Raman spectra suggest that the cations are formed by the addition of a proton to the nitrogen rather than to the oxygen atom and that the C—N bond in an amide is a pure single bond. Drs N S Ham and J B Willis (Division of Chemical Physics, Commonwealth Scientific and Industrial Research Organization) dealt with the infra-red and Raman spectra of some isothiocyanates. They have identified the symmetrical NCS stretching frequency in $-\text{CH}_2\text{NCS}$ types at about 670 cm^{-1} , and at about 930 cm^{-1} in aromatic $-\text{NCS}$ compounds. They also gave a detailed interpretation of the complex structure of the strong NCS characteristic band near 2100 cm^{-1} . A J Costoulas (Department of Chemistry, University of New South Wales) gave a complete vibrational assignment for methyl-isothiocyanate. He agreed with Ham and Willis in the reassignment of the band at 676 cm^{-1} to the symmetrical NCS stretching frequency.

Prof A N Hambly and R H Laby (Chemistry Department, University of Melbourne) discussed some criteria for allocating displacements of X—H bond stretching frequencies to the formation of hydrogen bonds. These are a double absorption band for weak intermolecular H-bonds and most weak intramolecular H-bonds, a double absorption band at low concentration in non-polar solvents for stronger intermolecular H-bonds, and a large displacement of frequency but no doubling on dilution for strong intramolecular H-bonds. Some exceptions were illustrated by the spectra of some ortho amino acetophenones and anthranilic esters. The stable conformations of a series of methyl-cyclo-hexanols were reported by Dr A R H Cole and G T A Muller (Chemistry Department, University of Western Australia). Small but significant differences in the stretching frequencies of axial ($3027\text{--}32\text{ cm}^{-1}$) and equatorial ($3622.5\text{--}23\text{ cm}^{-1}$) hydroxyl groups were used to determine the conformations. The methyl group was found to have a greater tendency to be equatorial than the hydroxyl group. A G Moritz (Department of Organic Chemistry, University of Adelaide) has examined the overall appearance of the 3000 cm^{-1} region in the infra-red spectra of a number of methyl-substituted polycyclic hydrocarbons. He has confirmed the general applicability of the correlation between the pattern of this region and the free valence number of the position of substitution in the parent hydrocarbon, a correlation first observed by Fuson and Josien for the methyl-1,2-benzanthracenes.

The results of a normal co-ordinate analysis of the 33 planar vibrations of naphthalene were presented by D E Freeman and Dr I G Ross (Physical

Chemistry Department University of Sydney) An iterative procedure of adjusting the force constants was used to force agreement with seven of the frequencies the assignment of which is most certain. This necessitates some reassignments, and the resultant interpolation is in general agreement with the work of Luther.

The simplest molecule discussed at the conference was hydrogen deuteride the weak dipole vibration spectrum of which was the subject of a paper by Dr R. A. Durie (Coal Research Station Commonwealth Scientific and Industrial Research Organization). The internuclear distance and the anharmonicity constants were calculated from measurements of the rotational structure of the (1,0), (2,0) and (3,0) vibration bands. Dr D. W. Posner (Division of Electrotechnology Commonwealth Scientific and Industrial Research Organization) presented the only paper on microwave spectroscopy. He has measured the electric field gradients at the oxygen and hydrogen nuclei in HDO and D₂O and has begun a measurement of the magnetic hyperfine splittings.

The following papers which were generally concerned with spectrographic apparatus and methods were also presented. Dr H. Gollnow (Mt Stromlo Observatory, Canberra) described a precision photoelectric setting device (accuracy about 0.5 μ) for the measurement of diffuse spectral lines. A fast scanning infra red (1-5 μ) spectrometer equipped with a cooled lead-tellurium detector was described by Dr J. Trenggall Williams (Defence Standards Laboratories, Maribyrnong). Another paper from the same laboratories by G. L. White discussed the application of polynomials fitted by 'least squares' methods, instead of the Friedel-McKinney equation, for the calibration of infra red spectrometers. Some molecular spectra excited by shock waves were shown by Dr C. L. Cook (Weapons Research Establishment Salisbury), and the part played by a photograph spectrograph in routine control in the steel industry was outlined by J. H. Savage (Australian Iron and Steel Port Kembla). Another paper on emission spectroscopy was given by J. M. Nobbs (Defence Standards Laboratories, South Australia), who described some of the effects of pulse shape on the spectral characteristics of pulsed discharges. He pointed out that the exponential shapes commonly used yielded lower sensitivities than most other shapes.

The final morning session of the conference took the form of a small symposium on atomic absorption spectroscopy, with a review and five research papers on the subject. A. Walsh (Division of Chemical Physics, Commonwealth Scientific and Industrial Research Organization) reviewed the present status of emission and atomic absorption spectroscopy. Recent advances in emission spectroscopy include better sources, the use of photomultipliers and the availability of vacuum instruments. The use by Margoshes and Scribner of a plasma jet as a spectroscopic source was a new development which will be followed with great interest. However, the need for standards remains. This results essentially from three types of interference namely, chemical, radiative and excitative. Atomic absorption spectroscopy avoids two of these but not the chemical interferences. In the opinion of the reviewer the value of atomic absorption spectroscopy has been established and it seems that any analysis that can be done by flame

emission methods using atomic lines can be done as well and often better by atomic absorption methods.

J. E. Allan (Department of Agriculture, Hamilton New Zealand) described the analysis of magnesium by atomic absorption. The measurement is carried out simultaneously with flame emission analyses for calcium, sodium and potassium the other major cations present in plants and soils. The magnesium determination can be performed with the same ease as and probably with greater reliability than calcium, sodium and potassium determinations. The minor elements zinc, iron and manganese have also been determined by atomic absorption directly on plant ash solutions or soil extracts but copper at present requires prior extraction with an organic solvent. D. J. David (Division of Plant Industry, Commonwealth Scientific and Industrial Research Organization) spoke about some of the chemical interferences encountered in applying atomic absorption to the analysis of plant material and soil extracts. In plant material analyses he finds no interference for zinc, iron, copper and magnesium but he finds that calcium absorption is depressed by phosphate, aluminium and silicate. This interference is eliminated with 0.6 per cent magnesium ions and 2 per cent, volume/volume sulphuric acid. With soil extracts the atomic absorption analysis is straightforward for sodium, potassium and magnesium but in this case the interference with calcium is controlled by 0.15 per cent strontium ions. These two papers showed that many analyses important in plant and animal nutrition can be carried out successfully by the atomic absorption method.

Dr J. B. Willis (Division of Chemical Physics, Commonwealth Scientific and Industrial Research Organization) discussed the determination of blood serum calcium and magnesium levels by atomic absorption. Large quantities of strontium ions or the disodium salt of ethylene diamine tetracetic acid are needed to overcome the interference of phosphate and protein. Duplicate measurements for calcium and magnesium can be made directly on about 0.25 ml of serum diluted 10-20 fold. Dr P. Brownell (Botany Department University of Adelaide) is interested in analysing very small quantities (about 0.01 p.p.m.) of sodium, which is a micro-nutrient for *Atriplex vesicaria*. The flame photometric results are misleading when the calcium concentration exceeds 0.02 M. The atomic absorption method using 'Siro spec', a simple instrument designed by Box and Walsh for this purpose at present enables accurate measurements of about 1 p.p.m. sodium in the presence of large excesses of calcium (4 M) and potassium.

The final contribution by Dr B. M. Gatehouse and Mr A. Walsh (Division of Chemical Physics, Commonwealth Scientific and Industrial Research Organization), was concerned with the direct analysis of metals and alloys. By sputtering from a metal surface in the presence of about 1 mm mercury pressure of neon they were able to obtain a calibration curve and to determine 1 p.p.m. silver in a copper-silver alloy. They suggested that this method may be suitable for elements such as aluminium and boron which do not give atoms in the flame.

In a concluding discussion members agreed unanimously that a standing committee should be set up to organize similar conferences at regular intervals.

NOELMAN R. HAM

PROTEIN BIOGENESIS

A COLLOQUIUM on "Specificity in Protein Biogenesis" was held in Louvain during June 8-9 by the Centre interuniversitaire de Recherches enzymologiques, a government-sponsored association grouping several Belgian biochemical laboratories. The aim of the organizers was to bring together scientists actively engaged in research on protein synthesis and to establish new contacts with the Belgian groups interested in this field. The meeting was arranged on an informal basis and the speakers were asked to discuss freely the current work of their laboratories, the lectures will not be published.

Present ideas on the relationship between deoxyribonucleic acid and protein structures were lucidly summarized and discussed by C. Levinthal (Massachusetts Institute of Technology). Since deoxyribonucleic acid and protein are both linear polymers, it would seem that a simple relation should exist between the arrangement of the amino-acids in the protein and that of the nucleotides in deoxyribonucleic acid of the corresponding gene—probably a point-to-point correspondence between the two sequences. Some of the characteristics of the coding system serving to translate one sequence into the other can be deduced from what is known about deoxyribonucleic acid and protein structure. It seems feasible at present to check experimentally the idea of collinearity between the structure of the two types of polymers. Find an organism in which genetic maps can be established with great accuracy, choose an enzyme molecule of moderate size produced by this organism and devise a good selection principle for recovering the useful mutants. Isolate several mutants of the genetic locus of the enzyme, map the mutation sites, isolate the abnormal proteins, if any, which are produced in place of the normal enzyme by the mutants, and locate the differences within the protein molecules. This gives a test of the correspondence between deoxyribonucleic acid and protein fine structure.

C. Levinthal described the progress of his own work on the genetic control of the formation of a phosphatase in *E. coli*. Thirteen different mutants resulting from mutations within the locus of the phosphatase have been isolated so far, the linear order of the mutation sites has been established by a very interesting use of the transfer of genetic material during bacterial conjugation. Unfortunately only one of the thirteen mutants produced a recognizable modified phosphatase protein. Both the normal and the abnormal enzymes have been isolated, and their structure is now being studied. Future developments along this line of research will be watched with great interest.

In bacterial systems, genetic analysis is ahead of chemical knowledge. In man, on the other hand, where genetic analysis is at a great disadvantage, brilliant success has been achieved on the chemical side. J. Hunt (Cambridge) reviewed the main results obtained by the Cavendish Laboratory group on the structure of abnormal haemoglobins. This work will undoubtedly become a classic of genetics and biochemistry. Haemoglobins S and C differ from the normal protein in only one detail—the replacement of one glutamic acid in the β chain by valine or lysine respectively. Haemoglobin E differs from

normal haemoglobin by the replacement of another glutamic residue by lysine, in haemoglobin G, still another glutamic is replaced by glycine. Thus genetic differences presumably arising from mutations can result in the replacement of individual amino acids at specified places in the polypeptides.

J. Hunt further described in detail his recent work on foetal haemoglobin. He has shown that one of the two polypeptide chains of foetal haemoglobin (chain α) is identical with that of normal adult haemoglobin. This discovery opens new perspectives and will certainly give important information on the mechanism of the genetic control of protein structure, for here is a simple case of differentiation at the molecular level. The structure of foetal haemoglobin of infants carrying genes of abnormal adult haemoglobins will be very informative. It might indicate whether the switch from foetal to adult haemoglobin during development results from the inhibition of the activity of a gene and the unveiling of another gene, or whether the change occurs somewhere between the gene and the protein-making system and consists in a change of expression of the same gene.

Other aspects of the control of the synthesis of specific proteins were discussed by B. Magasanik (Harvard University), who considered the phenomena of enzyme induction and repression and the function of ribonucleic acid in the synthesis of bacterial protein. B. Magasanik reported results obtained in his laboratory on various mutants which require amino-acids, nucleic acid precursors, or certain energy sources. By a very ingenious use of these mutants, several aspects of the correlation between ribonucleic acid content and level of protein synthesis were checked. Increased rate of protein synthesis goes together with an increased content of the bacteria in both soluble ribonucleic acid and ribosome ribonucleic acid. This is comparable to the well known relation found in higher organisms. Studies on ribonucleic acid and protein synthesis during adaptation, especially in 'diauxic' experiments, indicate that the synthesis of new ribonucleic acid does not accompany enzyme adaptation. The results are compatible with a catalytic function of ribonucleic acid in protein synthesis, and with the view that induction and repression of enzyme synthesis rest upon the control of the activity of pre-existing protein-forming centres, rather than on the formation or destruction of such systems.

The existence of specific ribonucleic acid molecules capable of carrying some sort of genetic information is established by the discovery that pure virus ribonucleic acid is able to cause infection. Present knowledge on the structure of tobacco mosaic virus was summarized by H. Fraenkel-Conrat (University of California), who presented results of his current work on the molecular size of the virus ribonucleic acid. End-group determination in the virus acid by a combination of tracer methods with specific enzymic degradation and controlled chemical oxidation indicates that each virus particle might contain one single molecule of ribonucleic acid made up of some 6,000 nucleotides in one chain. The polypeptide chain of the virus protein contains only about 150 amino acid residues. It would seem, therefore,

that the ribonucleic acid of the virus is large enough to carry much more information than that which is required for controlling the primary structure of the protein unit contained in the finished virus. This raises several problems for future research. H. Fraenkel-Conrat also reported very interesting results on a special state of the virus ribonucleic acid at the beginning of infection.

Another approach to the specific function of ribonucleic acid in protein synthesis is the artificial modification of the structure of the acid. This has been done by chemical means in the case of virus ribonucleic acid. In bacteria, composition of the acid can be changed by growing the organisms in the presence of analogues of the normal purines or pyrimidines. F. Groe (Institut Pasteur, Paris) gave a very clear account of research on the effects of fluorouracil on protein synthesis in *E. coli*. Incorporation of all the individual amino acids does not respond in the same way to fluorouracil. For example, the incorporation of proline and tyrosine is depressed whereas that of arginine is stimulated. These changes appear to reflect qualitative as well as quantitative modifications in the protein equipment of the organism, indicating that the analogue may actually interfere with the agents which control protein structure. A phosphatase formed in the presence of the analogue has a normal enzymic activity although it contains less proline than the normal enzyme, thus it is probably slightly modified at a place which is not important for the catalytic properties of the protein. On the contrary, β -galactosidase synthesis is abolished and replaced by the formation of some related inactive protein. It is striking that fluorouracil specifically reduces the fixation of proline

and of tyrosine on soluble ribonucleic acid at the same time as it reduces the incorporation of these same amino acids into the proteins. This indicates that soluble ribonucleic acid plays an important part in the specificity of protein formation. These results also support current views according to which activated amino acids are bound to soluble ribonucleic acid before condensing into polypeptides.

T. Hultin (Wenner-Gren Institute, Stockholm) reported observations on animal tissues which indicate that another pathway of amino acid incorporation might exist beside that passing through soluble ribonucleic acid. That the latter must also be operative was shown by several of his results which agree with the classical scheme. However, he obtained by means of new techniques of isolation of ribosomes and by fractionation of supernatant preparations, a system in which amino acids are incorporated into proteins in the particles in the absence of soluble ribonucleic acid. A protein of the supernatant is required for incorporation with this system. Protein synthesis which can occur in isolated mitochondria or nuclei appears to depend on the presence in these cell organelles of particles closely resembling the ribosomes of the cytoplasmic ground substance.

Of great benefit to the meeting was the presence in the audience of biochemists from different countries who had taken part a few days before in Brussels in the Solvay Conference on Nucleoproteins. All the lectures were followed by very good discussions. The meeting was closed by a general discussion which concerned the function of the various ribonucleic acid fractions, the transfer of information from gene to protein, and coding problems.

H. CHANTRENE

PROGRESS IN GAS CHROMATOGRAPHY

AN informal symposium of the Gas Chromatography Discussion Group (associated with the Hydrocarbon Research Group of the Institute of Petroleum) was held at the University of Bristol on September 25 under the chairmanship of Mr C. S. G. Phillips.

Dr F. H. Pollard commented on the enthusiasm and free interchange of ideas among workers in this field which was undoubtedly responsible for the present advanced state of the art. Having regard to the success achieved by him in the field of inorganic separations by paper chromatography, it was not surprising that he should mention the possible separation of such materials by gas chromatography.

The outstanding feature of the meeting was the demonstration by Mr R. P. W. Scott of the presentation of gas chromatographic data with a high persistence cathode ray tube. With capillary columns it is possible to effect separations of speeds much greater than the response of conventional recorders, and in order to take full advantage of the technique in its application to kinetic and other studies a means of high-speed recording is essential. Mr Scott, using a 70 ft column, demonstrated separations of 100°C boiling range samples in less than 1 min with his apparatus which inclusive of automatic repetitive sample injection system, cost less than £80 for materials.

The discussion which followed a paper by Mr C. L. A. Harbourn on quantitative determinations

showed that this aspect of the subject is one that affects most users of the technique. As yet, however, if one uses the published literature as a guide, it would appear to have received very little attention. The well-prepared paper covered methods of peak measurement, sources of error and repeatability of calibration, internal standard, and normalization methods, and interpretation of unresolved peaks. Recent developments in integrators and the use of analogue computers and tape recorders were also discussed.

Some of the practical aspects of the measurement of retention volumes were dealt with by Dr G. W. A. Rijnders, and Dr C. R. Patrick mentioned some of the problems attached to 'sealing up' analytical columns to sizes capable of handling up to 10 gm samples. The values of height equivalent of a theoretical plate (HETP) increase and the much higher volumetric flow rates necessitate modifications to the design of hot wire detectors. Mr D. H. Desty read a paper by Dr J. Janak, who unfortunately was unable to be present, describing the application of gas chromatography to the identification of structure of involatile substances by pyrolysis and subsequent analysis of the products.

Members attending among whom were some from the United States and Europe were able to inspect and see working a good selection of the commercial instruments now available for laboratory and process control work.

C. G. SCOTT

Sir George believes, however, that a Government department can function as the directing authority of a great operating service like the Hospital Service in Britain, and the vast expenditure involved could not and should not be removed from the direct control of a Minister responsible to Parliament. If, however, the Hospital Service is to remain the direct responsibility of a Minister and a Government department, Sir George considers that more attention must be given to the staffing of that department and to the arrangements for liaison between it and the decentralized formations, and that a central intelligence organization must be provided. Further, he suggests that on all three points lessons can be learned from the experience of other Government departments which have responsibilities in relation to operating services.

On the first point, he does not see how the Ministry can give the understanding leadership which is required unless the highest posts on its staff are held by officers who have had practical experience of hospital administration at operational level, and in support of his argument he quotes the staffing arrangements of the Fighting Service Ministries and of the Colonial Office. Sir George pays tribute to the value of the work done by many officers appointed before such experience was available, and he does not advocate immediate wholesale change but rather exchanges of staff on the lines of the Colonial Office arrangements. His stress is laid on the quality of the officers available to fill the various posts and the need in the National Hospital Service for new administrative skills, for which there is at present no readily available source of supply. Thus last, as he recognizes, is a need which often occurs elsewhere to-day as a result of modern development, and the Hospital Service must take deliberate action to meet this need as private enterprise has done in the field of industry.

It might be observed here that if this need for statesmanship is to be met in the Health Service, in industry, or elsewhere, those who meet that need must be treated as statesmen. There is no place for the type of party politics which seeks to misrepresent opponents or those who may be entrusted with the execution of schemes or policies which are not in line with party doctrine. It is significant that in supporting the Acton Society Trust's proposal that the Minister in charge of the Health Service should have a seat in the Cabinet, Sir George stresses the danger of frequent change of office, and his own proposals would make the chief permanent official in the Ministry a professional man.

This does not mean that Sir George is here advocating that the expert should be permanently at the top, but his suggestion goes far beyond the claim that the expert should be considered for the highest administrative posts. It implies that the expert by virtue of his expertise is particularly suited to supply the type of specialized administration needed. He must, of course, possess administrative capacity: there is nothing in Sir George Schuster's pamphlet to countenance incompetence in management or administration, but much to stimulate more thought about the way in which to meet the need for administrators and the type of training and experience they should receive.

On the second point, that of liaison between the Ministry and the hospital authorities, Sir George suggests that there are lessons to be learned from the best traditions of the inspectors of schools under the

Ministry of Education, but here again Sir George pleads for constructive thinking and refrains from specific proposals. His stress on joint consultation at the centre and once again on the quality of the liaison officers clearly has implications far beyond the Health Service, and his strongest criticism is reserved for the perfunctoriness with which liaison is often treated. Positive measures and constructive thought are always required to provide an effective two-way flow of ideas.

Sir George Schuster's major proposal is in regard to his third point and, in line with a main recommendation of the Guillebaud report, he recommends the establishment of a central intelligence and statistical department. This, however, should be an integral part of the executive, with its own creative role as a detector of problems and a productive source of wisdom. Sir George has in mind something on the lines of the Office of Special Enquiries and Reports under the direction of Michael Sadler at the Ministry of Education, equipped with an intelligence staff which would keep under constant review the development of hospital practice, in its social as well as its medical setting, in Britain and other countries, and which would publish a series of reports which might be accepted throughout the world as authoritative. With such a staff the Ministry could not only carry out its own investigations, but could also provide valuable stimulants to work by the hospital authorities. Particularly in its social aspects, the research here required needs central guidance and co-ordination, and Sir George's own experience as chairman of a regional hospital board has convinced him of the great flow of evidence of clinical, human and social interest which requires recording, co-ordination and interpretation.

Beyond this Sir George points to the need for creative thought, such as demands the services of men of wisdom and comprehension, combined with knowledge of medical affairs. How to produce such men and women is one of the real challenges which this rapidly changing world makes on professional organizations to-day, and there is much indeed in Sir George Schuster's comments that deserves careful study by professional men and women of professions other than that of medicine. So far as the National Health Service in Britain is concerned, Sir George Schuster's investigation suggests that this is very seriously understaffed as regards first-class administrators in comparison with large industrial organizations, and some improvement here may well be the first step required to implement his more specific proposals to remedying the alleged weakness of the voluntary committee system and to promote the intensive expert study of the hospital cost structure, the full use of efficiency techniques by the hospital authorities, including the introduction of work-study methods, and the application of operational research to some of the problems of the hospital service.

These last are clearly proposals limited specifically to the Hospital Service and to some of them an interested group of members of Parliament is already giving attention. The Minister of Health has stated that the Ministry's present experimental organization and methods unit is to be enlarged and made permanent, and that he has accepted the offer of a group of management consultants to undertake a series of surveys, at their own expense, to demonstrate the economies and improvements in efficiency which could be achieved in the hospital service by work study.

PREVENTING JUVENILE DELINQUENCY

SEVERAL years ago the United States Children's Bureau, as part of its programme on juvenile delinquency, published a report about the effectiveness of measures in delinquency prevention. The analysis was based on evaluative studies conducted over the previous twenty five years or so.

The review led to the conclusion that programmes for the prevention of juvenile delinquency had not been notably effective. This conclusion was tempered by two facts. First, few programmes, relatively speaking had been evaluated, and most of those not adequately. Secondly, many of the evaluative studies were out of date since they dealt with programmes and methods that to-day might not be considered the best. Moreover, there were hints that good results had been achieved with certain types of delinquent children in certain circumstances. This was notably the case in child guidance work and was perhaps also true of the kind of neighbourhood work associated with the name of Clifford Shaw.

Some of the newer programmes and methods seemed, however, to give promise of more favourable findings. Among those mentioned in the report were various devices for 'reaching out' to youngsters and their parents with services they were unlikely to seek for themselves, for example group work with delinquent and pre-delinquent gangs, case work or group work with 'resistant' families. These and other newly devised programmes seemed to be succeeding where older ones had failed and to be benefiting both from the experience of their predecessors and from recent advances in knowledge about human behaviour and motivation.

In an issue of the *Annals of the American Academy of Political and Social Science*, measures of delinquency prevention and their effectiveness are con-

tinued with reports from practitioners and research workers who have been closely associated with these efforts (322 March 1959).

The most striking change according to Helen L. Wilmer, of the U.S. Department of Health Education and Welfare is in the level of sophistication shown in the reports. This is shown in the way the work with delinquent youngsters and their parents is carried on, in the psychological and sociological knowledge underlying the work, and in the methods employed in its evaluation. Much has been learned in all these areas in recent years. These articles show programmes of delinquency prevention both benefiting from that advance and contributing to it.

Perhaps the most important contribution of this series of articles lies in the picture it provides of the kinds of young people who are likely to become chronically delinquent and of the kinds of homes and neighbourhoods they live in. The picture is not a new one but is drawn in a way that reveals, more vividly than usual, the fears the discouragement and the wish to be like other people that characterize these young people and their parents. The treatment measures described, both those that would improve the environment and those that are directed toward the individuals take their direction from this knowledge. The knowledge itself is rooted both in the social sciences and in psychology and demonstrates their interrelatedness.

The articles deal with small programmes and, in part, short-lived efforts. Few of them report scientifically established results. Nevertheless, in their conception of what needs to be done and in their suggestions for some ways of doing it, they hold the hope that the problem of delinquency can be reduced if communities are willing to put the effort required into the work.

THE ORIGINS OF LOVE

PSYCHOLOGISTS, sociologists and anthropologists commonly hold the view that the infant learns to love through the association of the mother's face, body and other physical characteristics with the alleviation of internal biological tensions, particularly hunger and thirst. Psychoanalysts have tended to emphasize the importance of attaining and seeking at the breast as the basis for affectional development. Recently a number of child psychiatrists have questioned such simple explanations. Some argue that affectionate handling in the act of nursing is a variable of importance, whereas a few workers suggest that the composite activities of nursing, contact clinging and even seeing and hearing work together to elicit the infant's love for his mother.

It is difficult, if not impossible, to use human infants as subjects for the studies necessary to break through the present speculative impasse. For several years a group at the Primate Laboratory of the University of Wisconsin has been using baby rhesus monkeys in a study that has begun to yield significant insights into the origin of the infant's love

for his mother. A report has been prepared by Harry F. Harlow*.

The interest in infant-monkey love grew out of a research programme that involved the separation of monkeys from their mothers a few hours after birth. The investigators were impressed by the deep personal attachments that the monkeys formed for the dimpler pads, and by the distress that they exhibited when the pads were removed briefly once a day for the purposes of sanitation. The behaviour of the infant monkeys was reminiscent of the human infant's attachment to its blankets, pillows or rag dolls. These observations suggested a series of experiments to compare the importance of nursing and all associated activities with that of simple bodily contact in engendering the infant monkey's attachment to its mother. Two surrogate mother monkeys were prepared. One is a bare welded wire cylindrical form surmounted by a wooden head with a crude face. In the other the welded wire is encased by a sheathing of terry-cloth. Eight new born monkeys

* *Scientific American*, 200, 6, June 1959.

were placed in individual cages, each with equal access to a cloth and a wire mother. Four of the infants received their milk from one mother and four from the other, the milk being supplied in each case by a nursing bottle, with its nipple protruding from the mother's 'breast'.

The two mothers quickly proved to be physiologically equivalent. The monkeys in the two groups drank the same amount of milk and gained weight at the same rate. But the two mothers proved to be by no means psychologically equivalent. Records showed that both groups of infants spent far more time climbing and clinging on their cloth-covered mothers than they did on their wire mothers. As the monkeys grew older, they tended to spend an increasing amount of time clinging to and cuddling her pliant terry-cloth surface. Those that secured their nourishment from the wire mother showed no tendency to spend more time on her than feeding required, contradicting the idea that affection is a response that is learned or derived in association with the reduction of hunger or thirst. These results indicate the importance of bodily contact and the immediate comfort it supplies in forming the infant's attachment for its mother, the cloth-covered mother surrogate is an eminently satisfactory mother.

The time that the infant monkeys spent cuddling on their surrogate mothers was a strong but perhaps not conclusive index of emotional attachment. Would they also seek the inanimate mother for comfort and security when they were subjected to emotional stress? With this question in mind the monkey infants were exposed to the stress of fear by presenting them with strange objects, for example a mechanical teddy bear which moved forward, beating a drum. Whether the infants had nursed from the wire or the cloth mother, they overwhelmingly sought succour from the cloth one, this differential in behaviour was enhanced with the passage of time and the acquisition of experience. All tests show that the infant monkey's relationship to its surrogate mother

is a full one. Comparison with the behaviour of infant monkeys raised by their real mothers confirms this view.

While bodily contact clearly plays the prime part in developing infantile affection, other types of stimulation presumably supplement its effects. A search has been made for these factors. Western culture parents appreciate that rocking a baby or walking with him somehow promotes his psychological and physiological well-being. The responsiveness of infant monkeys to two cloth mothers, one stationary and one rocking, was now compared. All preferred the rocking mother, though the degree of preference varied considerably from day to day and from monkey to monkey. Motion does appear to enhance affection, albeit far less significantly than simple contact. The act of clinging, in itself, also seems to have a role in promoting psychological and physiological well-being.

Still other elements in the relationship remain to be investigated systematically. The warmth of the mother's body would appear to play its part in strengthening the infant's ties to the mother. Observations have not yet confirmed this hypothesis. Heating a cloth mother does not seem to increase the attractiveness of the mother to the infant monkey and infants readily abandon a heating pad for an unheated mother surrogate. Visual stimulation may forge an additional link. It is also possible that particular sounds and even odours may play some part in the normal development of response or attention.

The depth and persistence of attachment to the mother depend not only on the kind of stimuli that the young animal receives but also on when it receives them. Experiments with ducks show that imprinting is most effective during a critical period soon after hatching; beyond a certain age it cannot take place at all. From preliminary experiments with monkeys it has been found that their affectional responses develop, or fail to develop, according to a similar pattern.

NORTH-SOUTH ANISOTROPY AND ANTICIPATORY INCREASE OF INTENSITY ASSOCIATED WITH THE COSMIC-RAY STORM OF FEBRUARY 11, 1958

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THE time variations of cosmic rays have been measured during the International Geophysical Year with standard instruments at a large number of places on the Earth, and several studies have been made of the energy dependence of the primary variations and the anisotropy which is often associated with primary variations of intensity. From an examination of Forbush-type decreases, Fenton, Fonton and Rose¹ have come to the conclusion that the cause of the transient intensity decreases is variable in its energy dependence from a few BeV to more than 30 BeV. The variation in response to

transient decreases observed with similar equipment at different stations suggests that a primary anisotropy is present at these times. Lockwood² has examined the detailed structure of several Forbush-type decreases in the intensity of local neutrons during 1955-58. He finds that in most of the decreases there was a magnetic storm at the onset. Flare activity during the preceding 30 hr was high and there was some indication of an intensity maximum during the 12-hr period preceding the start of the decrease. He comments that such an anticipatory effect might be due to the albedo of the moving magnetic gas cloud, but that further results are

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Table 1 CHRONOLOGY OF EVENTS ASSOCIATED WITH THE FORBUSH DECREASE OF FEBRUARY 11 1958

 ΔC and ΔH respectively indicate the change of cosmic-ray intensity (CR) and of the horizontal component of geomagnetic field at Virginia

| Date | UT | Solar event | UT | Terrestrial effect | Cosmic ray features |
|---------|-------------------------------|---|--------------------------------------|---|---|
| 9-2-58 | 0207 2053- 2120 2159 | *2+ Flare Type III and Type I radio bursts *2+ Flare E04.S20 | | Radio fade-out | |
| 10-2-58 | 1325 | *2+ Flare with major burst radio noise II 67 S12 | | Radio fade-out | |
| | | | 2100 | CR maximum + $\Delta C \approx +1$ per cent | (1) Anticipatory increase at equator only related to high energy |
| 11-2-58 | | | 0120 0123 0130 0154 0300 | B C storm + $\Delta H - \Delta C$ Aurora + $\Delta H - \Delta C$ CR minimum | (2) Decrease starts at high latitudes |
| | | | 0622 0635 | X ray $\Delta H = 0$ Maximum absorption, gal actic noise of 18 Mc/s | (3) 6300 minimum at equator (4) 0500 minimum in mesons |
| | | | 0730 0850 1600 1100 | X ray ends X-ray and ΔH Maxima aurora CR maximum | (5) 0700 minimum at high latitudes (6) Increase commences |
| | | | | | Seen in instruments with high end low energy response. Not observed in stations in 120° E. belt, nor in the southern hemisphere |

needed to substantiate any anticipatory effect McCracken and Parsons⁴ have made a very interesting analysis of a Forbush type event which occurred on October 21, 1957. They found that there was a preliminary depression prior to the commencement of the Forbush decrease and they comment that it was not due to the arrival of solar matter at the Earth since it occurred before the magnetic disturbances. They conclude from studies made at several stations that the preliminary depression must be attributed to a cause located at some distance from the Earth, and since it is not observed simultaneously at all stations its explanation requires some rather special form of short-lived primary anisotropy. McCracken⁴ has analysed the anisotropy of a number of Forbush type decreases which were preceded by decreases. Yoshida and Wada⁵ have directed attention to in

creases of intensity which occur after the onset of cosmic ray storms. They believe that the mesons are mainly isotropic and have an energy-dependence nearly the same as that of the decreases.

In connexion with the Forbush type decrease in cosmic ray intensity which occurred on February 11 1958 we have fortunately a large number of other solar and terrestrial observations which give us a unique set of data for following the event from the time it occurred on the Sun. These have been summarized by Trotter and Roberts⁶. During its second passage on February 9, 1958, a region 58 B at 15° S heliographic latitude then at the central meridian suddenly underwent very rapid changes in plage brightness and sunspot growth. The region flared rapidly throughout the day half a dozen of the flares were Class 1+ or greater. Five of these caused complete short wave radio fade-outs of considerable duration. In addition, these events were associated with unusual solar radio noise burst activity on 2,600, 470 and 167 Mc/s. The flux density on 167 Mc/s was very high during February 7-9. An extremely large number of high speed dark surges were observed on the solar disk, most of them in association with small flares. The mean integrated coronal (5303 Å) intensity was low during the period Region 58 B, which had very intense activity during the second passage in February, persisted with pronounced activity during the third and fourth passages in March and April respectively.

The strongest geomagnetic storm with sudden commencement (s.c.) of the present solar cycle began early on February 11, and almost simultaneously a very spectacular aurora that persisted throughout the night lit up the northern sky as far south as the 35th parallel. It was visible on the following night as well. In Table 1, the important events observed on the Sun and on the Earth are summarized in chronological order.

We have examined the effect in cosmic rays from data of the high counting rate meson detector at the Massachusetts Institute of Technology and from a grid of neutron monitor stations distributed (1) in two belts corresponding to the equator and the middle geomagnetic latitudes (2) in three meridional sections corresponding to 75-115° W

Table 2. PARTICULARS OF COSMIC-RAY NEUTRON MONITOR STATIONS USED IN ANALYSIS

| Code | Station | Geog. Lat. | Geomag. Lat. | Long. | Investigator |
|------|-------------------|---------------------|--------------|----------|----------------------------|
| A | Murchison Bay | 80° N | 76° N | 15° E | Dr A. E. Sandstrom Sweden |
| B | Churchill | 50° N | 60° N | 94° W | Dr D. C. Rose Canada |
| C | Leeds | 53° N | 67° N | 0° | Dr J. G. Wilson, England |
| D | Sulphur Mt. | 51° N | 58° N | 115° W | Dr D. C. Rose Canada |
| E | Wladimir | 41° N | 49° N | 0° E | Dr A. Ebert Germany |
| F | Ottawa | 45° N | 57° N | 76° W | Dr D. C. Rose Canada |
| G | Mt. Nori | 30° N | 26° N | 137° E | Dr Y. Miyazaki Japan |
| H | Kodakalankur | 10° N | 1° N | 77° E | Dr V. Sarabhai India |
| I | Makrerrre College | 0° | 2° E | 32° E | Dr D. M. Thomson, Uganda |
| J | Lae | 6° S | 10° S | 147° E | Dr A. G. Fenton, Hobart |
| K | Hinacayao | 12° S | 1° S | 75° W | Dr J. A. Simpson Chiriqui |
| L | Hermannus | 34° S | 33° S | 10° E | Dr A. M. Vanwijk Hermania |
| M | Mt. Wellington | 41° S | 45° S | 147° E | Dr A. G. Fenton, Hobart |
| N | Invercargill | 46° S | 52° S | 168° E | Dr N. V. Ryder New Zealand |
| O | Mawson | 67° S | 73° S | 62° E | Dr A. G. Fenton, Hobart |
| 1 | H. I. K. | Equator | 0-2° | | |
| 2 | E. O. D. | High latitude | 40-75° | | |
| 3 | D. F. K. | West longitude | | 75-115° | |
| 4 | C. E. I. | 0-Longitude | | 0-82° | |
| 5 | J. M. V. | East longitude | | 147-163° | |
| 6 | A. E. G. | Northern hemisphere | | | |
| 7 | L. M. O. | Southern hemisphere | | | |

0-32° E and 147-168° E, and (3) in the northern and southern hemispheres. In Table 2 are indicated the stations which are included in the grid, particulars of their location and the name of the principal investigator at each station through whose kindness the data have been made available to us. Assuming that the variations can be dependent on the primary energy response, on local time or longitude and on the hemisphere, we have grouped stations so as to study one variable at a time with, so far as possible, an equal contribution in each group due to the other two variables. The stations from which data have been combined for the various analyses are indicated in Table 2.

Fig. 1 shows the percentage deviations in the bi-hourly counting-rates of the neutron monitors during successive bi-hourly periods in UT from February 9-12, the deviations in each case being taken with respect to the mean intensity on February 10, which represents a period of 24 hr immediately preceding the onset of the Forbush decrease early on February 11. It is clear from Fig. 1A that the variation is strongly dependent on primary energy. It will be noticed that the meson detector at the middle latitude exhibits a variation which is intermediate between the variation of the neutron monitor intensity at the equator and at the middle latitude stations. The middle latitude stations have a much larger percentage decrease than the stations at the equator. A minimum intensity is reached at 0300 UT , at 0500 UT and at 0700 UT at the equator, with the meson detector and at the middle latitude stations respectively. Moreover, about 12 hr after the initial decrease, at the equator the intensity returns almost to normal before it decreases again, on the other hand, the recovery occurs only partially at middle latitude stations.

A most interesting aspect of the present event is the increase of intensity at 2100 UT on February 10, observed at equatorial stations only, about 4 or 5 hr before the arrival of the solar plasma at 0120 UT , indicated by the storm with sudden commencement and a number of other terrestrial effects. The second increase, or the recovery of intensity at 1100 UT on February 11, is seen to be much more significant at the equatorial stations and in the meson detector

at Cambridge than at the middle latitude stations. It would thus appear that both events, which appear to be increases, are particularly characteristic of the high-energy component of the primary radiation. In contrast, the first minimum of the Forbush event is larger and occurs later for low-energy than for high-energy primaries.

In Fig. 1B the variations of intensity at stations in the three meridional belts are compared. It is seen that there are significant differences in the initial decrease, indicating the existence of an anisotropy. The most remarkable feature is the complete absence of the second increase at 1100 UT on February 11 at stations in the east meridional section (147° E to 168° E longitude), as also at stations in the southern hemisphere for which a comparison with the northern hemisphere is shown in Fig. 1C. The second increase of intensity is thus characterized by a strong anisotropy not only parallel to the ecliptic, but also perpendicular to it. This is perhaps the first evidence for an anisotropy of the latter type. In contradiction to the view of Yoshida and Wada, we believe that the second increase is mainly anisotropic and has an energy dependence different from the mainly isotropic Forbush decrease.

The main event observed early on February 11 in cosmic rays, in geomagnetism, in the aurora and in X-rays at high altitudes is undoubtedly related to the major solar outburst from region 58-B between 2053 and 2139 UT on February 9. We would like to suggest here that solar plasma reached the interaction distance of the geomagnetic field at about 0120 UT on February 11, but that for several hours prior to that, there was a cosmic-ray effect which involved an increase of the radiation. During the second increase of cosmic-ray intensity on February 11, we have an increase of cosmic-ray intensity occurring with a strong aurora and change of the horizontal component H of the geomagnetic field. This contrasts with the association of the aurora and the change in magnetic field with the large decrease of cosmic-ray intensity about 10 hr earlier. From other geophysical evidence it is believed that the main plasma outburst streamed past the Earth in 10-12 hr and it appears that the second increase of cosmic-ray intensity is related to the departure of the plasma cloud. There was a 2⁺ flare with major burst of radio noise at 67° W heliographic longitude, which occurred at 1325 UT on February 10. It is worth while examining whether the second increase is related to the arrival of fresh solar particles from this flare. If, in order to explain the terrestrial influence of a solar event far removed from the central meridian to the west, one postulates the presence of a guiding path of solar magnetic lines of force stretched out to the Earth by earlier streams or an outward solar wind, it would be difficult to explain the 24-hr delay for solar particles of even a few MeV energy. We are thus inclined not to associate the second event with the solar outburst on February 10.

We believe that in the two increases and the main decrease observed with the cosmic-ray storm of February 11, 1958, we have essentially three types of modulation process. One is directly associated with the moving plasma, probably related to the magnetic fields in the shock front and gives increases as well as decreases of intensity along with anisotropy. The second gives decreases of intensity and is related to a process which has a sharp onset but a relatively long time constant of recovery. The first is often more effective for high primary energies than low,

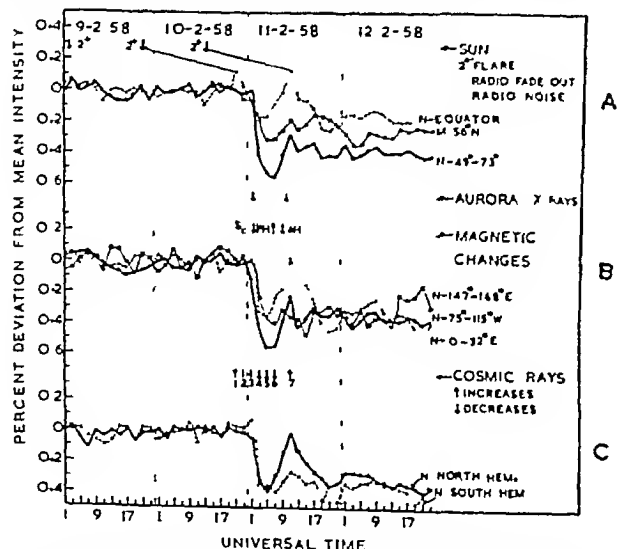


Fig. 1 Cosmic-ray intensity changes and associated solar and terrestrial effects for the cosmic-ray storm of February 11, 1958. Relationships of changes are indicated separately in A for low and middle latitudes and primary energy response, in B for meridional sections and in C for hemispheres.

but the second is much more effective for low than for high energies

The large anisotropy parallel to the north-south and east-west directions in the second increase poses an important problem. The different motions of solar particles trapped by the geomagnetic field have been discussed by Gold⁷, and before average conditions are established round the globe there is probably a basis for major differences in conditions over the hemisphere and at different meridional sections immediately following the arrival of a new cloud of solar particles. But the time involved is very short compared to the observed effect which shows up over periods of several hours. Moreover, even though changes in the Van Allen radiation belts could perhaps provide an adequate mechanism for the perturbation of the geomagnetic field and through it alter cosmic ray intensity, a quantitative evaluation of the effect has not so far been undertaken.

We are grateful to Mr S R Thakore and to the computation section at the Physical Research Laboratory and to Miss Britt at the Massachusetts

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MEASUREMENT OF THE EFFECTS OF PISTON MASS AND BURSTING PRESSURE ON THE MOTION OF A PISTON IN A HYPERSONONIC GUN TUNNEL

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A HYPERSONIC gun tunnel¹ is essentially a blow down tunnel with a shock compression heater to generate a high temperature reservoir of gas. This heater consists of a high pressure vessel separated from a long barrel by a diaphragm and light piston (see Fig 1). When the pressure is high enough the

diaphragm bursts and drives the piston down the barrel. A shock wave forms ahead of the piston and is reflected from the almost closed nozzle end of the barrel, causing several compressions of the gas within the barrel and raising the temperature. The piston finally comes to rest with the pressures on both

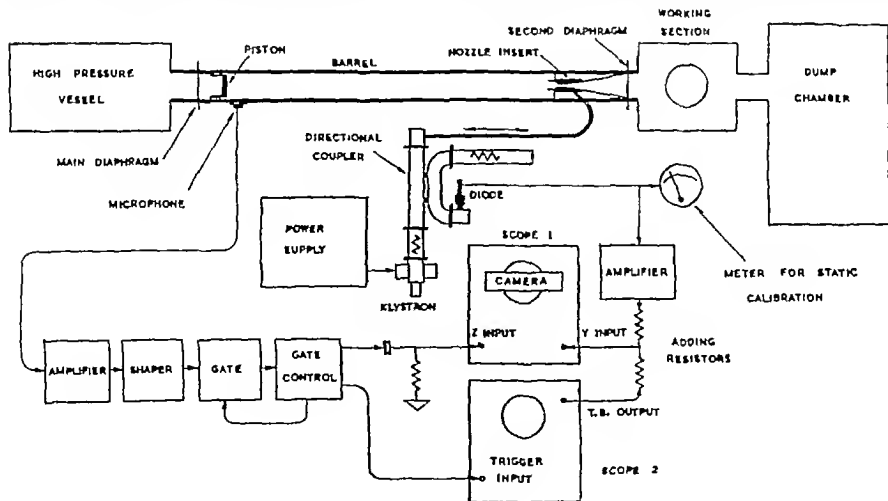


Fig 1. Layout

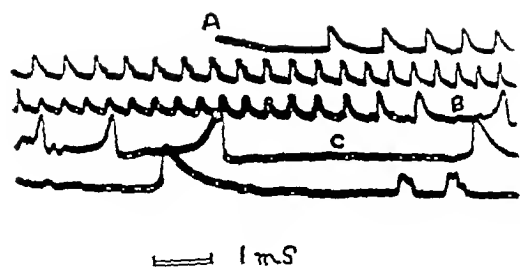


Fig 2 Typical oscilloscope record

sides equal. Both the mass of the piston and the bursting pressure will affect the performance of the tunnel.

One of the investigations into the operation of the gun tunnel at the Imperial College of Science and Technology, London, was to find how the bursting pressure and piston mass affect the motion of the piston down the barrel. This was done by a microwave technique², the barrel being turned into a long resonant cavity by coating the face of the piston with a conducting material, either a silver colloid paint or by gluing and screwing on a dural disk. Microwaves are injected at the nozzle end and resonance occurs with the piston at every half wave-length. By detecting and recording these resonances an analysis of the piston motion is possible.

The generator is a 200-mW, 10 cm klystron feeding a wave-guide directional coupler. To reduce the tendency for the klystron frequency to follow the changing resonant frequency of the barrel cavity, an attenuator is inserted between the klystron and the directional coupler. The purpose of the directional coupler is to sort out signals according to their direction, so that only the reflected waves coming from the barrel reach the diode. Power is fed from the klystron to the probes mounted in the nozzle insert through a co-axial cable. These probes are arranged not to interfere with the normal working

of the tunnel while still exciting a radially symmetric mode (TM_{01}) in the barrel. During a run the probes are protected by a nylon block. The probes are matched to the barrel cavity so that under conditions of resonance there is little power reflected back along the co axial feeder. However, when the piston moves from the resonant position the subsequent mismatch causes power to be reflected and is detected by the diode on the directional coupler. Hence a resonant point is indicated by a drop in the voltage output from the diode. The drop in voltage is recorded by an oscilloscope and camera. About fifty resonant points have to be measured and, as one sweep of the cathode ray tube has insufficient resolution, a raster type of display was used with a second oscilloscope providing the vertical time-base. Oscilloscope 1 was arranged to sweep continuously but with the beam blanked off, and oscilloscope 2 brightened up the first beam when triggered from a bursting signal picked up by a microphone. The time-base from the second oscilloscope was then added to the diode output to displace consecutive lines on the recording tube, producing a raster display. One trouble encountered was that the time-base voltage biased off the diode and reduced the signal to nothing. This was cured, with the attendant advantages of a larger signal, by inserting a small self-contained transistor isolating amplifier between the diode and the adding resistors (see Fig 1). The amplifier has a voltage gain of 17, a frequency response of 15 c/s to 500 kc/s ± 3 db with a high input and low output impedance. Two OC 45 transistors are used. A similar amplifier was also used as a microphone amplifier. Because of the resulting 'ring' and general noise of a burst, several traces were superimposed for each run as the second oscilloscope triggered more than once. To ensure that only one trace was obtained a trigger and gate system was adopted. This amplifies and shapes incoming signals from the microphone and passes them to a gate. A pulse coming from this gate closes the gate

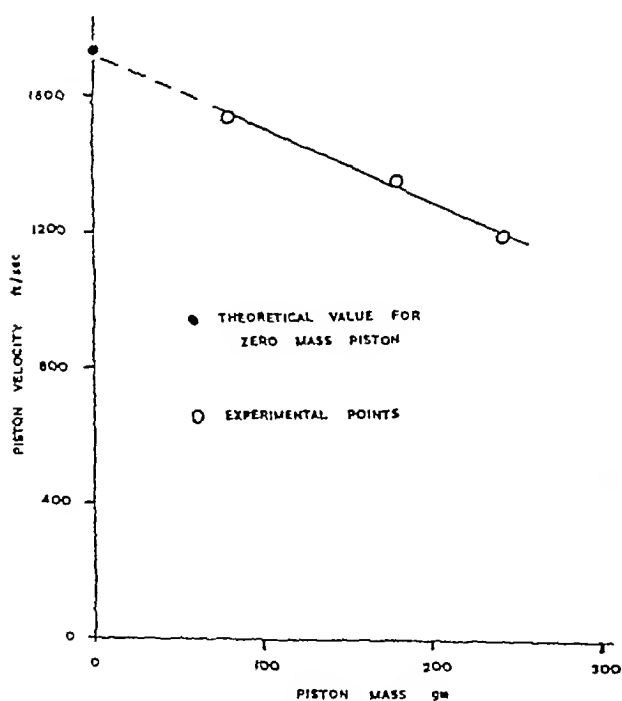


Fig 3 Variation of piston velocity with mass

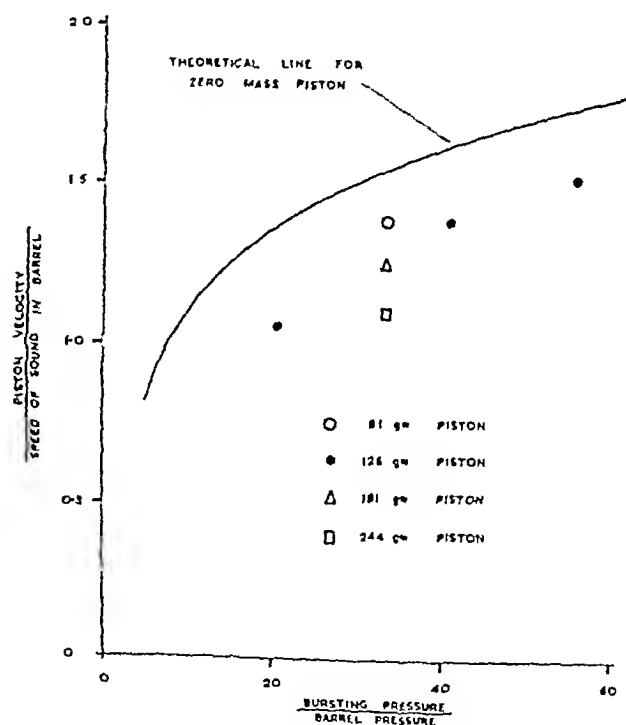


Fig 4 Variation of piston velocity with bursting pressure

and triggers the second oscilloscope. Hence only one trace is possible before the system is reset by opening the gate manually.

A typical record is shown in Fig. 2. Starting at A, which is arranged to be on a resonant point for reference, the distance between pips becomes less, indicating acceleration of the piston, until the third line down where after a rapid deceleration the wave shape is seen to reverse at B, indicating that the piston has reversed and is now going the other way down the tube. On the fourth line at C another reversal is evident. The resonant points are indicated by positive pips because the amplifier reverses the sign of the signal.

These film records were analysed to give a plot of piston position (x) against time (t). From such plots

the maximum piston velocity is taken. Figs. 3 and 4 summarize these results. Initial acceleration was also measured from the $x-t$ plots assuming the acceleration to be constant over the first few stations, the results being

| Bursting pressure (lb./sq. in.) | Acceleration |
|------------------------------------|--------------|
| 800 | 4 000g |
| 485 | 5 400g |
| 800 | 7,200g |
| 825 | 15 000g |

I am indebted to Mr J. L. Stollery for his direction and help in the foregoing work, and to Mr P. D. Church for his analysis of the traces.

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A STRUCTURAL MODEL FOR MONATOMIC LIQUIDS INCLUDING METALLIC LIQUIDS

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ALTHOUGH the melting point (T_m) is generally determined thermodynamically, it is interesting that Lindemann's geometrical law¹ is effective in determining the melting condition of solids. So we have studied the structure of liquids at their melting points in the hope of finding some similar law.

So far, radial distribution curves for 18 monatomic liquids near their melting points have been obtained by X-ray or neutron diffraction measurements and they give coordination numbers (Z) and the distance (r_1) of the nearest neighbour. However, the values of Z so far obtained are less reliable than those of r_1 , it is probable that in some cases we obtained low values. Therefore, we calculated Z from r_1 and the bulk density (measured) assuming a quasi face-centred cubic lattice. The calculated values Z_{cal} were between 10 and 11.5 (mean value 10.85, about 90 per cent of 12, Table 1).

Table 1. DATA FOR RADIAL DISTRIBUTION CURVES NEAR T_m

| | r_1 (Å) | Z_{exp} | Z_{cal} | r_1 (Å) | Z_{cal} (Å) | r (Å) |
|--------|-----------|-----------|-----------|-----------|---------------|---------|
| He (a) | 3.85 | 10.5 | 10.5 | 2.85 | 8.36 | — |
| Ar (b) | 3.66 | 8.0 | 10.5 | 3.40 | 3.47 | — |
| Ne (c) | 4.43 | 9.4 | 10.4 | 3.61 | 8.87 | — |
| Li (d) | 3.24 | 9.8 | 12.7 | 2.60 | 2.63 | 2.74 |
| Na (e) | 3.83 | 9.6 | 11.2 | 2.83 | 3.84 | 3.43 |
| K (f) | 4.94 | 8.0 | 10.8 | 3.95 | 4.05 | 4.36 |
| Ag (g) | 2.86 | 11.0 | 10.4 | 3.42 | 2.40 | 2.62 |
| Zn (h) | 2.94 | 10.8 | 13.7 | 3.33 | 2.67 | 2.76 |
| Cd (i) | 3.06 | 8.3 | 10.4 | 2.60 | 2.67 | 2.76 |
| Al (j) | 3.10 | 8.3 | 10.3 | 2.68 | 2.70 | 2.78 |
| Ga (k) | 2.95 | 10.9 | 11.5 | 2.60 | 2.58 | 2.59 |
| Sn (l) | 2.77 | 11.0 | 0.6 | 2.43 | 2.42 | 2.45 |
| In (m) | 3.30 | 8.5 | 11.3 | 2.85 | 2.85 | 2.96 |
| Tl (n) | 3.30 | 8.0 | 10.1 | 2.85 | 2.83 | 3.06 |
| Ge (o) | 2.70 | 9.1 | — | 2.66 | 2.66 | 3.07 |
| Si (p) | 3.23 | 9.1 | 10.7 | 2.79 | 2.82 | 3.77 |
| Pb (q) | 3.40 | 9.4 | 10.3 | 2.93 | 2.95 | 3.02 |
| Bi (r) | 3.40 | 8.0 | 9.6 | 2.90 | 2.97 | 3.04 |

(a) Gordon Shaw and Daunt, *J. Phys. Chem. Solids* **5**, 117 (1958).
(b) Eisenstein and Gingrich, *Phys. Rev.*, **63**, 261 (1942). (c) Campbell and Hildebrand, *J. Chem. Phys.* **11**, 534 (1943). (d) Gamsater, *Rev. Sci. Instr.* **28**, 1038 (1957). (e) Trumble and Gingrich, *Phys. Rev.* **84**, 278 (1952). (f) Thomas and Gingrich, *J. Chem. Phys.* **6**, 411 (1938). (g) and Gingrich and Wall, *Phys. Rev.*, **86**, 338 (1953). (h) Hildebrand, *Sci. 505* (1947). (i) Vignard, *J. Chem. Phys.* **22**, 1635 (1954). (j) Takenouchi and Furukawa Meeting of Japan Inst. Metals (April 1958). (k) Sharratt and Smith, *J. Chem. Phys.* **21**, 228 (1953). * $Z_{cal} = r_1^3(1.5)^{-1}$.

The shape of the curves was analysed by Wall's theory² using the spherical free volume of radius a . According to this theory, $(r_1 - a) = A$ corresponds to the position on the shorter side branch at a height of 34.4 per cent of the maximum value in the first peak of the curve $4\pi\rho(r)$ where $\rho(r)$ is the atomic number density at a distance r from any atom. Hence we measured A_{ob} from radial distribution curves and obtained the empirical formula $r_1/A_{ob} = (1.5)^{1/3}$ (Table 1).

Assuming a molecule to be a sphere (nearly rigid)³ of diameter A at T_m , the following model can be postulated: Let V_c be the volume at closest packing of spherical molecules of diameter A , then the volume of liquid at T_m is $1.5 V_c$ for quasi face-centred cubic lattice. But about 10 per cent of the sites in this quasi lattice are empty, and these spaces are distributed through all interstices, explaining the second peak at $1.0 r_1$ of the distribution curves. Thus the total volume is about $1.05 V_c$.

Using this model of a reduced form independent of materials, several properties of liquids can be explained as follows. Self diffusion and viscous flow in liquids are easily explained. The self-diffusion coefficient of a liquid at its melting point may be expressed^{4,5} as $D_m = \gamma r_1^2 \nu_m \exp(\Delta S_D/R) \exp(-H_D/RT_m)$, where γr_1^2 is the mean square of jump distances, ν_m the frequency of the liquid at T_m and ΔS_D and H_D the activation entropy and energy of diffusion respectively. Now $\gamma \Delta S_D$, H_D/RT_m and $D_m/(r_1^2 \nu_m)$ must all be constants independent of the material. If ν_m is calculable from Lindemann's formula, $\nu_m = 3.8 \times 10^{12} T_m^{-1/2} M^{-1/2} V_m^{-1/3}$, where M is the molecular weight and V_m the molar volume, $D_m/(r_1^2 \nu_m)$ is obtainable from experimental values of D_m , and is nearly constant (Table 2).

The experimental values of H_D/T_m and H_f/T_m are also nearly independent of the material where H_f is an activation energy of viscosity (Table 2). Differences between the liquid metals and other material may be explained by the expansion co-

Table 2 SELF-DIFFUSION AND VISCOSITY DATA (O.C.S.)

| | $(D_m/r_1^2 v_m) \times 10^3$ | H_D/RT_m | $H\eta/RT_m$ | $\eta_{m,ob} \times 10^3$ | $\eta_{m,cal} \times 10^3$ |
|-------------------------------|-------------------------------|------------|--------------|---------------------------|----------------------------|
| Na | 0.72 (a) | 3.28 (a) | 2.2 (d) | 0.71 (d) | 0.59 |
| Hg | 0.83 (a) | 2.15 (a) | 1.41 (d) | 2.1 (d) | 2.07 |
| In | 0.73 (a) | 2.83 (a) | 1.80 (c) | 1.94 (c) | 1.97 |
| Ga | 0.79 (a) | 1.85 (a) | 1.61 (d) | 2.14 (d) | 1.63 |
| Sn | 1.32 (b) | 3.06 (b) | 1.78 (c) | 1.05 (c) | 2.19 |
| Ag | 0.74 (c) | 3.30 (c) | 1.91 (f) | 3.88 (f) | 4.00 |
| Ar | 0.05 (a) | | 3.12 (g) | 0.28 (g) | 0.11 |
| N ₂ | | | 3.09 (g) | 0.31 (g) | 0.23 |
| CO | | | 3.50 (g) | 0.32 (g) | 0.23 |
| CH ₄ | | | 4.14 (h) | 0.23 (h) | 0.20 |
| C ₂ H ₆ | 0.41 (l) | 4.00 (l) | 4.31 (i) | 0.83 (i) | 0.90 |
| O ₂ | | | 3.70 (j) | 0.81 (j) | 0.27 |
| CCl ₄ | 1.87 (a) | 0.00 (a) | 4.74 (j) | 2.0 (j) | 0.55 |

(a) See ref. 12 concerning the experimental values of D_m . (b) Carerl and Pnoletti, *Nuovo Cim*, II, No. 3, 574 (1955). (c) Yang, Kado and Derge, *Trans. Met. Soc. A.I.M.E.*, 212, 628 (1955). (d) Liquid Metal Handbook (1952). (e) Culpin, *Proc. Phys. Soc. B*, 70, 1069 (1957). (f) Gebhardt and Wörwag, *Z. Metall.* 42, 358 (1951). (g) Rudenko and Schubnikow, *Phys. Z. Sowjet.*, 6, 470 (1954). (h) *ibid.*, 8, 179 (1955). (i) Grunberg and Nissan, *Trans. Farad. Soc.* 45, 125 (1949). (j) Thorpe and Rodgen, *Phil. Trans. Roy. Soc. A*, 185, 307 (1894). (l) See ref. 6.

efficients the ratio of which is of the order of 10^{-2} . In fact, under the condition of constant volume H_D/RT_m becomes 2.14 for CCl_4 , and 1.26 for C_2H_6 , from isobaric experiments, and becomes 2.07 for Hg, 1.63 for Ga, 1.65 for CCl_4 , and 1.40 for C_2H_6 , by computation from isothermal experiments using their expansion coefficients and compressibilities.

So putting $H_D/RT_m \equiv 1.6$ at constant volume, we obtain $\Delta S_D/R = -3.1 \pm 0.3$ independent of the materials from their values $D_m/(r_1^2 v_m)$ of Table 2. $\Delta S_D < 0$ can easily be explained by a more regulated activated-complex configuration composed of planar 4 or 5 atoms in the closest contact than the ordinary irregular configurations. Considering the above, it is of interest that A nearly coincides with the metallic bond-lengths of co-ordination number 3 calculated by Pauling's theory⁷ ($r(3)$ in Table 1).

Combining these facts with the Sutherland-Einstein formula⁸, $D\eta = kT/(2\pi A)$, we can easily deduce Andrade's formula⁹ $\eta_m = 5.7 \times 10^{-4} M^{1/2} T_m^{1/2} V_m^{-2/3}$ putting $D_m/(r_1^2 v_m) = 0.0067$. The calculated viscosity coefficients at T_m , $\eta_{m,cal}$, are in good agreement with the experimental values $\eta_{m,ob}$ (Table 2).

Table 3 ENTROPY OF LIQUIDS AT T_m (CAL/DEG/MOLE)

| | Calculated | | | Observed | |
|----|------------|------------|----|------------|------------|
| | Calculated | Observed | | Calculated | Observed |
| Ar | 12.458 | 12.594 (a) | K | 18.154 | 17.810 (c) |
| Xe | 18.704 | 10.04 (b) | Au | 23.613 | 23.32 (d) |
| Li | 11.170 | 11.001 (c) | Al | 16.820 | 17.00 (d) |
| Na | 15.130 | 15.507 (c) | Pb | 22.412 | 22.28 (d) |

(a) Clusius and Frank, *Z. Elektrochem.* 49, 308 (1943). (b) Clusius and Roccobini, *Z. phys. Chem.* 38B, 81 (1937). (c) Evans *et al.*, *J. Res. Nat. Bur. Stand.*, 55, 83 (1955). (d) See Borellus, "Solid State Phys.", 6, 55 (1958).

Moreover, using Wall-Harashina's free volume theory^{2,10}, and adding the entropy of random arrangement of vacancies as a cruder treatment of this model, the entropies of the liquids at their melting points were calculated, the values agreed with the observed ones (Table 3).

The above discussion shows that the metallic liquid is not a special liquid. Thus we need not consider the ionic unit^{4,11,12} in the transport phenomena.

The model will become more complete when combined with the recent work of Bernal¹³, who explained the essential difference between regular and irregular close-packing arrangements having a volume difference of about 10 per cent, which agrees with our model.

A detailed description including further applications will be published elsewhere.

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POLYNUCLEAR COMPLEXES OF MOLYBDENUM(II)

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ALTHOUGH molybdenum(II) chloride and its co-ordination complexes have been known for a century, they have received but little attention. As a result of the virtual absence of physical studies on these compounds, not only was nothing known of their constitution until a few years ago, but incorrect molecular formulae were even adopted. The relatively recent X-ray diffraction studies by Brosset¹⁻³ have done much to improve the position, though the bonding present in molybdenum(II) chloride derivatives has never been seriously discussed and many simple physical measurements remain to be done and correlated with the proposed structures. A re-investigation of these compounds is now particularly important as they appear to possess a stereochemistry quite different from that indicated

for d^4 metal complexes by ligand field theory. Therefore molybdenum(II) chloride and its derivatives are being re-examined and it is now possible to summarize some new experimental results and propose a bonding scheme for these compounds. This bonding scheme is able to explain why only certain types of ligands form molybdenum(II) chloride complexes.

The crystalline compounds studied by Brosset were formulated on the basis of his structure determinations as $[(Mo_2Cl_2)(OH)_4(H_2O)_2] \cdot 12H_2O$ ¹ and $[(Mo_2Cl_2)(Cl_2(H_2O)_2)] \cdot 6H_2O$ ². The structure of the $(Mo_2Cl_2)^{4+}$ group, fully named octa- μ_2 -chlorohexamolybdenum(II) and henceforth referred to as the chloromolybdenum(II) group, is given in Fig. 1. It is convenient for most purposes to regard the group

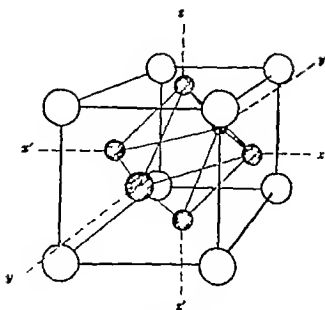


Fig. 1 The chloromolybdenum(II) group White circles Cl shaded circles Mo

as a regular face-centred cube and it is presented in this manner in the figure. Though the octahedron described by the molybdenum atoms is almost regular, the cube described by the chlorine atoms is somewhat distorted and it is possible that the deviation from strict equivalence of these chlorine atoms may be of some chemical significance. Brosset has emphasized that six groups given in braces in the formulae above, appear closely associated with the chloromolybdenum(II) unit. Fig. 1 shows that each molybdenum atom is surrounded by a square planar configuration of chlorine atoms, and can accept one ligand normal to the cube face to achieve co-ordinative saturation. The effective co-ordination number of each molybdenum atom, taking into account the four molybdenum close neighbours would be nine, and it is therefore improbable that more than one ligand could donate to each molybdenum atom. Thus six ligands may be accepted by the chloromolybdenum(II) group along the axes xx' , yy' and zz' . Whereas the identity of the central (MoCl_6) unit is seldom affected, the six ligands are freely variable. There is possible a novel range of octahedral complexes, their general character being of the type familiar to the inorganic chemist, but possessing a polyatomic nucleus.

The chloromolybdenum(II) group is stable over a wide range of conditions. In the form $(\text{Mo}_2\text{Cl}_8)\text{Cl}_2$, that is, MoCl_5 , it is not affected by boiling aqua regia or concentrated sulphuric acid heated to fuming other than the displacement of the chlorine ligands. It is stable to more than 800°C *in vacuo* with probable disproportionation to metal and higher halides above this temperature. It is not oxidized by air below 300°C , but above this temperature a dark product is formed. However it is much more sensitive to aqueous alkali giving molybdenum(V) hydroxide and hydrogen. At room temperature and pH 12, a chloromolybdenum(II) solution shows some signs of decomposition in about 10 hr, though at higher pH and temperature decomposition can be complete in a few minutes. It is noteworthy that the reagents most disruptive for the (Mo_2Cl_8) group are the strong electronegative complexing agents, namely, OH^- , F^- and NCS^- , though attack by these is rapid only at high temperatures. It is therefore possible that the decomposition of the chloromolybdenum(II) group under these conditions proceeds by the formation of an unstable substituted chloromolybdenum(II) nucleus. As this group retains its identity under most conditions, it is proposed to designate it as 'M' in formulae.

The present work strongly supports the view that the chloromolybdenum(II) group invariably possesses six groups bound to it. The following are typical examples of the new compounds isolated $[\text{MCl}_6(\text{C}_2\text{H}_5\text{N})_2]$, $[\text{MCl}_6(\text{C}_2\text{H}_5)_2\text{N}_2]$ and $(\text{H}_2\text{O})_2[\text{MCl}_6(\text{C}_2\text{H}_5\text{O})_2]$. Compounds with compositions corresponding to the following have also been reported $[\text{MCl}_6(\text{H}_2\text{O})_2]$, $[\text{MCl}_6(\text{C}_2\text{H}_5\text{OH})_2]$, $\text{K}_2[\text{MCl}_6] \cdot 6\text{H}_2\text{O}$, $[\text{MBr}_6(\text{H}_2\text{O})_2]$ and $(\text{H}_2\text{O})_2[\text{MBr}_6] \cdot 6\text{H}_2\text{O}$. The parent acid of the hexachloro chloromolybdenum(II) series has been known in the crystalline form as $(\text{H}_2\text{O})_2[\text{MCl}_6] \cdot 6\text{H}_2\text{O}$ for some time⁴. It is the most soluble hexachloro-complex, the salts of this acid being sparingly soluble or completely insoluble. Typical salts include those of the alkali metals ammonium and pyridinium⁴. The insoluble salts derived from large organic cations for example, tetraethylammonium and triphenylphosphonium, have been prepared in the present work. The salts of the hexabromo- and hexaiodo-acids are less well known but are undoubtedly similar to those of the hexachloro acid. The hexahalogeno-acids and their salts are rapidly hydrolysed in aqueous solution and an excess of hydrohalogenic acid must be maintained for stable solution. Solvolysis of these compounds is not observed in ethanol and solubilities often prove to be much higher in this solvent.

In addition to MCl_6 , it has now been possible to prepare MBr_6 , MI_6 and $\text{M}(\text{OH})_6$ by heating the appropriate hexahalogeno-acid or hydrated chloromolybdenum(II) hydroxide *in vacuo* at 250°C . As there appears to be only four ligands per chloromolybdenum(II) nucleus it is reasonable to suppose that these compounds are polymeric using some ligands for bridging between chloromolybdenum(II) groups and thus satisfying the proposed octahedral requirements. However it is interesting to note that Brosset has shown the hydrates of MCl_6 and $\text{M}(\text{OH})_6$ to consist of discrete octahedral complexes. In passing it may be mentioned that the four simple chloromolybdenum(II) compounds referred to above are found to be hygroscopic and undergo a lightening of colour on gaining water. The materials may be obtained anhydrous again by reheating *in vacuo*.

Complexes of the type $[\text{M}(\text{OH})_6]^{2-}$, $[\text{M}(\text{H}_2\text{O})_6]^{2+}$ and $[\text{M}(\text{NCS})_6]^{2-}$ are of interest but attempts to prepare solid compounds of the first two have failed so far. Such compounds undoubtedly exist in solution as chloromolybdenum(II) hydroxide is soluble in 2 N acid and 0.1 N alkali. It has been possible to confirm the existence of $[\text{M}(\text{OH})_6]^{2-}$ in solution by the pH titration involving the precipitation of the hydroxide by standard acid from a standard alkaline solution. Fig. 2 shows a typical titration curve in which two equivalents of nitric acid precipitate one of $\text{M}(\text{OH})_6$. Thus chloromolybdenum(II) hydroxide dissolves in alkali to give the complex $[\text{M}(\text{OH})_6]^{2-}$. The addition of $[\text{MCl}_6]^{2-}$ to a concentrated potassium thiocyanate solution gives a crystalline precipitate possessing a chloride and thiocyanate content reasonable for $\text{K}_2[\text{M}(\text{NCS})_6] \cdot 6\text{H}_2\text{O}$. However the compound is soluble in water, precipitating only in excess thiocyanate, and attempts to free the precipitate from the contaminating potassium thiocyanate have not proved successful so far.

The ideas expressed above might be criticized on the grounds that the chloromolybdenum(II) nucleus or its proposed co-ordination complexes are *in fact* ionic assemblages rather than covalent compounds. Though this is inconsistent with the chemical data already given, there is good evidence to settle this

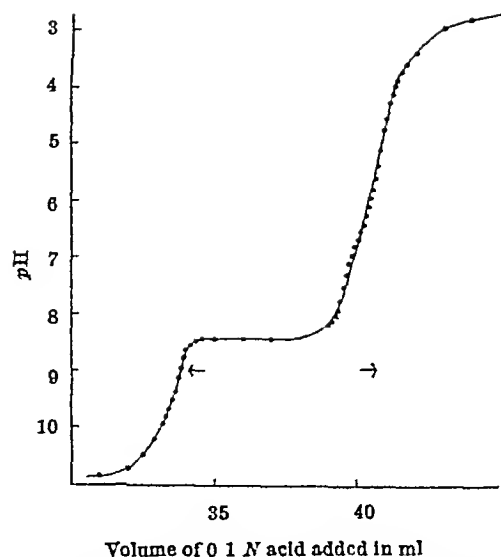


Fig 2 The precipitation of 3.29×10^{-4} moles of $M(OH)_6.6H_2O$ occurred in the region between the arrows

point Brosset has established that the hexachloro-acid exists as $[MCl_6]^{2-}$ in ethanolic solution by an X-ray diffraction technique⁷. Molecular weight determination of molybdenum(II) chloride in boiling ethanol has been found to give just over half the required value for MCl_4 .⁸ Under these conditions, it is very probable that some alcoholysis occurred, but ionization to a degree suggested by $M^{4+}(Cl^-)_4$ as the true constitution of molybdenum(II) chloride is ruled out. Thus, in a moderately strong solvating solvent, like ethanol, the $M-Cl$ bonds retain their identity. A number of chlorine-36 exchange studies to determine the lability of the chlorine atoms in the $[MCl_6]^{2-}$ ion have been carried out in the present investigation. The first experiments were carried out in 5.65 *N* hydrochloric acid to avoid hydrolysis. The hexachloro-acid was allowed to exchange with labelled hydrochloric acid, and the complex separated from solution either by freezing out at 0° C as the crystalline acid or precipitated as the triphenylphosphonium salt. The first separation method gave a very pure material, the second gave a rapid quantitative precipitation. It was found that the exchange fraction corresponded closely to the exchange of only six out of the fourteen chlorine atoms in $[MCl_6]^{2-}$ for exchange times of 2–800 min at 25° C. For times of exchange less than 2 min, less than six out of fourteen chlorine atoms exchanged, but the data are inaccurate. It is reasonable to conclude that all fourteen chlorine atoms in $[MCl_6]^{2-}$ are covalently bound, but the ligand chlorine atoms are much more labile than the nuclear chlorine atoms in 5.65 *N* hydrochloric acid. The inertness of the eight nuclear chlorine atoms is striking, for on refluxing the hexachloro-acid for 1½ hr in hydrochloric acid, only six out of fourteen had exchanged.

At this point it is logical to consider whether chloromolybdenum(II) should have a chemistry analogous to some mononuclear cation, or whether the resemblance is superficial. It is true that if the molybdenum(II) atoms were held together by a cage of shared chlorine atoms, it may well be that the compounds resembling octahedral complexes could be isolated. However, these would have the properties expected of divalent molybdenum, frequently displaying paramagnetism, ligand field spectra and a strong tendency to oxidation. This is in striking con-

trast to what is observed, for chloromolybdenum(II) complexes are very stable to oxidation and are all diamagnetic. Solution absorption spectra give no indication of ligand field spectra, only one or more bands at about 300–350 $m\mu$, $\epsilon \sim 3 \times 10^3$, which account for the deep yellow colour of the compounds. It is possible, however, that these charge transfer bands may be superimposed on some very weak $d-d$ transition bands. Fig 3 gives the absorption curves assigned to the species $[MCl_6]^{2-}$ and $[MBr_6]^{2-}$ in 5 *N* hydrochloric and hydrobromic acid, respectively, and $[M(OH)_6]^{2-}$ in 0.01 *N* alkali. It is important to bear in mind that the properties suggested above for molybdenum(II) are hypothetical as no paramagnetic molybdenum(II) compounds are known and complexes of the type $[Mo(II)X_6]$, from which $[MX_6]$ might be considered to be derived, do not exist. Furthermore, mononuclear molybdenum(II) compounds are very rare (see below). If molybdenum(II) is spin-paired in chloromolybdenum(II), accounting for its diamagnetism, combination of this group with carbon monoxide-like ligands would be expected, and again this is not found. There is no evidence that MCl_4 is affected by carbon monoxide at 40 atm and 110° C. or by triphenylphosphine at 200° C. It is significant that among the few mononuclear molybdenum(II) complexes known, $[Mo(II)(diarsine)(CO)_2I_2]$, $[Mo(II)(diarsine)_2(CO)_2I_2]$ and similar compounds have recently been prepared by Nyholm and co-workers by linlogenation of tetracarbonyl-(*o*-phenylene-bis(dimethylarsine))molybdenum(0).⁹ These compounds are diamagnetic, contain carbon monoxide-like ligands and possess ligand field spectra and co-ordination number seven. Therefore, the chloromolybdenum(II) group behaves quite differently from that reasonably expected on molybdenum(II), and moreover, differently from any transition metal other than one with a d^0 configuration. It is then justifiable to regard the chloromolybdenum(II) group as a particular and distinct chemical entity and not as an assemblage of atoms in a rather special geometry.

The non-appearance of typical transition metal properties is not difficult to explain. The intermolyb-

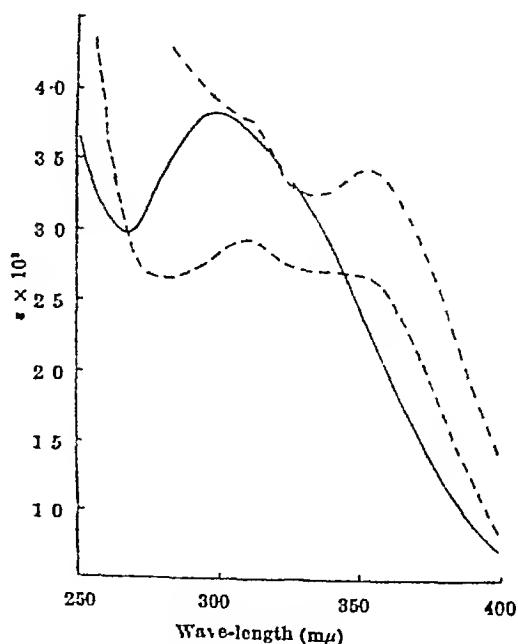


Fig 3 — —, $[MBr_6]^{2-}$, —, $[M(OH)_6]^{2-}$, - · - ·, $[MCl_6]^{2-}$

dendum distance is 2.03 Å to be compared with 2.73 Å for molybdenum metal, and therefore Mo-Mo bonds must exist along all sides of the Mo₆ octahedron. The highly symmetrical arrangement of the Mo₆ group allows convenient consideration of the intermolybdenum bonds as delocalized and best represented by molecular orbitals. For the purposes of discussion the [MoCl₄]²⁻ complex will be considered. Each molybdenum atom is surrounded by a tetragonal pyramid of chlorine atoms, bonded probably by d_{xy}, d_{yz}, d_{zx} hybrid orbitals. Of the remaining four d -orbitals, the d_{xz} and d_{yz} possess lobes directed exactly along the intermolybdenum axes and it is possible for each of four co-planar molybdenum atoms to combine one of these orbitals to give a molecular orbital system. There are three such sets of co-planar atoms, each forming such orbitals. The contribution of two d -electrons per molybdenum atom to forming such intermetallic bonds gives molybdenum a valency higher than the oxidation number two. The disposition of the two remaining electrons in the d_{xy} and d_{z^2} orbitals must be consistent with the observed properties of chloromolybdenum(II) compounds. Pairing the electrons in one of the two remaining orbitals may account for diamagnetism, but possibly not the other properties. Furthermore, the proximity of the molybdenum atoms to each other also suggests that there would be some repulsive interaction between non bonding pairs in either the d_{xy} or d_{z^2} orbitals. It is concluded that the two remaining electrons occupy the orbitals singly, and that these contribute a little more to the intermolybdenum bonding by coupling their spins.

Therefore, chloromolybdenum(II) can best be regarded as a compound of molybdenum(VI) employing all nine orbitals. This is quite consistent with crystallographic evidence, for Broset reports that each molybdenum atom possesses nine neighbours

all closer than 2.7 Å. The hexavalency of molybdenum explains the absence of observable $d-d$ transitions in spectra and the inability to form complexes with π bonding ligands. The apparent conflict of the stereochemistry of chloromolybdenum(II) with ligand field theory is removed. Though the theory suggests a number of favoured arrangements for d^4 complexes, it seems unable to account for the arrangement in chloromolybdenum(II). This difficulty disappears when the compounds are recognized as d^0 complexes.

In conclusion, the following points are re-emphasized. Molybdenum(II) chloride complexes contain the chloromolybdenum(II) group, (Mo₆Cl₆)⁴⁺, which functions as a nucleus for octahedral complexes of the form [M₆X₆]. The chloromolybdenum(II) group exhibits intermetallic bonding and though the oxidation number of molybdenum is two, the valency is effectively six. Consistent with the d^0 character of the molybdenum is co-ordination number nine. Furthermore, this d^0 character explains the diamagnetism, absence of both ligand field spectra and complexes with π bonding ligands of chloromolybdenum(II) compounds.

I wish to acknowledge the award by the University of London of an I.C.I. Research Fellowship during the tenure of which this investigation was conducted and also to express my indebtedness to Prof R. S. Nyholm and Dr J. Lewis for their suggestion and support of the research.

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MASSIVE INCORPORATION OF 5-FLUOROURACIL INTO A BACTERIAL RIBONUCLEIC ACID

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IN the course of studies on the correlation of the mechanisms controlling the production of cellular high polymers, we have investigated the effects of 5-fluorouracil on the synthesis of protein and nucleic acid in several strains of *Escherichia coli*. We have reported elsewhere (ref. 1, and unpublished work by the same authors) on the ability of the fluoro compound to substitute, in part, for uracil in a mutant requiring this pyrimidine. In the absence of uracil, the addition of 5-fluorouracil resulted in the doubling of the protein content; a slight increase in ribonucleic acid, but none in deoxyribonucleic acid took place. In *E. coli*, strain B, as well as in the uracil auxotroph supplemented with uracil, the fluoro pyrimidine inhibited the synthesis of deoxyribonucleic acid completely, but permitted the formation of both protein and ribonucleic acid.

The formation, in the presence of 5-fluorouracil, of several constitutive or inducible enzymes was also examined. The activity of two of the enzymes,

catalase and succinate dehydrogenase, increased, the induction of β -galactosidase by lactose was, on the other hand, almost entirely blocked in the presence of 5-fluorouracil. The fluoropyrimidine prevented, moreover, any further rise of the β -galactosidase activity in cells that had previously been treated with the inducer or in a strain of *E. coli* in which this enzyme is constitutive. Other observations, soon to be published in collaboration with Drs F. Goodman and J. J. Saukkonen, showed that 5-fluorouracil prevented the multiplication of *T2* bacteriophage and the intracellular synthesis of the phage nucleic acid in *E. coli*, strain B, whereas it had less influence on the growth of *T3*.

These findings, as well as the recent reports on the incorporation of 5-fluorouracil into the ribonucleic acids of animal tissues² and of tobacco mosaic virus³ made it of interest to ascertain whether also in *E. coli* the biological effects of the fluoro compound are accompanied or caused by its

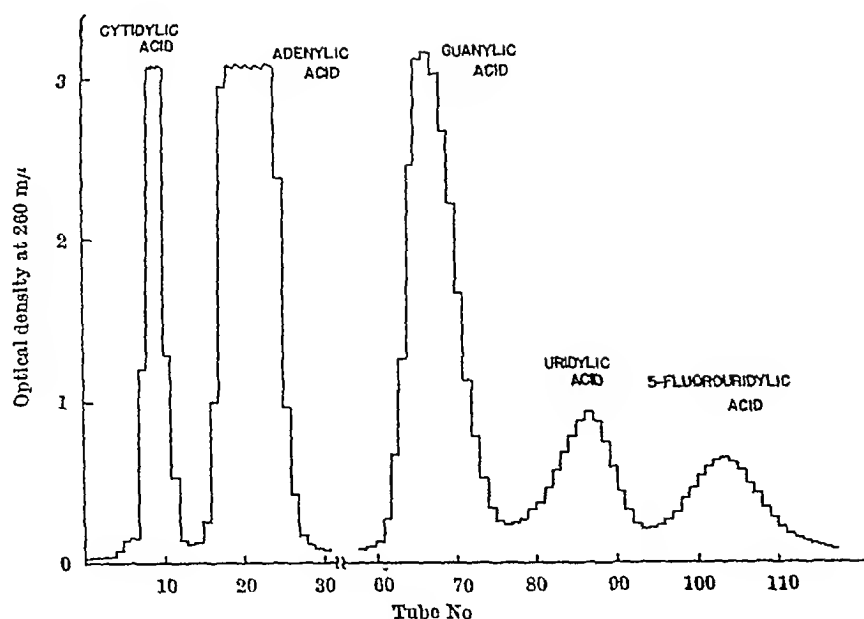


Fig. 1. Elution diagram of the hydrolysate of the ribonucleic acid of *E. coli*, strain *B*, formed in the presence of 5-fluorouracil. Dowex 2 formate⁸ (8 times), 200–400 mesh, 23 cm × 0.9 cm diameter, gradient elution (mixing chamber 500 ml water, reservoir 2.5 N formic acid), 7 ml fractions.

introduction into the ribonucleic acid. The results presented here show that a considerable amount of this uracil analogue does indeed find its way into the ribonucleic acid of the organism, where it may replace nearly one-half of the normally present uracil.

To cultures (37°, glucose-salts medium, early logarithmic phase) of *E. coli*, strain *B*, or of the uracil-deficient mutant 63–86, supplemented with uracil (20 μgm/ml), 5-fluorouracil (50 μgm/ml) was added and the cell suspensions were kept at 37° for varying periods. If the action of the inhibitor on the uracil auxotroph was to be tested in the absence of uracil, the cells were harvested and starved before the addition of the fluoropyrimidine¹. At the conclusion of the treatment, the organisms were collected and prepared for analysis (removal of mononucleotides, lipids, etc.) by procedures described previously⁵. The hydrolysis of the ribonucleic acid was carried out with 0.3 N alkali (30°, 18 hr.) with the use of either sodium hydroxide, in which case the hydrolysate was acidified with hydrochloric acid in order to precipitate protein and deoxyribonucleic acid, or of potassium hydroxide, in the latter case perchloric acid was employed, care being taken to avoid losses through the co-precipitation of nucleotides during the removal of potassium perchlorate in the cold. The ribonucleotide composition was determined by electrophoresis on filter paper or by ion-exchange chromatography.

A typical elution pattern (Fig. 1) shows five components, with the new nucleotide leaving the column after uridylic acid, as expected for a mixture of the 2'- and 3'-phosphates of 5-fluorouridine³. The combined eluates of this component collected in several runs were again subjected to chromatography, the experimental conditions were as in Fig. 1 except that *N* ammonium formate was used for gradient elution. A single sharp peak was observed and the nucleotide identified as 5-fluorouridylic acid. The hydrolysis of the compound with 72 per cent perchloric acid (1 hr., 100°) liberated 5-fluorouracil, which was identified by chromato-

graphy and spectrophotometry, the molar ratio of 5-fluorouracil to phosphorus was found to be 1:1.17. The treatment of the nucleotide with prostatic phosphatase resulted in the liberation of 5-fluorouridine, which was identified by the comparison of its spectral and electrophoretic (0.1 M borate buffer of pH 9.2⁹) properties with those of the authentic nucleoside. The ratio of 5-fluorouridine to phosphate released by the enzymic hydrolysis was 1:1.1. That the nucleotide consisted of a mixture of the 2'- and 3'-phosphates of 5-fluorouridine and had, therefore, formed part of a polynucleotide, was shown by its behaviour towards 3'- and 5'-nucleotidases. It was not attacked by the 5'-nucleotidase of Russell's viper venom, whereas 3'-nucleotidase⁷ hydrolysed about 60 per cent of the nucleotide to fluorouridine within 20 hr. 5-Fluorouridylic acid has its absorption maximum at 268 mμ in 0.01 N hydrochloric acid with a

molar extinction coefficient of 9,400, the absorbance ratios in the same solvent are A_{250}/A_{260} , 0.64, A_{280}/A_{260} , 0.82, A_{290}/A_{260} , 0.32.

The nucleotide composition of the ribonucleic acid synthesized, both in the presence and the absence of 5-fluorouracil, by the two *E. coli* strains under investigation is shown in Table 1. It will be seen that one-quarter to nearly one-half of the nucleic acid uracil can be replaced by the fluoropyrimidine. This takes place without an essential disturbance of the equality of the molar sums of 6-amino and of 6-keto nucleotides¹⁰. The large quantities of 5-fluorouracil built into the ribonucleic acid of strain *B* offer a convenient method for the preparation of the 2'-, 3'-, and 5'-phosphates of 5-fluorouridine. It is noteworthy that 5-fluorouridylic acid was also found in the ribonucleic acid of the uracil-requiring mutant incubated with the fluoropyrimidine in the absence of uracil, although the amount of nucleic acid synthesized under these conditions is slight (ref. 1, and unpublished work by the same authors). Owing to the relatively small number of analyses it is not yet clear what importance should be attached to the fluctuations in nucleotide proportions recorded in Table 1, nor is it yet known whether 5-fluorouracil is incorporated preferentially into any particular fraction of the total ribonucleic acid or into certain positions on the polymer chain.

In contrast to the known metabolic fate of uracil, we have found no indication that 5-fluorouracil gives rise also to a 5-fluorocytidylic acid component of the nucleic acid. Preliminary evidence would, in fact, seem to speak against the presence of the latter fluoro nucleotide, at least in amounts comparable to those of 5-fluorouridylic acid. Neither elution peak nor chromatographic zone corresponding to 5-fluorocytidylic acid was seen, the spectra of the separated nucleotides showed no evidence of such a contaminant. Moreover, orienting experiments on the uptake of uracil-2-¹⁴C by the ribonucleic acid of the uracil auxotroph exclude the occurrence of appreciable quantities of 5-fluorocytidylic acid. As shown in Table 2, 5-fluorouracil depresses the incorporation of

Table 1 NUCLEOTIDE COMPOSITION OF RIBONUCLEIC ACID OF *E. coli* STRAINS

| No. | Specimen* | Analytical procedure† | Moles per 100 moles nucleotide in ribonucleic acid | | | | |
|-----|--|-----------------------|--|-----------------|----------------|---------------|-----------------------|
| | | | Adenylic acid | Guanilylic acid | Cytidylic acid | Uridylic acid | 5-Fluorouridylic acid |
| 1 | Strain B normal | I | 26.3 | 29.6 | 25.1 | 19.0 | — |
| 2 | Strain B treated with 5-fluorouracil 21 hr | II | 23.1 | 30.4 | 25.2 | 11.4 | 0.8 |
| 3 | Uracil auxotroph 63-86 normal | III | 23.7 | 32.3 | 23.0 | 20.8 | — |
| 4 | Uracil auxotroph 63-86 treated with 5-fluorouracil to the presence of uracil 3 hr | III | 24.6 | 30.4 | 24.8 | 16.0 | 4.8 |
| 5 | Uracil auxotroph 63-86, treated with 5-fluorouracil in the absence of uracil 16 hr | II | 23.8 | 32.7 | 22.5 | 17.4 | 4.0 |

* The figures for No. 1 averages of many determinations are taken from a previous publication (ref. 8). Those for No. 3 are based on several hydrolysis experiments. Specimens No. 2 and 4 and 6 were single preparations. Preparations of strain 63-86 treated with 5-fluorouracil to the presence of uracil for 1 and 2 hr gave results very similar to those reported for specimen No. 4.

† The following procedures were employed: (I) chromatography on filter paper in the isobutyrate solvent (ref. 8); (II) separation of nucleotides liberated by sodium hydroxide on Dowex 2 formate columns by gradient elution with formic acid (ref. 3); (III) separation of nucleotides liberated by potassium hydroxide through electrophoresis on filter paper in 0.02 M citrate buffer of pH 3.6 (ref. 9). In the last-mentioned system uridylic and 5-fluorouridylic acids migrate together. The fluoronucleotide was therefore determined separately by electrophoresis in 0.1 M borate buffer of pH 9.16 to which it migrates as the fastest component (ref. 4) and the estimates of uridylic acid were suitably corrected.

uracil into the uridylic acid, but not its utilization for the cytidylic acid, of the ribonucleic acid of the mutant. It may also be mentioned that we have encountered no indication of the entrance of 5-fluorouracil into the deoxyribonucleic acid of *E. coli*.

Table 2. EFFECT OF 5-FLUOROURACIL ON INCORPORATION OF URACIL-2-¹⁴C INTO *E. coli* RIBONUCLEIC ACID

Exponentially growing cells of the *E. coli* mutant 63-86 were washed and starved of uracil (ref. 1). After the addition of uracil-2-¹⁴C (20 μ M/ml) specific activity 25,000 c.p.m./mmole) the preparation was divided into two equal parts one of which received 5-fluorouracil (50 μ M/ml). During the subsequent incubation at 37°C for 3 hr equal amounts of ribonucleic acid were formed in both preparations. The radioactivity found in the purine nucleotides and in 5-fluorouridylic acid amounted to less than 5 per cent of that incorporated into the pyrimidine nucleotides. The results are reported per ml of cell suspension.

| Specimen | Uracil-2- ¹⁴ C incorporated (μ mole per ml) | | Incorporation ratio uridylic acid to cytidylic acid |
|-----------------------------|---|----------------|---|
| | Uridylic acid | Cytidylic acid | |
| Normal | 25.1 | 20.6 | 0.85 |
| Treated with 5-fluorouracil | 14.5 | 30.0 | 0.48 |

We are indebted to Dr J. A. Aeschlimann, Hoffmann-La Roche, Inc., Nutley, N.J., for specimens of the fluoro compounds used in these studies. The uracil requiring mutant originally isolated by Prof. B. D. Davis of Harvard University, was given us by Dr E. Borek. We are grateful to Dr J. J. Saukkonen for helpful discussions and to Mr R. L. Cooper for technical assistance. The work was supported by grants from the United States Public Health Service and the National Science Foundation.

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MEASUREMENTS OF TEMPORAL ADAPTATION TO SPATIAL DETAIL VISION

By A. J. SEYLER and Z. L. BUDRIKIS

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THERE is neurophysiological and psychological evidence¹⁻³ that temporal as well as spatial adaptation processes are involved in visual perception. From this we argued that after the presentation of a new visual pattern a certain time may be required for a viewer to recognize spatial detail in this new pattern.

A quantitative measure of the perceptual time delay versus the size of detail would be a significant design parameter for a variety of control and communication systems involving the human sense of vision. Tachistoscopic visual recognition tests and reaction time measurements have been reported^{4, 5}, but we think that these have a different significance, because the object, and thus the design, of the experiments are different.

The idea behind our experiments was that, if the viewer requires a definite adaptation time to perceive

spatial detail in a newly presented visual scene it should be possible to measure this effect by presenting the new scene in such a way that the detail size is decreased progressively in time after the instant of presentation. In other words, the new scene is 'blurry' when it is presented to the viewing subject and is made increasingly 'sharper' as function of time. If this temporal increase in objective sharpness occurs faster than the subjective adaptation to the perception of detail, the viewer will not notice the effect. If, however, the temporal adaptation process of the viewing subject proceeds faster than the objective increase in sharpness, it will be noticed by the subject that the scene had been blurred initially. It will be recognized that this approach contains certain elements of transient response testing of electrical systems where the response to a finite transition (in time and amplitude) is given by the

convolution of excitation and transfer function. Hence, for our tests, we argued that the finite temporal increase in sharpness will not be noticed, when the perceptual time response to it is not 'noticeably' slower than what it would have been to a scene which was sharp from the instant of its presentation (response to an ideal stimulus).

Because the 'sharpness' of a picture can be conveniently varied (along the horizontal dimension) by varying the band-width of a television picture signal using a variable low-pass filter, television-type presentation was chosen. This also facilitated rapid change-over from one scene to another by electronic means. The test scenes were stationary (slides) while between presentations of these was displayed an 'interlude' of a normal television programme without sound received from local stations. Thus, we found, prevented staring at the display area, provided relaxed viewing conditions with no specific bias towards any one fixation point and introduced a close similarity to actual viewing in everyday situations.

The experimental conditions were as follows. Television pictures in accordance with the CCIR Standard (625/50/25) having a maximum signal band-width of 5 Mc/s were displayed on a studio monitor of 9 in. \times 12 in. picture dimensions. The monitor was surrounded by a flat grey surface, 48 in. \times 68 in. Indirect ambient lighting was used in the test area. The brightness of the surround was 0.2 foot-lambert, picture peak white 4 foot-lambert and picture black 0.1 foot-lambert (measured with SEI-Photometer). Two different viewing distances were used, one at four times, the other at eight times, picture height. Correspondingly, the maximum picture dimension (width) had a subtended angle of 19° and 9° 30' for the two distances and minimum detail size for any signal band-width of B Mc/s is given by $11.4/B$ and $5.7/B$ minutes of arc respectively.

By means of a voltage controlled continuously variable low-pass filter⁶ the signal band-width was varied from a minimum B_m Mc/s at the time of scene change-over, $t = 0$, to the system band-width of $B_s = 5$ Mc/s at $t = T$ in accordance with the following time function

$$B(t) = B_m \exp\left(\frac{t}{T} \log \frac{B_s}{B_m}\right) \text{ Mc/s, } 0 < t < T$$

Thus the minimum detail size in minutes of arc subtended angle varied for the two viewing distances as

$$S(t)_4 = \frac{11.4}{B(t)} \text{ and } S(t)_8 = \frac{5.7}{B(t)}$$

The minimum band-width B_m (degree of blurriness) and the recovery time T as well as the test slide were preset by the experimenter without the subject knowing the conditions. After being prompted by the experimenter the subject pressed a control button by which the interlude scene was replaced by the test scene. The equipment was controlled so that change-over took place during the suppression interval (of approximately 1.5 msec) between television frames following the pressing of the button. This instant being time $t = 0$ was also the beginning of the recovery of the filter from the preset minimum to full system band-width, which caused the increasing of the objective picture sharpness over the interval $0 < t < T$. Shortly afterwards, the subject announced by 'Yes' or 'No' whether a blurring of the picture was

'seen' or not. The test slide display was then changed back to the interlude by the experimenter before the next experimental condition was established. An average of not more than 150 decisions were made by each subject during a single session in order to prevent tiring. The sequence of the three experimental parameters was selected from a table of random numbers.

In tests of this nature it is desirable to have approximately equal frequencies for 'Yes' and 'No'. We therefore carried out exploratory tests at a viewing distance of four times picture height by which we intended to find values for B_m for which the decisions went from 100 per cent 'No' to 100 per cent 'Yes' when T was varied. For B_m ranging from 0.28 to 4 Mc/s and T from 20 to 2,600 msec, full transitions from 100 per cent 'No' to 100 per cent 'Yes' could only be obtained for B_m less than 1 Mc/s. At this particular setting the percentage 'No' never fell below 60 per cent and seemed to vary in an unsystematic way for recovery times exceeding 1 sec. We therefore concentrated on the two values of 0.28 and 0.5 Mc/s for B_m , corresponding to 40.6 and 22.8 minutes of arc for the maximum detail size at four times picture height and 20.3 and 11.4 minutes of arc at eight times picture height viewing distance. The minimum detail size for the two distances and $t > T$ was 2.28 and 1.14 minutes of arc. For each setting of B_m eight different recovery times were used, being $50 < T < 2,600$ msec and $40 < T < 2,080$ msec for $B_m = 0.28$ and $B_m = 0.5$ Mc/s respectively.

Three different test slides were displayed. One of these depicted a group of three children, the second an aerial view of a city and the third a stone hut, all three contained fine detail and sharp contours of good contrast but different distribution over the picture area. Since the experiment was not concerned with a semantic recognition, the pictorial content of the slides was of less significance than the availability of detail to which the subject's perception would adapt itself.

Four male subjects belonging to the staff of the Laboratories were tested. They were all familiar with the experiment and the appearance of the reduced detail presentation. Therefore, they may be classed as skilled and critical observers.

The 'percent not seen' ('No') for each experimental condition were computed taking the decisions of all subjects on all test slides together. The resulting

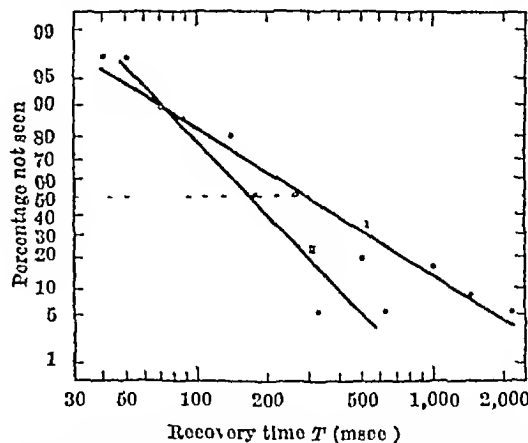


Fig. 1. Percentage not seen versus recovery time. Viewing distance, four times picture height. 1, (O—O) $B_m = 0.5$ Mc/s, $S_{max} = 22.8$ min. of arc, 11, (●—●), $B_m = 0.28$ Mc/s, $S_{max} = 40.6$ min. of arc.

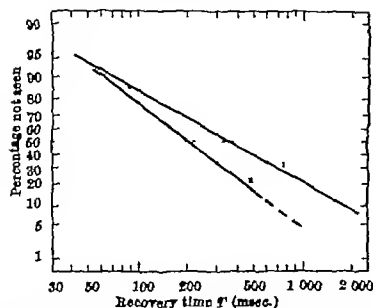


Fig. 2. Percentage not seen versus recovery time. Viewing distance eight times picture height. T (O—O) $B_m = 0.5$ Mc./s. $S_m = 11.4$ min. of arc. T (●—●) $B_m = 0.28$ Mc./s. $S_m = 20.3$ min. of arc.

experimental points were fitted to a normal distribution versus the logarithm of recovery time (T) as shown in Figs 1 and 2, using the method of least squares. Each point represents 30 decisions. The permissible recovery times for which the mutual lack of sharpness in detail was not seen in 50 per cent of the presentations are listed with the respective experimental conditions in Table 1.

Although within the same viewing distance the permissible recovery time increases approximately in the same ratio as the initial detail size decreases, for the doubling of the viewing distance (that is, halving of detail size for the same B_m) the recovery time increases only by a factor 1.25.

From what is known about human sensual phenomena we cannot expect linear behaviour over any extended range of inputs and stimulus conditions. Hence we consider it unjustified to attempt an extra

Table 1

| Viewing distance (picture height) | 4 times | 8 times |
|--|---------|---------|
| Minimum detail (min. of arc) | 2.23 | 1.14 |
| Maximum detail (min. of arc) | 40.6 | 22.8 |
| Recovery time (msec.) for 50 per cent No | 100 | 290 |
| | 200 | 360 |

polation from the restricted data at our disposal at this time. However, the main conclusions which we may draw from the results of the experiment are that a certain time is required after the presentation of a new and remaining visual display before the perception threshold for fine detail is reached, and that due to this effect it is possible to expand the time interval within which detail in changing complex visual displays is offered to the viewer without noticeably interfering with the normal perception process.

It must be left to further extended experiments to attempt a determination of the functional relationships between the relevant parameters.

We are indebted to the Supervising Engineer Research, Postmaster General's Department of Australia, for permission to publish the material contained in this communication.

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EFFECT OF OXYGEN TENSION ON HÆM AND PORPHYRIN BIOSYNTHESIS

By J. E. FALK, R. J. PORRA and ANN BROWN

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F. MOSS and HELEN E. LARMINIE

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THE adaptive synthesis of cytochromes in aerobic and anaerobic conditions of culture is well known¹. It has been shown by one of us² that as the oxygen tension in the culture medium is increased, the synthesis of cytochrome a_2 by *Aerobacter aerogenes* increases to a maximum, and then decreases when still higher oxygen tensions are applied. The maximum was reached when the oxygen concentration in the medium was of the low order of 0.1 M. It was suggested that a self-regulatory mechanism may operate, the formation of cytochrome a_2 being controlled in accordance with the respiratory requirements imposed by the prevailing oxygen tension.

It occurred to us that prosthetic group synthesis might be affected by the oxygen tension. The prosthetic group of cytochrome a_2 is an iron-chlorin, and nothing is yet known about the biosynthesis of this cytochrome or its prosthetic group. It has now been found however, that the biosynthesis of

protoporphyrin and hœm, in chicken erythrocyte preparations *in vitro*, appears to be regulated by oxygen tension.

Whole blood (25 ml.) from normal chickens was shaken with glycine (final concentration 0.055 M) and 1 mgm. each of heparin, penicillin and streptomycin, at 38° C. The gas mixtures all contained 5 per cent carbon dioxide and the relevant concentration of oxygen; nitrogen was used as diluent. The mixtures were made in aspirators, and by displacement with water were bubbled through the incubation mixture at the rate of 2 l./hr. The conical incubation flasks were closed with Bunsen valves and frothing was controlled by a few drops of octanol. When washed cells were used, 25 ml. of blood was centrifuged and the serum and the 'buffy coat' removed. The erythrocytes were washed three times with isotonic sodium chloride and resuspended in isotonic sodium chloride to a final volume of 25 ml. Substrate and

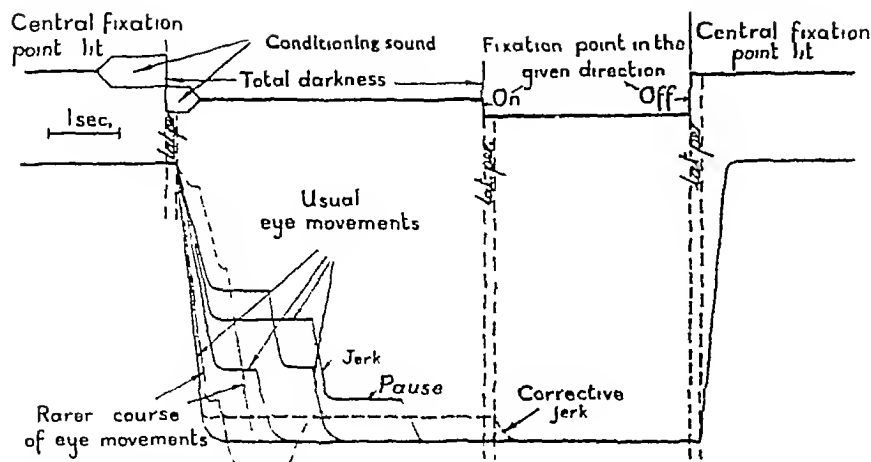


Fig 1 Representative scheme showing typical variability of equally directed precise (—) or imprecise (---) conditioned eye fixation movements in successive trials. Abscissa: time, ordinates: eye displacement during trials. From more than 2,000 records of conditioned eye movements in the dark of six subjects, in various given directions from 0° to 35° off the centre in the horizontal plane. Optically elicited and conditioned changes in fixation are preceded by latent periods of about 0.15 sec. lat per = latent period.

to (a) the number of single eye jerks in it (for example, from 1 to 3, and up to 6 jerks in the total saccade), (b) the size of these jerks (varying, most generally, from 30 to 100 per cent of the total fixation movement, and in extreme cases from 15 per cent up to 120 per cent of its total size), (c) the duration of pauses between successive jerks in the saccades (habitually, from 0.04 to 0.7 sec, and up to 1.92 sec), (d) the angular speed of the eye movement in jerks of equal size (from 60 to 140 per cent, and not infrequently up to 200 per cent of its mean value). In some cases reversals have been observed in the usual succession of diminishing jerks, and in some other cases excessive jerks have been recorded, followed by corrective jerks in the opposite direction.

Such a fundamental variability of the composition of equally directed saccadic fixation movements characterizes conditioned eye rotations of every size in the horizontal plane as well as in vertical and in diagonal planes. We may conclude that conditioned eye movements of equal total size and direction, just like motor acts of the organism as a whole, are generally produced by essentially variable sequences of innervation impulses, which is inconsistent with the innervation theory. On the other hand, the now well-known proprioceptors⁶ of the extrinsic eye muscles are the only sensory organs firing during eye rotations in total darkness, and thus proprioceptive feedback is used to bring the position of the eyes into accordance with the temporary central changes brought about by the conditioning stimulus. Thus the observations strongly support the hypothesis that the 'muscle sense' of the eyes is mainly controlled by temporary changes in the higher proprioceptive centres, and it must be noted that such a mechanism would form a physiological basis for visual illusions arising in cases of dissociation between the actual eye position and the evaluation of the line of regard, which in fact depends on conditioned fixation reflex training.

Because of the restriction of nerve connections engaged and the constancy of mechanical load during movement, the conditioned eye fixation reflex may be considered as a simple physiological model of more complicated motor behaviour acts.

It appears that to remove apparent contradictions between 'peripheral' theories of behaviour control

(like Sherrington's) and 'central' theories (like Holmholtz's), Pavlov's theory must be applied to sensory arcs of the conditioned reflex. Fig 2 represents a hypothetical scheme based on Pavlov's concept of temporary cerebral kinesthetic feedback. The external stimuli, having formerly coincided with reactions fulfilled and reinforced, on eliciting a reaction by the way of its effector centre, simultaneously produce in the higher proprioceptive centres changes just like those which, beforehand, became reinforced at the fulfilment of the reactions. During the course of the reaction, the impulses ascending to the higher proprioceptive centres from the sensitive endings in the effector organs are constantly re-coded according to the functional state of these centres and, being thus transformed into signals of cor-

rection, take part in the regulation of the reaction until its fulfilment and repeated reinforcement. Thus, it appears that behaviour acts remain on the whole adequately directed, because of the regulation during their course of the efferent nerve supply by the higher proprioceptive centres, according to changes brought to these centres by conditioning stimuli.

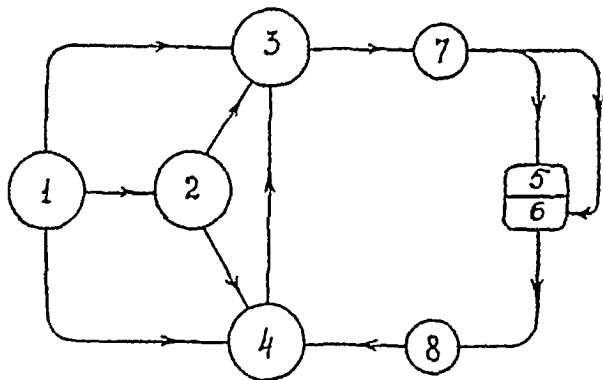


Fig 2 Hypothetical scheme of the central sensory control of behaviour, 1, cortical representation of the conditioning stimulus, 2, cortical centre of the unconditioned reaction, 3, cortical effector and 4, cortical sensory centre of the conditioned reaction, 5, effector organ and 6, sensory endings in it, 7, 8, subcortical centres. Arrows show the supposed directions of the main innervation flows engaged.

It is only in the frame of the conditioned changes in the higher sensory centres that the afferent impulses from the effector organs get their full meaning for the organism. 'Muscle sense' arises from co-operation and mutual control, as behaviour acts are going on, of certain sensory events of external and internal origin, thus co-operation and mutual control being rendered possible by the conditioned reflex mechanisms. Thus, the mechanisms of elaboration of temporary changes in the higher proprioceptive centres may be regarded as probably the more general physiological basis of psychic space perception phenomena.

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FORTHCOMING EVENTS

(Meetings marked with an asterisk * are open to the public)

Monday, November 30

ROYAL SOCIETY (at Burlington House Piccadilly London W 1) at 2.30 p.m.—Anniversary Meeting

INSTITUTE OF METAL FINISHING (in the Canterbury Room of the Claridge Hotel London W 1) at 2.45 p.m.—Mr J. A. B. Harvey "The Role of the Scientific Society" (Presidential Address)

UNIVERSITY COLLEGE (in the Physiology Theatre Gower Street, London, W 1) at 5 p.m.—Prof. E. J. Kennedy (University of Chicago) "The Biosynthesis of Complex Lipids" (First of two lectures in Biochemistry Further lecture on December 7)

ROYAL INSTITUTION LIBRARY CIRCLE (at 21 Albemarle Street London W 1) at 5.30 p.m.—Dr L. Pearce Williams "Paradise Through His Manuscripts"

ROYAL GEOGRAPHICAL SOCIETY (at 1 Kensington Gore, London, S W 7) at 8.30 p.m.—Prof. O. von Furer-Haimendorf "Shoreland of Eastern Nepal"

Tuesday December 1

UNIVERSITY OF LONDON (in the Anatomy Theatre University College Gower Street, London W 1) at 1.15 p.m.—Prof. R. E. D. Bishop "Vibration Problems in Engineering"

INSTITUTE OF ELECTRICAL ENGINEERS MEASUREMENT AND ELECTROTECHNICAL SECTIONS (at Savoy Place London W 2) at 5.30 p.m.—Dr L. Eason Mr J. V. L. Parry and Mr J. McE. Steele "Frequency Variations of Quartz Oscillators and the Earth's Rotation in Terms of the N.P.T. Cesium Standard"

UNIVERSITY OF LONDON (at Imperial College of Science and Technology London S W 7) at 6.30 p.m.—Prof. H. K. Porter "Physiology has No Frontiers" (Inaugural Lecture)

UNIVERSITY OF LONDON (at the London School of Hygiene and Tropical Medicine Keppel Street Gower Street London W 1) at 5.30 p.m.—Dr J. L. Gowers "The Lymphocyte" (Twelfth of fifteen lectures on "The Scientific Basis of Medicine" organized by the British Postgraduate Medical Federation Further lectures on December 3 & 10)

PLASTICS INSTITUTE (at the Wellcome Building, 183-193 Euston Road London N W 1) at 6.30 p.m.—Mr M. E. B. Ashenden "Plastics and the Law"

ROYAL AERONAUTICAL SOCIETY (at 4 Hamilton Place London W 1) at 7 p.m.—Dr L. M. Hall "Transonic Flow Over Swept Wings"

Wednesday December 2

INSTITUTE OF PETROLEUM (at 21 New Cavendish Street London W 1) at 5.30 p.m.—Mr J. Marechal and Mr P. de Radatsky "Petrochemicals of Urea in Dewaxing Middle and Heavy Distillates"

INSTITUTE OF INFORMATION SCIENTISTS (at the Berners Hotel 10 Berners Street London W 1) at 6 p.m.—Discussion on Languages in Information Work—To What Extent is Competence in a Foreign Language an Essential Qualification for an Information Scientist?

Wednesday, December 2—Thursday December 3

IRON AND STEEL INSTITUTE (in the Great Hall Caxton Hall, Garton Street London E 1) and the Hoare Memorial Hall Church House Great Smith Street London S W 1) at 9.30 a.m. daily—Autumn General Meeting

Thursday December 3

UNIVERSITY OF LONDON (in the Anatomy Theatre University College Gower Street London W 1) at 1.15 p.m.—Mr P. R. Bell "The Origin of Indian Corn"

ROYAL SOCIETY (at Burlington House Piccadilly London, W 1) at 3 p.m.—Mr J. H. C. Edgcombe and Prof. R. C. W. Norrish F.R.S. "A Study of the Mechanism of Photochemical Electron Transfer Processes in Solution" Mr J. M. Dawson and Mr H. A. C. Follett "An Electron Microscope Study of Synthetic Graphite"

INSTITUTE OF MARINE ENGINEERS (joint meeting with the INSTITUTE OF NAVAL ARCHITECTS, in the Water Hall 10 Upper Belgrave Street London, S W 1) at 4.15 p.m.—Prof. G. Aerias "New Sea Trials on the Sandblasted Lubricant"

UNIVERSITY OF LONDON (at the London School of Economics and Political Science, Leighton Street London W 2) at 5 p.m.—Dr E. H. Leach "Rethinking Anthropology" (Malinowski Memorial Lecture)

ROYAL SOCIETY OF ANTS, COMMONWEALTH SECTION (at John Adam Street, Adelphi London W 2) at 5.15 p.m.—Mrs. Mildred Valley Thornton "Indians of British Columbia"

INSTITUTE OF ELECTRICAL ENGINEERS (at Savoy Place London W 2) at 6.30 p.m.—Mr C. B. H. Wood and Mr J. J. Shelley "The Transmission of News Film over the Trans Atlantic Cable"

SOCIETY OF CHEMICAL INDUSTRY MICROBIOLOGY GROUP (joint meeting with the SOCIETY FOR APPLIED MICROBIOLOGY at the Royal Society of Medicine 1 Wimpole Street, London W 1) at 6.15 p.m.—Dr P. Brown "Infective Ribonucleic Acid from the Virus of Foot and Mouth Disease"

Friday December 4

INSTITUTE OF ELECTRICAL ENGINEERS MEDICAL ELECTRONICS DISCUSSION GROUP (at Savoy Place, London W 2) at 6 p.m.—Discussion on "X-ray Magnetics Resonance" opened by Dr V. Sheppard and Dr R. E. Richards

SOCIETY OF DYERS AND COLOURISTS (at the Royal Society Burlington House, Piccadilly London W 1) at 6 p.m.—Mr R. C. Oakley "Dyeing of Ribbons" Mr B. Woods "Dyeing of Carpet Knots"

ROYAL INSTITUTION (at 21 Albemarle Street London W 1) at 8 p.m.—Dr H. A. Thomas "Electronic Brains"

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned

LECTURERS OR ASSISTANT LECTURERS (suitably qualified graduates) with some experience in any of the branches of electrical engineering in the Department of Electrical Engineering—The Registrar The University Manchester 13 (November 21)

LECTURER IN TELECOMMUNICATION to undertake undergraduate and postgraduate teaching and to supervise research involving information analysis and experimental work Industrial element—Head of the Electrical Engineering Department Imperial College of Science and Technology Exhibition Road London S W 7 (November 24)

LECTURER with a degree in psychology or equivalent and experience of teaching and clinical work in EDUCATIONAL PSYCHOLOGY—The Registrar University College Swansea (November 28)

SENIOR LECTURER and a LECTURER (preferably with a major interest in applied thermodynamics or applied mechanics especially the theory of machines) in Engineering (Mechanics)—The Registrar The University Manchester 13 (November 23)

SENIOR LECTURER LECTURER and an ASSISTANT LECTURER in the DEPARTMENT OF MECHANICAL ENGINEERING—The Registrar Royal Technical College Belfast Lancs (November 28)

ASSISTANT LECTURER (DEMONSTRATOR) in ANATOMY, to undertake teaching and research and a RESEARCH ASSISTANT (with an honours degree in zoology or medical sciences and preferably a knowledge of German) in the DEPARTMENT OF ANATOMY for work mainly on the central nervous system—The Registrar University College London Gower Street London W 1 (November 30)

LECTURER with a degree in zoology at Victoria University of Wellington New Zealand—The Secretary Association of Universities of the British Commonwealth 30 Gordon Square London W 1 (New Zealand, November 30)

RESEARCH OFFICER (with veterinary qualifications) for studies on the epidemiology of diseases in the field of the Research Institute (Animal Virus Diseases) Pirbright Surrey (November 30)

SENIOR LECTURER in CHEMISTRY at Victoria University of Wellington New Zealand—The Secretary Association of Universities of the British Commonwealth 30 Gordon Square London W 1 (New Zealand November 30)

RESEARCH ASSISTANT (with a first or second-class honours degree in chemistry or alternatively graduate member of the Royal Institute of Chemistry) in CHEMISTRY—The Principal Coventry Technical College, Coventry (December 1)

LECTURER (with experience in either heavy electrical machinery or of power transmission and distribution) in ELECTRICAL ENGINEERING—The Registrar University College of South Wales and Monmouthshire Cathays Park Cardiff (December 4)

ASSISTANT or ASSOCIATE PROFESSOR of APPLIED MATHEMATICS—The Chairman Department of Mathematics McMaster University Hamilton, Canada (December 10)

SENIOR LECTURER, or LECTURER (Grade 1) in BOTANY at University College, Ibadan Nigeria—The Secretary Inter University Council for Higher Education Overseas 29 Woburn Square London W 1 (December 12)

SENIOR LECTURER or LECTURER in EXPERIMENTAL PHARMACOLOGY—The Secretary The University, Aberdeen (December 14)

CHAIR of PHYSICS CHAIR of GEOLOGY CHAIR of ZOOLOGY and CHAIR of BACTERIOLOGY in the University of Khartoum—The Registrar, University of Khartoum, c/o Inter University Council for Higher Education Overseas 29 Woburn Square London W 1 (December 15)

EMPIRE RHEUMATISM COUNCIL FELLOW (with medical or scientific qualifications) to prosecute research in the field of rheumatism. The General Secretary, Empire Rheumatism Council, Faraday House 8-10 Charing Cross Road London W 2 (December 15)

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LETTERS TO THE EDITORS

CHEMISTRY

Photolysis of Thionine in Rigid Medium—
Measurement by Spectrofluorimetry

The quantum efficiency of photo decomposition in rigid solvents at liquid nitrogen temperature is for many substances quite low, and it is customary to expose the photolyte directly to the concentrated beam from a mercury lamp to produce sufficient photo product for the measurement of its absorption spectrum. When measuring the quantum efficiency, it is difficult to produce a sufficiently high intensity of monochromatic light at a series of wave-lengths and covering the whole area of the reaction cell. A further difficulty is the absorption of the irradiating light by the products of the reaction. This can produce a large inner filter error if comparatively high concentrations are photolyzed to a significant degree. With thionine in E.P.A. glass the quantum efficiency is less than 0.005 and to avoid these difficulties the application of spectrofluorimetry was investigated. As an analytical technique spectrofluorimetry is much more sensitive than absorption spectroscopy¹ and allows the use of dilute solutions, so that a comparatively small proportion of the photolyzing light is absorbed. A further advantage is that light from a monochromator can be focused on a small area of the reaction cell so that much higher intensities can be obtained than if the whole cell face were illuminated. After irradiation, comparison of the intensity of the red thionine fluorescence from the irradiated area with that from unirradiated areas on either side gives a direct measure of the proportion of dye-stuff consumed. The spectrofluorimeter can also be used to observe the fluorescence emission and excitation spectra of fluorescent photo products. At the concentrations used ($< 10^{-5}$ M), complications due to energy transfer processes are negligible.

The spectrofluorimeter previously described¹ was used both for photolysis with monochromatic light and for fluorescence measurements. The cuvette was replaced by a quartz Dowar vessel having two windows in line for the passage of the irradiating beam and for absorption measurements and one window in a position at right angles to the irradiating beam for the observation of the fluorescence. The reaction cell had a square face, 2.9 cm \times 2.9 cm and an optical depth of 0.5 cm, the fluorescence being observed through the flat edge of the cell. The exciting light was chopped at 800 c/s and the fluorescence was detected by means of an 800 c/s tuned amplifier so that phosphorescence of duration greater than a few msec was rejected.

The quantum efficiencies for the photodecomposition of thionine in other-ethanol-septentano glass (2:2:1) were found to be as in Table 1.

The quantum efficiency is low at all wave-lengths observed. It is highest at 248 m μ , on the high frequency side of the second absorption band of thionine. At 578 m μ , in the visible absorption band, there was no detectable decomposition, the quantum yield being less than one thousandth of that at 248 m μ . This wave-length effect thus runs parallel to that observed in the flash photolysis of dilute solutions of thionine at room temperature² where a

long lived species, tentatively identified as the semi-thionine free radical, was observed when ultra violet light was used.

Table 1 QUANTUM EFFICIENCY FOR THE PHOTOLYSIS OF THIONINE
(Ethanol-septentano glass at 77° K)

| Wave-length (m μ) | Dose rate incident on reaction cell (micro-einstein per min.) | Time of irradiation (min.) | Quantum efficiency $\times 10^3$ |
|---------------------------|--|----------------------------------|-------------------------------------|
| 578 | 0.33 | 120 | < 0.002 |
| 578 | 0.34 | 240 | < 0.001 |
| 302 | 0.032 | 270 | 0.01 |
| 302 | 0.11 | 285 | 0.04 |
| 283 | 0.009 | 240 | 0.47 |
| 283 | 0.028 | 120 | 0.63 |
| 248 | 0.018 | 270 | 2.0 |
| 248 | 0.027 | 100 | 3.0 |
| 248 | 0.053 | 40 | 2.9 |

The fluorescence emission spectra of the photolyzed glasses showed a band with maximum at 510 m μ . The corresponding excitation spectra showed three well-defined maxima at 260, 320 and 455 m μ . The absorption spectra of the photo products, obtained by photolysing larger concentrations of thionine (10^{-4} – 10^{-3} M) showed well defined peaks at 410, 425 and 635 m μ , none of which corresponded to the excitation maximum, and it thus appeared that more than one product of photolysis could be obtained. Measurements of the thionine recovered after molting the irradiated glass, and also after aeration of the resulting solution, suggested that about 50 per cent of the photolyzed dye-stuff was converted into the semiquinone free radical.

A detailed account of these experiments will be published elsewhere.

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June 24

¹ Parker C. A. *Nature* 182 1092 (1958)

² Parker C. A. *Nature* 182 130 (1958)

BIOCHEMISTRY

Monamycin A New Antibiotic

In 1944 Meredith reported¹ the results of an extensive screening programme designed to select soil micro-organisms with antagonism towards *Fusarium oxysporum cubense*, the causative agent of the Panama disease of the banana plant. An examination of a selection of Meredith's cultures has led to the separation, from a mixed culture, of a new species which we have named *Streptomyces jamaicensis*. The species grows readily on a medium containing neopeptone and glucose both in stationary and in aerated, submerged cultures to produce an antibiotic which is distributed in the culture medium and the mycelium.

This antibiotic has been isolated by a procedure which includes the following essential stages. The crude product is extracted from the culture fluid and the mycelium with ether or butanol. The extract after removal of solvent, is concentrated with respect to antibiotic by two countercurrent distributions using in turn, the systems ethyl acetate-cyclohexane

methanol, water (12 10 10 7) and light petroleum (boiling point 60–80° C), methanol, water (10 10 1) followed by chromatography using the ion exchange resin 'Amberlite' C G 45. The product is crystallized from light petroleum as needles, melting point 126° C. This compound to which we have assigned the name monamycin, has properties which distinguish it from known antibiotics.

Monamycin is a base which gives a crystalline monohydrochloride [melting point 187° C, $[\alpha]_D^{18} - 62 \pm 5^\circ$ (c 0.9 in ethanol)]. Analysis results are in good agreement with those required by the molecular formula $C_{22}H_{36-38}N_4O_5$ with one N-methyl and three C-methyl groups. The ultra-violet spectra of the base and its salts exhibit only end absorption. The infra-red spectrum of monamycin shows no evidence of aromatic character but suggests the presence of an amide linkage. It does not react with sodium metaperiodate or with hydrogen in the presence of platinum catalyst.

Monamycin is active at high dilution against a variety of Gram-positive organisms, including strains of *Staphylococcus aureus* which are resistant to penicillin, aureomycin, chloramphenicol and sulphamethazine. There is no significant activity against any of the Gram-negative organisms which have been examined. Table 1 shows the activity towards typical organisms.

Table 1

| Organism | Highest effective dilution (gm./ml.) |
|--|---|
| <i>Staphylococcus aureus</i> (A T C C 9144) | 1/20,000,000 |
| <i>Bacillus subtilis</i> (A T C C 6033) | 1/15,000,000 |
| <i>Streptococcus pyogenes</i> (A T C C 8108) | 1/10,000,000 |
| <i>Streptomyces lavendulae</i> | 1/8,000,000 |
| <i>Escherichia coli</i> | <1/100,000 |
| <i>Pseudomonas fluorescens</i> | <1/100,000 |

in terms of the highest effective dilution as measured by the agar-streak method².

This antibiotic is a relatively stable compound. There is no loss of activity after autoclaving in aqueous solution at pH 9 for 10 min. at 114° C, but losses occur at pH values lower than 7. It is not inactivated by human serum. Acute toxicity studies involving injection into mice by the subcutaneous route showed no unfavourable reactions at a dosage of 850 mgm/kgm. This was the highest dose tested.

We are grateful to Miss L. Wong and Mrs S. Smith for technical assistance, to the Tropical Products Institute for financial support and to both the National Research Development Corporation and the Microbiological Research Establishment (Ministry of Supply), Porton, for facilitating and undertaking the larger-scale production of monamycin.

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¹ Meredith, C. H., *Phytopath.*, **34**, 406 (1944).

² Waksman, S. A., and Reilly, H. C., *Ind. Eng. Chem. (Anal. Ed.)*, **17**, 556 (1945).

Transplantation Immunity: Separation of Antigenic Components from Isolated Nuclei

EXTRACTION of transplantation antigens, introduced and substantially improved by Billingham, Brent and Medawar^{1,2} has always been performed by

exposing the cells to ultrasonic oscillations in distilled water or solutions of low ionic strength. We here report results obtained with less drastic techniques more usual in biochemistry. The test for antigenicity is based on the ability of active components to provoke a 'second set' reaction in a skin homograft of the donor strain¹.

All extraction procedures are conducted in the cold. Thymus and spleen nuclei isolated according to Billingham *et al.*¹, represent a suitable and constant basic material. They are extracted four times with 0.14 M sodium chloride, 0.01 M sodium citrate, pH 7, in a Waring blender, for 75 sec. each time. The 4 supernatants, after centrifugation for 10 min. at 15,000 g, are collected for subsequent manipulation. The residue, mostly deoxyribonucleoprotein, is still slightly active after four such treatments, but has no detectable activity after six extractions. If allowed to stand for some time, the collected supernatants show a faint opalescence which may be cleared by centrifuging at 15,000 g for 30 min. The sediment, which seems to contain some kind of deoxyribonucleic acid-protein complex, is antigenically active, but the greater part of the antigenic activity remains in solution.

Various purification procedures may then be applied. Antigen may be precipitated by lowering the pH to 5. Fractional precipitation shows the best yields to occur between pH 7 and 6 and between pH 6 and 5.5. The precipitate, most of it consisting of ribonucleoprotein, also contains haemoglobin which is a regular contaminant of our nuclei suspensions. Though it dissolves most of the ribonucleoprotein, citrated saline does not bring back the antigen into solution. This insoluble fraction is highly antigenic and represents a useful preparation for many purposes.

Alternatively, antigen may be precipitated from the initial supernatants by ammonium sulphate up to 50 per cent saturation. The sediment is completely soluble in citrated saline. This procedure eliminates most of the haemoglobin which precipitates at 60–80 per cent saturation. This method has the advantage of securing soluble antigenic matter which may be easily handled for analysis, particularly by chromatography and electrophoresis. Selective chromatography on calcium phosphate has shown the identity of the antigen with one of the first peaks. This probably represents a very high degree of purification.

Enzymic assays have been performed, very often with the insoluble fraction after precipitation at pH 5. Deoxyribonuclease, ribonuclease, trypsin, actinomycin *F*₁ B and lysozyme were tested. Only the last enzyme significantly reduced the antigenic activity. However, this is probably due to a non-specific complexing effect, for it was not accompanied by a corresponding increase in reducing sugars. In other experiments enzymic assays were combined with separation procedures. Although they permitted a higher degree of purification, they failed to solve the fundamental problems of the chemical nature of the antigen, which, according to the latest hypothesis of Billingham, Brent and Medawar², seems to be a complex polysaccharide of comparatively low molecular weight. This and other problems are discussed in detail elsewhere.

It is of interest to note that a toxic component may be extracted from the nuclei. Constantly recovered from the same fractions, it seems to be a glycoprotein.

We are greatly indebted to Profs V. Desreux and

M. Wolsch for helpful advice and criticism throughout this work and to Miss M. Protin for technical assistance

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¹ Dillingham, R. T., Brent, L., and Medawar, P. B. *Nature* 178 514 (1956)
² *idem Transp. bull.* 5 377 (1958)

Electrophoretic Heterogeneity of Trypsin

In a previous communication¹ it was reported that crystalline trypsin, when submitted to paper electrophoresis at pH 2.6, shows the presence of three different and proteolactically active fractions, even in the absence of calcium ions.

The present work was undertaken to investigate further the electrophoretic behaviour of crystalline trypsin and of the trypsin fractions separated by paper electrophoresis.

Our results seem to indicate that the behaviour of crystalline trypsin in free boundary electrophoresis at pH 2.5 is fundamentally similar to that obtained with paper electrophoresis. They show also that the fractions separated by paper electrophoresis at pH 2.6 bear no relation to those separated by free electrophoresis at pH 5 in the presence of calcium ions. These facts are interpreted as resulting from the presence in crystalline trypsin of at least four electrophoretic components.

The crystalline trypsin and the technique used for paper electrophoresis were the same as described previously¹. For preparative purposes, however, sheets of Whatmann No. 3 paper measuring 32 cm. × 54 cm. were used. The localization of the trypsin fractions was obtained by dyeing three guiding stripes, one cut from the middle and one from each side of the sheet. The part of the paper containing the main trypsin fraction was cut and extracted with 3 ml. of 0.001 *M* hydrochloric acid. This extract was dialysed for 48 hr. against two changes of the proper buffer solution and then submitted to free electrophoresis in a Perkin Elmer Model 38 instrument.

Two buffers were used in these experiments: a glycine (0.05 *M*), hydrochloric acid (0.025 *M*) and sodium chloride (0.05 *M*) buffer of pH 2.5 and a sodium acetate (0.04 *M*) and acetic acid (0.04 *M*) buffer of pH 5, to these solutions calcium chloride up to a concentration of 0.04 *M* was added when necessary.

The results of the analyses, by free electrophoresis, of the main component of crystalline trypsin separated by paper electrophoresis at pH 2.6 are given in Table I.

They show that this component is homogeneous when analysed by free electrophoresis at pH 5, at pH 2.6 in the presence of calcium ions and also by paper electrophoresis at pH 2.6. However, by free electrophoresis at pH 5 in the presence of calcium ions two fractions were obtained. These results indicate that trypsin contains at least four distinct electrophoretic fractions, namely, F_1 and F_2 migrating together as the main component during paper electrophoresis at pH 2.6, and separated only when in the presence of calcium at pH 5 by free electrophoresis, and fractions F_3 and F_4 which are resolved directly by paper electrophoresis at pH 2.6. Another point that emerges from these experiments is that the fractions obtained by paper electrophoresis at pH 2.6 seems to bear no relation to those shown by free electrophoresis at pH 5 in the presence of calcium.

The experiments of fractionation of crystalline trypsin by free electrophoresis are shown in Table 2. Fraction E_4 is present in crystalline trypsin and amounts to about 3 per cent of the total proteins, this component, however, is precipitated almost entirely during dialysis against pH 5 buffer and is therefore absent from the electrophoretic diagrams obtained at pH 5. Adding the precipitate F_4 to crystalline trypsin resulted in an increase in the amount of the slower fractions which is separated by free electrophoresis at pH 2.5. Since F_1 and F_2 are not separated at this pH either by paper electrophoresis or by free electrophoresis (Table 1), we may conclude that F_4 at this pH, migrates together with F_2 during free electrophoresis. The composition of the fractions in this case, namely, free electrophoresis at pH 2.5, are considered to be ($F_1 + E_4$) for the faster, and ($F_3 + F_4$) for the slower one; thus result being independent of the presence of calcium ions.

At pH 5, F_4 is absent and in the presence of calcium ions F_1 is separated from F_2 . The ratio between the percentages of F_1 and F_2 —found after fractionation at this pH—of the main paper electrophoretic component indicates that F_2 migrates together with F_1 and not with F_3 . Accordingly, the components of the fractions observed at pH 5 in the presence of calcium ions should be ($F_1 + F_2$) for the faster and F_3 for the slower fraction.

It is necessary, however, to point out that no conclusive evidence exists for identifying F_2 obtained by direct electrophoresis of crystalline trypsin, with F_3 resulting from the fractionation of the main component separated by paper electrophoresis inasmuch as their mobilities are different. We have not found satisfactory explanation for this result beside admitting further heterogeneity of these three fractions.

Another point of interest is the pronounced effect of calcium ions on the mobility of both trypsin fractions during electrophoresis at pH 2.5 indicating that at

Table 1. ELECTROPHORETIC ANALYSIS OF THE MAIN COMPONENT ($F_1 + F_2$) OF CRYSTALLINE TRYPSIN

| | | | | | |
|--|-------------------------------|---|---|---------------|--|
| Fractions obtained by paper electrophoresis of crystalline trypsin ($F_1 + F_2 + F_3 + F_4$) at pH 2.6 | (F_1) (14 ~ per cent) | | Paper electrophoresis at pH 2.6 | one fraction | $(F_1 + F_2)$ |
| | $(F_1 + F_2)$ (52.7 per cent) | { | Free electrophoresis at pH 5 + Ca^{++} | two fractions | (F_1) (63 per cent, $\mu = 4.38$) (F_2) (33 per cent, $\mu = 5.95$) |
| | | | Free electrophoresis at pH 2.5 + Ca^{++} | one fraction | $(F_1 + F_2)$ ($\mu = 5.93$) |
| | | | Free electrophoresis at pH 5 | one fraction | $(F_1 + F_2)$ ($\mu = 5.1$) |
| | (F_3) (2.6 per cent) | | | | |

* The probable composition of each electrophoretic fraction is given inside brackets.

Table 2. FREE BOUNDARY ELECTROPHORESIS OF CRYSTALLINE TRITIN

| Buffer* | pH 5 | pH 5 + Ca ⁺⁺ | pH 2.5 | pH 2.5 + Ca ⁺⁺ |
|---|--|------------------------------------|-------------------|---|
| Probable composition of electrophoretic fractions | (F ₁ + F ₂ + F ₃)§ | (F ₁ + F ₂) | (F ₁) | (F ₁ + F ₂) (F ₃ + F ₄) (F ₁ + F ₂) (F ₃ + F ₄) |
| Mobility† | 5.03 | 4.07 | 4.50 | 7.00 5.81 6.00 4.37 |
| Percentage Composition‡ | 100 | 77 | 23 | 77.5 22.5 78 22 |

* See text for the composition of the buffers

† Mobility $\times 10^{-4}$ of the ascending boundary

‡ Based on the areas of the ascending boundary

§ See text for explanation

this pH, as should be expected, both fractions are reacting with calcium ions

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† Perrone, J C, Disitzer, L V, and Domont, G, *Nature*, 183, 605 (1959)

Inhibition of Reduced Diphosphopyridine Nucleotide Oxidation by Ammonia

THE toxic responses of plants to ammonia supplied as anhydrous or aqueous ammonia or ammonium salts are well documented¹⁻³, but relatively little is known regarding the means by which toxicity to either plant or animal cells is brought about⁴. In the course of an investigation of this problem it was found that ammonia strongly inhibits the exogenous utilization of glucose, pyruvate, citrate, α -ketoglutarate, succinate and malate by a number of intact tissues and particulate preparations from plant sources. Of the Krebs' cycle substrates, succinate was inhibited less by ammonia than the others used. This partial resistance of succinate oxidation to ammonia inhibition pointed toward a possible effect on diphosphopyridine nucleotide since this does not serve as a co-factor for succinate oxidation. To investigate this question further, studies were made of the effect of ammonia on the reduction and oxidation of diphosphopyridine nucleotide in homogenates of red beet-root, using the 340 m μ absorption peak of the reduced diphosphopyridine nucleotide. Homogenates of the fresh root of red beet (*Beta vulgaris*) were prepared in the cold by hand grinding and centrifugation. The suspending medium was 0.2 M tris (hydroxymethyl) aminomethane buffer at pH 8.5 containing 1.0 M sucrose and 5×10^{-3} M ethylenediamine tetra acetic acid.

The reduction of diphosphopyridine nucleotide was carried out in a preparation containing 0.2 ml of the homogenate, diphosphopyridine nucleotide, 3 μ M, malate, 3 μ M, and 0.5 M tris buffer to make 3 ml. The oxidation of reduced diphosphopyridine nucleotide was measured in a preparation containing a similar amount of homogenate, adenosine diphosphate, 3 μ M, potassium ascorbate, 15 μ M, and reduced diphosphopyridine nucleotide, 0.6 μ M in a total volume of 3 ml. The substrate and co-factors were prepared fresh daily from commercial materials. A limited amount of reduced diphosphopyridine nucleotide oxidation was demonstrated by the homogenate without the addition of either adenosine diphosphate or ascorbate, but the presence of these materials, particularly ascorbate⁵, greatly enhanced the rate obtained.

Changes in the absorbance of this preparation at 340 m μ were followed by means of a Beckman model DU spectrophotometer fitted with a recording attachment. Maximum rates of reaction and the most reproducible results were obtained when the homogenates were supplied with either nitrogen or oxygen during the measurements. For this purpose a capillary

tube drawn to an extremely fine orifice was inserted into the silica cell. For studies of diphosphopyridine nucleotide reduction, nitrogen gas was passed through this tube and for oxidation of reduced diphosphopyridine nucleotide, oxygen was used. Ammonia gas obtained from an atmosphere in equilibrium with 4 M ammonium was supplied through another tube, with either oxygen or nitrogen used as a carrier for the ammonia.

The inhibitory effect of ammonia on reduced diphosphopyridine nucleotide oxidation is shown in Fig. 1. The reversible nature of this inhibition is demonstrated by the resumption of oxidation upon removal of the ammonia supply. This recovery of activity also indicates that a form of ammonia in close equilibrium with ammonia is the effective agent of inhibition, since when the supply of ammonia is stopped, oxidation is quickly resumed as the ammonia is washed out of solution by the aerating oxygen supply. The results in Fig. 1 also show that pH in this range has relatively little effect on the rate of reduced oxidation diphosphopyridine nucleotide. Measurements made with a similar preparation under the same conditions showed that from an initial pH of 8.4, during the first minute of treatment with ammonia, the pH rose to 8.6, which was maintained until the second 2-min application which resulted in a rise to the final pH of 9.1.

The increase in the rate of oxidation of reduced diphosphopyridine nucleotide shown by the preparation treated with ammonia after removal of the first application of ammonia has been consistently found in a number of experiments. It is possible that this might be due to an effect of the altered pH of the medium on the reaction, but when the pH is changed over the same range by additions of potassium hydrox-

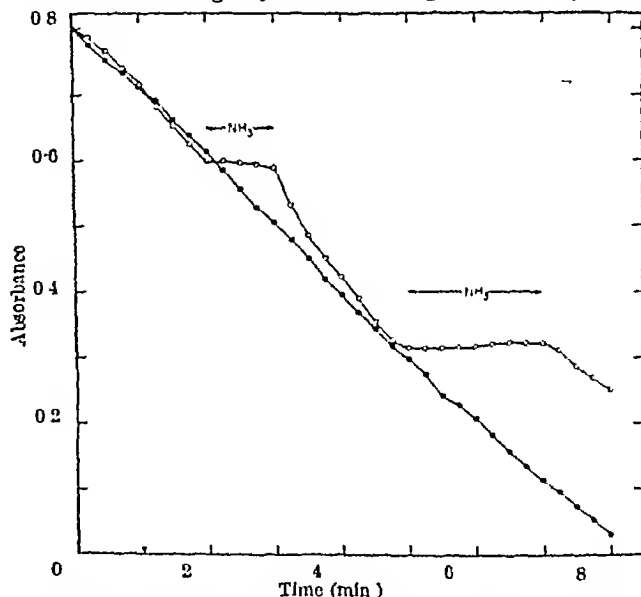


Fig. 1. The effect of gaseous ammonia on the oxidation of reduced diphosphopyridine nucleotide by red beetroot homogenates. O, treated with ammonia for the periods indicated; ●, untreated.

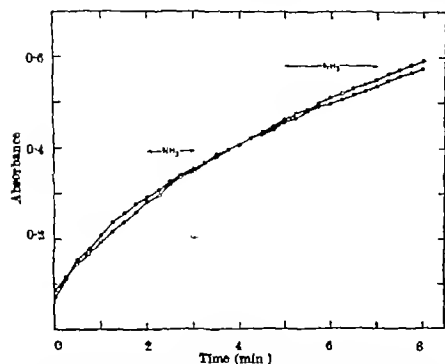


Fig. 3. The effect of pyruvate ammonia on the reduction of diphosphopyridine nucleotide by red beetroot homogenates: ○ treated with ammonia for the periods indicated; ● untreated.

ido, no such stimulation is found. Another possibility is that some intermediate accumulates during the ammonia inhibition period and upon removal of the inhibitor this intermediate is converted to diphosphopyridine nucleotide at a rate faster than the overall reduced diphosphopyridine nucleotide \rightarrow diphosphopyridine nucleotide reaction.

The specificity of ammonia inhibition for oxidation of reduced diphosphopyridine nucleotide is illustrated by Fig. 2, which shows the reduction of this substance by two preparations of beetroot one of which was treated with ammonia at the times indicated. It may be seen that exposure to ammonia has little effect on the rate of the reaction in this experiment.

The means by which ammonia interferes with electron transport in the diphosphopyridine nucleotide system of beetroot homogenates is not clear. Ammonia may be serving as an uncoupling agent for oxidative phosphorylation, but the present evidence does not clearly show this to be the case. The rapid equilibrium which can exist between ammonia and ammonium suggests that the forms may in some way serve as a preferential hydrogen donor and thus be 'sparing' reduced diphosphopyridine nucleotide. It is also possible that ammonia is competing with the hydrogen ion during oxidation of reduced diphosphopyridine nucleotide, or with this substance itself for a site on the oxidative enzyme.

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Binding of the Sulphydryl Group in D-Amino-Acid Oxidase Apo-Protein with Flavin Adenine Dinucleotide

The importance for the enzymatic activity of the sulphydryl group in D-amino acid oxidase apo protein has been reported by several authors¹⁻⁴, but their conclusions concerning the binding site of the sulphydryl group differed. Singer and Barron¹ and Singer² suggested that the protein sulphydryl group might be involved directly in the binding of the

substrate. Frisell and Hellerman³ concluded, however, that the enzyme sulphydryl group is not needed for the direct binding of the substrate. A D-amino acid Kubo *et al.*⁴ considered that the protein sulphydryl group binds with the imino NH(3) group of flavin adenine dinucleotide.

In our laboratory, the binding between D-amino acid oxidase apo protein and the coenzyme flavin adenine dinucleotide has been studied in detail^{5,6} but a decision as to the exact binding of the protein sulphydryl group is still needed. For this purpose a detailed kinetic analysis of the mechanism of inhibition by *p*-chloromercuribenzoate was carried out.

The enzyme protein and flavin adenine dinucleotide were purified by the methods of Negelein and Brömel⁷ and that of Yagi *et al.*⁸, respectively. The oxidase activity was measured with a conventional Warburg manometer.

It was confirmed^{5,6} that *p*-chloromercuribenzoate inhibits the oxidase interfering with both the substrate and flavin adenine dinucleotide. Since our recent results⁵ demonstrated that the phenyl carboxyl group is essential for the competition of benzene derivatives with the substrate and that it does not affect the binding of flavin adenine dinucleotide with the oxidase protein, it may be concluded that the inhibitory action of *p*-chloromercuribenzoate connected with the substrate is due to its phenyl carboxyl group, as Frisell and Hellerman supposed³, and that the inhibitory action of *p*-chloromercuribenzoate connected with flavin adenine dinucleotide is due to its property of reacting with the sulphydryl group.

The dissociation constant of flavin adenine dinucleotide with the protein (K_f) was calculated to be 1.1×10^{-7} M using the Michaelis-Menten equation. The reaction velocity of the oxidase (v) in the presence of a concentration (i) of inhibitor which competes with flavin adenine dinucleotide for the protein can be shown to be

$$v = \frac{Vf}{K_f(1+i/K_f)+f} \quad (1)$$

where f is the rate limiting concentration of flavin adenine dinucleotide, V is the maximum velocity obtained in the presence of excess flavin adenine dinucleotide and K_f is the dissociation constant of the inhibitor combining with the protein in competition with flavin adenine dinucleotide.

Nonetheless, Burk plots in the presence of 2.8×10^{-7} M *p*-chloromercuribenzoate, the rate limiting concentration of flavin adenine dinucleotide and excess DL-alanine (0.15 M) are on a straight line with the intercept $1/V$. From the slope of this line, K was calculated to be 1.6×10^{-7} M.

From equation (1) and the Michaelis-Menten equation, the following equation can be derived

$$\frac{v_0}{v} = 1 + \left\{ \frac{v_0}{V} \right\} \frac{i}{K} \quad (2)$$

where v_0 and v are the reaction velocities in the absence and presence of the inhibitor. Measured values of v_0/v plotted against the concentrations of *p*-chloromercuribenzoate were on a straight line with intercept 1, as shown in Fig. 1, curve III. The value of K obtained from the slope of this line agreed with that found above.

These results show that *p*-chloromercuribenzoate combines with the sulphydryl group of the oxidase protein in competition with flavin adenine dinucleotide. The question then arises of whether

p-chloromercuribenzoate competes with the riboflavin monophosphate part or the adenylic acid part of flavin adenine dinucleotide, in other words Which part of flavin adenine dinucleotide actually combines with the protein sulphhydryl group? To solve this problem, we devised a kinetic method using riboflavin-5'-monosulphate and adenosine-5'-monosulphate which, respectively, compete specifically with the riboflavin monophosphate part and the adenylic acid part of flavin adenine dinucleotide. The specific inhibitors were synthesized by the methods of Takahashi, Yagi and Egami⁹ and of Egami and Takahashi¹⁰, respectively.

Assuming that the reaction mixture contains two inhibitors, one of which competes with the riboflavin monophosphate part of flavin adenine dinucleotide, and the other with the adenylic acid part (case I), the reaction velocity can be shown to be

$$v = \frac{Vf}{K_f(1 + i_1/K_1 + i_2/K_2 + i_1i_2/K_1K_3) + f} \quad \text{or} \quad (3)$$

$$v = \frac{Vf}{K_f(1 + i_1/K_1 + i_2/K_2 + i_1i_2/K_2K_4) + f}$$

where i_1 , i_2 are the concentrations of two inhibitors, and K_1 , K_2 are the dissociation constants of the complexes (i_1 -enzyme protein) and (i_2 -enzyme protein), respectively. K_3 is the dissociation constant for (i_1 , i_2 -enzyme protein) $\rightleftharpoons i_1 + (i_2$ -enzyme protein), and K_4 is that for (i_1 , i_2 -enzyme protein) $\rightleftharpoons i_2 + (i_1$ -enzyme protein).

On the other hand, if the reaction mixture contains two inhibitors both of which compete with the same part of flavin adenine dinucleotide, (case II), the reaction velocity can be shown to be

$$v = \frac{Vf}{K_f(1 + i_1/K_1 + i_2/K_2) + f} \quad (4)$$

From the Michaelis-Menten equations and (3) or (4), equations (5) and (6) can be derived. These formulae show that the plots v_0/v against the

concentrations of inhibitors give a second-order curve in case I and a straight line in case II.

$$\frac{v_0}{v} = 1 + \left\{ 1 - \frac{v_0}{V} \right\} \left\{ \frac{i_1}{K_1} + \frac{i_2}{K_2} + \frac{i_1i_2}{K_1K_3} \right\} \quad \text{or} \quad (5)$$

$$\frac{v_0}{v} = 1 + \left\{ 1 - \frac{v_0}{V} \right\} \left\{ \frac{i_1}{K_1} + \frac{i_2}{K_2} + \frac{i_1i_2}{K_2K_4} \right\}$$

$$\frac{v_0}{v} = 1 + \left\{ 1 - \frac{v_0}{V} \right\} \left\{ \frac{i_1}{K_1} + \frac{i_2}{K_2} \right\} \quad (6)$$

In the actual measurements of the inhibition by *p*-chloromercuribenzoate and riboflavin-5'-monosulphate, v_0/v plotted against the concentrations of both inhibitors gave a second-order curve as shown in Fig. 1, curve V, whereas *p*-chloromercuribenzoate and adenosine-5'-monosulphate gave a straight line (Fig. 1, curve IV).

From these results, it may be concluded that *p*-chloromercuribenzoate combines with the protein in competition with the adenylic acid part of flavin adenine dinucleotide. Thus, it may be supposed that the protein sulphhydryl group combines with the adenylic acid part of flavin adenine dinucleotide, most probably with the amino group of its adenine nucleus.

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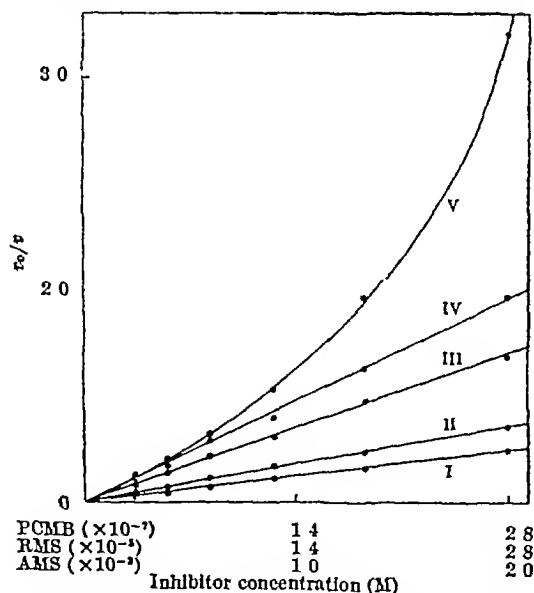


Fig. 1 The inhibitory action of *p*-chloromercuribenzoate on D-amino-acid oxidase. The reaction mixtures contained 15 μ gm of the oxidase protein, excess DL-alanine (0.15 moles), flavin adenine dinucleotide (1.7×10^{-3} moles), and graded concentrations of inhibitors: I, Adenosine-5'-monosulphate (AMS), II, Riboflavin-5'-monosulphate (RMS), III, *p*-Chloromercuribenzoate (PCMB), IV, *p*-Chloromercuribenzoate and adenosine-5'-monosulphate, V, *p*-Chloromercuribenzoate and riboflavin-5'-monosulphate. v was 132 μ l oxygen uptake/30 min and v_0 was 80 μ l oxygen uptake/30 min.

Lack of Direct Effect of Erythropoietin on Human Erythroid Cells *in vitro*

THE existence in the plasma and urine of anæmic patients and animals, of a substance which is capable of increasing the rate of production of red cells in normal recipients is now an undisputed fact. However, the mechanism by which this substance exerts its stimulatory effect is still obscure. Two mechanisms for its action can be postulated. A direct action of the hormone on erythroid cells to stimulate rate of cell division as well as rate of differentiation, that is to say, hæmoglobinization, would increase the rate of turnover of marrow. Alternatively the hormone could accelerate the rate of differentiation of stem cells into the erythron to expand the volume of active marrow without affecting the rate of turnover.

By application of the techniques of auto-radiography to bone marrow cells *in vitro*, the first hypothesis was investigated. The rate of synthesis of deoxyribonucleic acid and the length of the cell cycle were measured with ³H-thymidine or ¹⁴C-formate, the rate of hæmoglobin synthesis with iron-59. The methods and their application have been described previously¹.

Urinary erythropoietin from the urine of a patient with aplastic anaemia was used. The residue from

processing a quantity of normal urine was used as an inactive control substance. The marrow samples which were used were obtained from patients in the course of normal diagnostic investigations.

A number of treatment schedules were tried. The pre-treatment with erythropoietin ranged from 0 to 23 hr before addition of the label, but in no case were significant differences found between cultures treated with active and inactive urinary preparations. Table 1

Table 1. EFFECTS OF HUMAN URINARY ERYTHROPOIETIN ON DNA SYNTHESIS AND CELL CYCLE IN HUMAN BONE MARROW CULTURES. Auto-radiographic estimation of radio-activity in basophilic normoblasts after incubation with either active or inactive urinary erythropoietin. ³H thymidine (0.25 µg./ml. medium) or ¹⁴C-formate (1.25 µg./ml. medium) as deoxyribonucleic acid label, added at times shown.

| Incubation time | Grain counts/Labelled cell | | Percentage of cells labelled |
|---|----------------------------|----------|------------------------------|
| | Mean | Median | Maximum |
| 6 hr | | Active | |
| (30 µgm./ml.)* 3H thymidine added at 0 hr | 16 | Inactive | 90 |
| 8 hr | | Active | |
| (30 µgm./ml.) 3H-thymidine added at 4 hr | 14 | 8 | 64 |
| 8 hr | 7 | Inactive | 37 |
| (15 µgm./ml.) 3H-thymidine added at 2 hr | 10 | 8 | 49 |
| 24 hr | | Active | |
| (60 µgm./ml.) 3H thymidine added at 23 hr | 12 | 7 | 80 |
| 24 hr | 36 | Active | 24 |
| (60 µgm./ml.) 3H thymidine added at 23 hr | 26 | Inactive | 20 |
| 24 hr | | Active | |
| (60 µgm./ml.) 14C-formate added at 22 hr | 63 | 63 | 164 |
| | 63 | 69 | 143 |
| | | | 70 |

* Concentration of active or inactive urinary preparation added at zero time

summarizes the results and shows that neither the grain count per cell, an index of the rate of synthesis of deoxyribonucleic acid, nor per cent labelled cells, a measure of the ratio of the length of the period of synthesis of deoxyribonucleic acid to the length of the generation time, is affected. In order to give an impression as to the character of the distribution of the grain counts, the mean the median, and the maximum or highest observed grain count are given.

Table 2. EFFECT OF HUMAN URINARY ERYTHROPOIETIN ON THE INCORPORATION OF IRON-59 IN HUMAN BONE MARROW CULTURE. Bone marrow cultures were treated for the times shown with active or inactive urinary erythropoietin preparations and with 0.25 µg./ml. of iron-59. Cultures were run in triplicate. Separation, washing, plating and counting techniques are described elsewhere.

| Incubation time (hr) | Iron 59 added at time (hr) | Counts/min./ml. of final washed cell suspension |
|------------------------|----------------------------|---|
| 4 hr with 30 µgm./ml.* | 0 hr | Erythropoietin 2147 |
| 18 hr with 30 µgm./ml. | 6 hr | Inactive 1451 |
| 60 µgm./ml. | 5 hr | 1210 |
| 125 µgm./ml. | | 4220 3350 |

* Concentration of active or inactive urinary preparation added at zero time

In Table 2 are shown the radio activity determinations on washed cells after exposure to iron 59. In this case also there is no significant difference between the incorporation by the control or by cultures treated with erythropoietin. In one experiment in which iron 59 was added at 6 hr to a 24 hr culture, auto-radiographic analysis of the iron incorporation into basophilic normoblasts was undertaken. The mean grain count for erythropoietin treated cells was 186, control cells had a mean grain count of 192. Again no direct action could be demonstrated.

It must be concluded from these observations that erythropoietin has no observable direct actions on the two processes measured, namely, relationships of deoxyribonucleic acid synthesis and cell cycle, and haemoglobin synthesis. An aliquot of the preparation

used in bone marrow culture was assayed by the measurement of iron incorporation in starved rats according to the technique of Hodgson² and the urinary preparation from the aplastic anemic patient was found to be highly active. The injection into 200 gm rats of 2.5 mgm twice daily for two days produced a three-fold increase in the incorporation of a tracer dose of iron 59. The normal urine preparation was inactive. As the dose used *in vivo* was 60 µgm/gm of body weight, the dose used in culture for approximately 5×10^6 cells was of equivalent size or higher.

Recently Schroeder, Gurney and Wackman³ reported that 'amniotic plasma increased radio iron incorporation as much as four fold in bone marrow suspensions. Our observations do not substantiate their conclusions that erythropoietin stimulates haemoglobin synthesis *in vitro*. It is felt, however, that their failure to control the final specific activity of the isotope in the culture medium provides the explanation for their results.

We cannot exclude the possibility that the urinary erythropoietin is not identical with plasma erythropoietin, and that hydrolysis of a conjugated product is necessary for activity of the urinary product. Gordon⁴ reported, however that the urinary erythropoietin is active in his isolated hind limb preparation. Unless tissue esterases which would be capable of liberating an active product are present in the hind limb, a conjugated form would not be active.

As a consequence, we feel that stimulation of red cell production with erythropoietin is effected not through direct action on nucleated red cells, but by some other mechanism. Evidence for a mechanism involving the increased rate of differentiation of primitive stem cells into the early erythroid population of cells has been described elsewhere⁵.

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A Cardiolipin-like Compound in Rat Liver Mitochondria

MARINETTI *et al*¹ found that rat liver mitochondria readily incorporate radioactive orthophosphoric into a phosphatidic acid like polymer. They have further suggested² that this compound may be important in oxidative phosphorylation.

In the course of a study of the lipids of rat liver cell organelles, we have found in the lipids of rat liver mitochondria (extracted with chloroform-methanol 2:1 (v/v)) a fraction which is eluted off a silicic acid chromatography column³ with chloroform-methanol 7:1 (v/v) and which resembles in many respects the cardiolipin first isolated from ox heart by Pangborn⁴.

and more recently studied by Gray and MacFarlane⁵. This fraction constituted 7 per cent of the mitochondrial lipid carboxylic acid esters and 10 per cent of the lipid phosphorus recovered from the silicic acid column. Amino nitrogen was virtually absent from this fraction, the amino nitrogen phosphate molar ratio being less than 0.01. The glycerol/phosphate/carboxylic ester molar ratio was 1.4115 or 1.4121 when the ester estimation was performed on the methyl esters of the fatty acids prepared by interesterification of the intact lipid⁶. This latter ratio suggests a compound containing 4 glycerols, 3 phosphates and 4-6 fatty acids. Gray and MacFarlane found values of 3.24, Taylor and McKibbin⁷ obtained values of 3.23 for a similar lipid isolated by them from dog liver phospholipids and Pangborn⁸ reported a 4.3 glycerol/phosphate ratio.

The methyl esters of the fatty acids of this fraction prepared as indicated above, were analyzed by gas liquid chromatography using both 'Apiezon L' and an adipate ester of polyethylene glycol as stationary phases. The results (together with those of Gray and MacFarlane for comparison), are presented in Table 1 using the fatty acid notation suggested by Ahrens *et al.*⁹, as percentages of the total fatty acid methyl esters.

| | TABLE 1 Present work (rat liver mitochondria) | Gray and MacFarlane (whole ox heart) |
|---------------------|---|---|
| C12-15 | 0.86 | 0 |
| C16-0 (palmitic) | 1.09 | 0.40 |
| C16-1 (palmitoleic) | 1.93 | 5.23 |
| C17-0 | 0.20 | 1.22 |
| C18-0 (stearic) | 0.43 | 0.79 |
| C18-1 (oleic) | 11.93 | 11.0 |
| C18-2 (linoleic) | 79.5 | 80.0 |
| C20-4 (arachidonic) | 0.71 | 0.74 |
| C20-3 | 1.22 | |
| C20-2 | 0.762 | 0.74 |
| C22-6 | 0.79 | |
| Total saturated | 3.3 | 2.5 |
| Total unsaturated | 96.84 | 97.7 |

It is remarkable that compounds of such similar composition, even with respect to the major fatty acids, should have been found in two such different sources. The rat brain contains hardly any of this compound, at least with this fatty acid composition (L. A. Biran, unpublished from this laboratory). While the relation of this fraction to the phosphatidic acid-like polymer of Marinetti *et al.* (they reported an ester/phosphate molar ratio of 0.04) is not clear, it would be of considerable interest to determine the turnover of both the phosphate and fatty acid moieties of this lipid.

This work was aided by a grant from the Rockefeller Foundation. One of us (G. S. G.) thanks the Nuffield Foundations Trust for the award of a Nuffield Dominiions Demonstratorship during the tenure of which this work was done.

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A Reduced Triphosphopyridine Nucleotide-linked Cystine Reductase in the Clothes Moth, *Tineola bisselliella* (Humm)

In the course of studies on the digestion of wool by insects we have examined the clothes moth for the presence of reductases of disulphide bonds. Enzyme preparations were made by cold homogenization of whole larvae of the clothes moth followed by centrifugation at 30,000 *g* for 30 min and dialysis of the supernatant for 20 hr against cold 0.05 *M* *tris* (hydroxymethyl)-aminomethane-hydrochloric acid buffer at pH 7.3. Cystine reductase activity was demonstrated by measuring the decrease in absorption at 340 m μ of reduced triphosphopyridine nucleotide (California Foundation) using anaerobic cuvettes in a Beckman DU spectrophotometer. Also the production of SH-groups was measured by a modified Grunert and Phillips colorimetric nitroprusside method¹, and confirmed by titration with phenyl mercuric nitrate.

The decrease in absorption at 340 m μ due to oxidation of reduced triphosphopyridine nucleotide in the presence of cystine is rapid compared with the control without cystine (Fig. 1). A slight decrease in the control even under the anaerobic conditions used may be explained by the presence of endogenous substrates in the insect extract which are not removed during the preparation. The production of SH-groups by the enzyme in the absence of cystine is negligible, however the addition of cystine and di- or tri-phosphopyridine nucleotide causes a slight increase in SH-groups. Some activation is caused by reduced di- but considerably more by reduced triphosphopyridine nucleotide. High reductase activity follows the addition of a substrate for a triphosphopyridine nucleotide-linked dehydrogenase (glu-

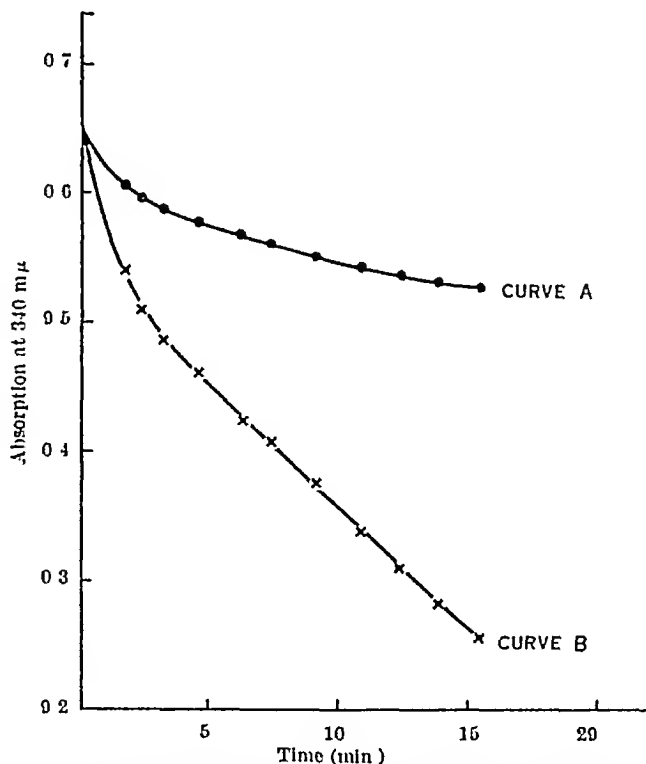


Fig. 1. Effect of 1-cystine on oxidation of reduced triphosphopyridine nucleotide by dialysed *Tineola* extract. Reaction mixture for curves A and B contained 1 ml extract, 270 μ moles *tris* (hydroxymethyl)-aminomethane (pH 7.3 with hydrochloric acid), 9.34 μ moles reduced triphosphopyridine nucleotide in a final volume of 3.2 ml. The mixture for curve B contained, in addition, 2.1 μ moles 1-cystine. The reaction was carried out in anaerobic Beckman cuvettes.

Table 1 CYSTINE REDUCTASE IN DIALYZED *Tineola* EXTRACT PREPARATION

| Reaction mixture | Cystine reductase activity (μ moles SH-groups produced) |
|------------------|---|
| Enzyme alone | 0.06 |
| " + cystine | 0.36 |
| " + DPN | 0.48 |
| " + TPN | 0.48 |
| " + DPNH | 0.76 |
| " + TPNH | 1.64 |
| " + G-6-P | 2.76 |
| " + G-6-P + TPN | 4.10 |

Reaction mixtures: 1 ml. enzyme 125 μ moles tri (hydroxymethyl) —acetoacetate (pH 7.3 with hydrochloric acid, diluted to final volume 2.5 ml. and containing the following where indicated: 4.2 μ moles L-cystine 3.2 μ moles glucose-6-phosphate (G-6-P) 0.07 μ moles triphosphopyridine nucleotide 0.07 μ moles diphosphopyridine nucleotide 1 μ mole reduced triphosphopyridine nucleotide, 1 μ mole reduced diphosphopyridine nucleotide. Incubated for 1 hr. at 25°C. under anaerobic conditions in Thurnham tubes. SH-group estimations by the colorimetric nitroprusside method.

case 6 phosphate) which, in the presence of added triphosphopyridine nucleotide yields the highest activity observed (Table 1). Since addition of glucose 6 phosphate alone activates the cystine reductase it appears that triphosphopyridine nucleotide is not completely removed by the dialysis under the conditions employed. Enzymic reduction of triphosphopyridine nucleotide by glucose 6 phosphate isocitrate and malate, and of diphosphopyridine nucleotide by malate has been demonstrated spectrophotometrically in these *Tineola* preparations. These dehydrogenase activities were retained on storage but the cystine reductase activity was lost under the same conditions.

Other disulphide bond reductases are also present in the insect preparation for example, cystine reduced diphosphopyridine nucleotide (Table 1) glutathione reduced triphosphopyridine nucleotide and glutathione reduced diphosphopyridine nucleotide reductase but these are all of relatively low activity. Glutathione tri¹ and di phosphopyridine nucleotide² reductase activities have been described in plants and the reduced triphosphopyridine nucleotide linked enzyme in animal tissues.³ The reduced triphosphopyridine nucleotide linked cystine reductase which has not previously been described, may be compared with similar enzymes from other sources which are reduced diphosphopyridine nucleotide specific.⁴ It is not possible from the present work to say whether the activity with reduced tri and reduced di phosphopyridine nucleotide is due to different enzymes or to the same enzyme having different specificity for the pyridine nucleotide coenzymes.

It is thought that these enzymes particularly the cystine reduced triphosphopyridine nucleotide reductase, are involved in the process of digestion of wool by clothes moths and other insects. Cystine is an important component of wool and it is known that wool which has a proportion of its disulphide bonds reduced becomes more easily digestible.⁵

Full details of this work will appear elsewhere

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Production of Ethylene by Mitochondria from Tomatoes

EVOLUTION of ethylene by ripening fruit and acceleration of ripening by application of the gas to green fruit has been of interest for many years. However, little more than the gross aspects of these phenomena has been known until recently when Burg and Thumann¹ used gas chromatography to study the evolution of ethylene by apple tissue slices. In our laboratories we have been able to observe the production of ethylene by a mitochondrial fraction from tomatoes.

All steps in the preparation of the mitochondria were conducted at 0–1°C. Since the pH of whole ground tomatoes is about 4, rapid neutralization is necessary during preparation of the homogenate. This was best accomplished by grinding tomatoes with an equal weight of phosphate buffer (0.5 M potassium dihydrogen phosphate 0.25 M sucrose, adjusted to pH 8.1 with sodium hydroxide) at low speed in a Waring blender. The homogenate was filtered through cheesecloth and the filtrate centrifuged at 4,000 g for 7 minutes to remove cell fragments. The supernatant was then centrifuged at 35,000 g for 10 minutes. (A force of 15,700 g was sufficient to separate the mitochondria but 35,000 g which separated no additional particles packed the mitochondria into easily handled pellets.) These were suspended in 0.5 M sucrose 0.01 M phosphate buffer of pH 7 by means of a Sorvall Omnimixer, and recentrifuged at 35,000 g for 10 min. The washed mitochondria were then suspended in buffer-substrate mixture (0.5 M sucrose 0.125 M potassium dihydrogen phosphate, 10⁻³ M magnesium sulphate 10⁻³ M manganese sulphate 1.98 $\times 10^{-3}$ M adenosine triphosphate 0.25 M malic acid 3.3 $\times 10^{-4}$ M diphosphopyridine nucleotide, pH 7.0).

This mitochondrial suspension was used for determination of the rate of production of ethylene by a method described previously,² the only difference being that in order to prevent contamination by micro-organisms, the air stream entering the respiration chamber was passed through columns of glycerol on glass wool and cotton and the respiration chamber and stopper were sterilized prior to use. (All buffer solutions used in the preparation of the mitochondrial fraction were also sterile except that adenosine triphosphate and diphosphopyridine nucleotide were added after sterilization.) No evidence of growth of micro-organisms was obtained when nutrient agar and Pratt's medium³ were inoculated with the mitochondria-substrate mixture.

The ethylene producing system appeared to be relatively stable for after 26 hr. storage of the mitochondrial-substrate mixture at 0–1°C it produced ethylene at about one half the original rate.

Typical results are presented in Table 1. Comparisons are made with ethylene production by whole fruit of the same variety, determined previously.⁴

No ethylene was detectable from mitochondria from green tomatoes or those in the early stages of ripening. Maximum production of this gas occurred

Table 1 PRODUCTION OF ETHYLENE BY 121 TOMATOES (WHOLE FRUIT AND MITOCHONDRIAL FRACTIONS) AT VARIOUS STAGES OF MATURITY

| Stage of ripeness | Ethylene (μ l./gram/4 hr) Whole fruit Mitochondria |
|-------------------|--|
| ~ | ~ |
| Immature green | 0.5 None detected |
| Medium turning | 10 10 |
| Advanced turning | 15 15 |
| Firm ripe | 15 15 |

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with mitochondria from tomatoes in the advanced turning stage (one-half to three-quarters of the surface red). Production of ethylene by mitochondria appears to follow the pattern obtained with the whole fruit, where evolution of ethylene reaches a peak at the 'advanced turning' stage and then decreases to low amounts as the fruit reaches full ripeness.

I acknowledge the technical assistance of T. A. Tribe

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Duration of Protective Action of Interferon Against Infection with West Nile Virus

INACTIVATED influenza virus has been shown to inhibit the growth of western equine encephalitis virus in eggs¹ and in the mouse brain² and it seemed likely, therefore, that interferon, which appears to mediate viral interference³ should also inhibit the growth of viruses of this group. We have found that interferon strongly inhibits the growth of West Nile virus in cultures of chick fibroblasts, and our colleague Dr. J. S. Porterfield has shown⁴ that it prevents plaque formation by a number of 'arbo' viruses, including West Nile and yellow fever viruses. In this paper we describe experiments carried out with West Nile virus, on the duration of the protective action of interferon.

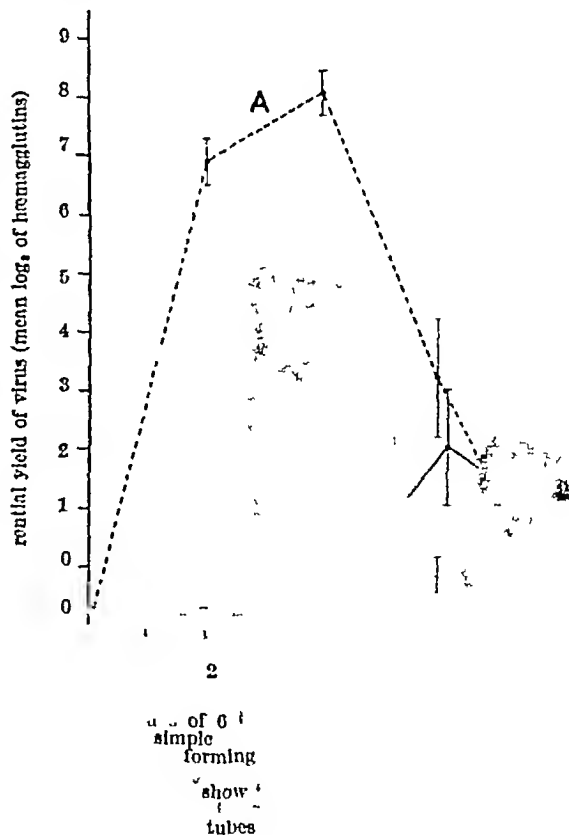
Cell suspensions were prepared from 10-day old chick embryos by a slight modification of the trypsinization technique described by Dulbecco⁵. Test tubes were planted with 5×10^6 cells in 1 ml. of Gey's buffered salt solution plus 0.5 per cent lactalbumin hydrolysate, and kept stationary at 37°C. Six tubes were used for each experimental group. After 24 hr. each tube received an addition of 0.5 ml. of a dilution of West Nile virus (Egypt 101 strain) containing 3.2×10^5 plaque forming units, from a capillary stock of mouse-brain virus kept at -78°C. The medium was changed daily or every second day and each fluid was titrated individually for viral haemagglutinin by diluting it serially in borate buffer at pH 7.0 and adding an equal volume of a 0.25 per cent suspension of goose erythrocytes in phosphate buffered saline, pH 6.6. At the same time, cell cultures were examined by low-power microscopy and cell degeneration noted. In cultures where large yields of viral haemagglutinin were obtained within the first 3 or 4 days' incubation (see curve A) when the cells degenerated completely.

Similar cultures were then set up except that interferon was added to the medium in the initial 24 hr. incubation. The interferon was prepared by the method of Lindenmann and Burke⁶ and the amount added was 10 per cent of the PR8 strain. The medium was changed daily or every second day and each fluid was titrated individually for viral haemagglutinin by diluting it serially in borate buffer at pH 7.0 and adding an equal volume of a 0.25 per cent suspension of goose erythrocytes in phosphate buffered saline, pH 6.6. At the same time, cell cultures were examined by low-power microscopy and cell degeneration noted. In cultures where large yields of viral haemagglutinin were obtained within the first 3 or 4 days' incubation (see curve A) when the cells degenerated completely.

produced. (Controls showed that interferon did not inhibit viral haemagglutination.) In other experiments where the medium was changed either daily or every second day only 2 tubes out of 78 examined showed the presence of haemagglutinin on the seventh day, the others showed no haemagglutinin when examined repeatedly over the period of 3-11 days after the initiation of viral infection. It seems therefore that when the cells are suspended in a simple maintenance medium a single dose of interferon given before the start of infection protects them from West Nile virus infection for almost the whole of their life-time.

When similar experiments were carried out with medium enriched by the addition of 5 per cent calf serum and 1.5 per cent chick embryo extract, viral haemagglutinin production and interference similar to that described above were noted during the first 2 or 3 days' incubation, but the cells degenerated rapidly. (In order to demonstrate viral haemagglutination it was necessary to absorb the serum and embryo extract with kaolin⁷ to remove inhibitors of viral haemagglutination.) Rapid cell degeneration occurred in similar cultures without virus and seemed to be due to the fact that the cells metabolized very actively, with rapid cell division, the new cells being detached from the glass. This behaviour was quite different from that of the cells kept in maintenance medium and it raised the possibility that the lengthy resistance to viral infection induced by a single dose of interferon might be due to the fact that the cells kept in maintenance medium were unable to divide.

In order to test this possibility cells treated with interferon were kept in maintenance medium and infected with West Nile virus, and after 3, 4 or 5 days'



incubation, serum and chick embryo extract were added to stimulate cell division. The cultures at once showed active metabolism and in one experiment a distinct fall in pH was noted within 75 min of adding the enriched medium. However, the resistance to viral infection broke down partially, as shown by the appearance of viral haemagglutinin in the medium (Fig. 1, curve B shows the type of result found). The most likely explanation of these findings is that in cells which are unable to divide, sufficient interferon to prevent virus multiplication is retained for a long period of time within the cells. But when cell division occurs, the interferon which is unable to replicate², is diluted until the concentration within cells is lower than that required to inhibit virus multiplication. In support of this hypothesis, the resistance of cells could be largely maintained by incorporating further interferon along with the serum and embryo extract each time the medium was changed (Fig. 1 curve C).

These experiments provide a model system which may be helpful in planning experiments on the protective effect of interferon in virus infections in animals.

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Glycosidases in the Mammalian Alimentary Tract

EPITHELIAL mucous secretions in mammals are comprised mainly of mucosubstances¹ consisting of some or all of the carbohydrates, glucosamine, galactosamine, galactose, fucose and sialic acid bound to protein². In some secretions there are also small amounts of acidic aminopolysaccharides containing hexosamine, uronic acid and sometimes ester sulphate. Mucosubstances with the above composition, but excluding sialic acid, resemble blood group substances, and fractions with high blood group activity have been

obtained from various secretions, including gastric juice, as well as from gastric mucosa.

In view of the prevalence of mucosubstances in the alimentary tract, and the widespread occurrence of the four glycosidases α -mannosidase, β -galactosidase, β -N-acetylglucosaminidase and β -glucuronidase in animal tissues³ an investigation has been made of the distribution of these enzymes throughout the alimentary tract of several mammalian species the wall itself and the contents of the lumen each being examined. Values for some sections of the alimentary tract and their contents, together with figures for pancreas and parotid gland are given in Table 1. The same assay methods as before were employed³, but the concentration of *p*-nitrophenyl α -mannoside used was 6 mM. Generally figures for the alimentary tract tissue were fairly constant for each species throughout the length of the tract. For purposes of comparison, some values for liver and kidney are included, in some cases these or similar figures have already been published. A study of β -glucuronidase in alimentary tract contents has already been made⁴. It was also observed that in rats after a period of starvation (24 hr), or several hours after ether administration, there was a definite though some what variable, tendency for the glycosidase activities of the alimentary tract contents to rise. This may have been due to mechanical factors, rather than increased enzyme secretion.

While β -galactosidase may also have lactase activity the presence of the other glycosidases in tissues known to secrete mucosubstances, together with the absence of any simpler glycoside molecule, suggests that such mucosubstances may well be natural substrates for this group of enzymes. Although not detected in the alimentary tract, mannose is a frequent component of mucoproteins from other sources.

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Table 1 GLYCOSIDASE ACTIVITIES IN THE ALIMENTARY TRACT, PANCREAS AND PAROTID GLAND OF VARIOUS SPECIES
Results are expressed as μ g *p*-nitrophenol (β -galactosidase), p -nitrophenol (α -mannosidase) and β -N-acetylglucosaminidase or phenolphthalein (β -glucuronidase) liberated per gm. moist tissue in 1 hr at 37°C from the appropriate glycoside

| | α -Mannosidase | | | | β -Galactosidase | | | | β -N-Acetylglucosaminidase | | | | β -Glucuronidase | | | |
|--------------------|-----------------------|--------|---------|---------|------------------------|-------|-------|--------|----------------------------------|--------|-------|----|------------------------|-------|--------|-------|
| | Sheep | Ox | Pig | Rat | Rabbit | Sheep | Ox | Pig | Rat | Rabbit | Sheep | Ox | Pig | Rat | Rabbit | Sheep |
| Stomach (abomasum) | 4.920 | | 3.900 | 3.935 | 813 | 371 | | 4,870 | 2,270 | 750 | | | 50 | | 3 | |
| Stomach contents | 347 | | 222 | 129 | 29 | 135 | | 212 | 145 | 49 | | | 52 | | 4 | |
| Ileum | 8.050 | 6.780 | 1.669 | 0.223 | 4,370 | 672 | 1,310 | 2,630 | 3,031 | 5.4.0 | | | 81 | 2,810 | 769 | |
| Ileum contents | 523 | 5.930 | 2,431 | 166 | 2,140 | 0 | 3,280 | 7,070 | 4.100 | 2,041 | | | 31 | 260 | 250 | |
| Colon | 2,210 | 5,450 | 4.470 | | 1,093 | 651 | 1,090 | | 3.400 | 2,095 | | | 89 | 3.400 | 278 | |
| Colon contents | 693 | 676 | | 945 | 110 | 80 | | 237 | 224 | 0 | | | 63 | 2,935 | 1,444 | |
| Pancreas | 2,100 | 1,416 | | | 517 | 423 | | 456 | 1,150 | 204 | | | 216 | 860 | 103 | |
| Parotid | 2,630 | 1,224 | | | | 2,090 | | | | | | | | | | |
| Liver | | | 2,953 | | 4.190 | | | 4,530 | 4.710 | 1,012 | | | | | | |
| Kidney | | | 4.500 | | 3,040 | | | 16,800 | 11.400 | 4.460 | | | | | | |
| Stomach (abomasum) | Sheep | Ox | Pig | Rat | Rabbit | Sheep | Ox | Pig | Rat | Rabbit | Sheep | Ox | Pig | Rat | Rabbit | Sheep |
| Stomach contents | | | 1,630 | 23,725 | 11,030 | 1,065 | | 50 | | 3 | | | 52 | | 4 | |
| Ileum | 33,850 | 42,900 | 42,100 | 35,213 | 63,300 | 782 | 1,037 | 31 | 2,810 | 769 | | | 89 | 3,400 | 278 | |
| Ileum contents | 1,890 | 40,500 | 43,500 | 429 | 27,230 | 110 | 890 | 81 | 2,935 | 1,444 | | | 216 | 860 | 103 | |
| Colon | 19,890 | 36,000 | | | 55,000 | | | | | | | | | | | |
| Colon contents | 4,290 | 1.75 | | | 2,090 | | | | | | | | | | | |
| Pancreas | 8,100 | 6.190 | 4.630 | | 12,930 | 240 | 63 | | | | | | | | | |
| Parotid | 18.030 | | | | 2,210 | | 216 | | | | | | | | | |
| Liver | | | 69,700 | 44.610 | 36,600 | 7,210 | | 620 | 16,310 | 6,290 | | | | | | |
| Kidney | | | 306,800 | 125,650 | 60,300 | | | 22 | 8,470 | 201 | | | | | | |

Isolation of Echinochrome A from the Spines of the Sea Urchin, *Diadema setosum* (Leske)

THE naphthoquinone biochromes in the animal kingdom are only found in the group of sea urchins the various colours (green, red, violet or black) of the spines and the tests of sea urchins arise from the calcium salts of these naphthoquinone pigments.^{1,2}

Echinochrome A^{3,4} (7-ethyl-2, 3, 5, 6, 8,-penta-hydroxy-1, 4-naphthoquinone) which was recognized as the naphthoquinone pigment in the ovaries of the sea urchin *Arbacia lixula* (Linn), has been found in the tests and the spines of the four species of sea urchins *Strongylocentrotus purpuratus* (Stimpson)⁵, *Paracentrotus lividus* (Lam)^{1,5}, *Echinus esculentus* (Linn)⁶ and *Echinarrachnus mirabilis* (Ag)⁷. Recently, a naphthoquinone pigment isolated from the dark violet-black spines of the sea urchin, *Diadema setosum* (Leske) (Japanese name, 'gan gazo uni') was identified with echinochrome A.

Spines washed with water were dissolved in dilute hydrochloric acid and the pigment was extracted therefrom with ether and transferred into saturated sodium bicarbonate solution. The pigment was extracted again in ether, after acidification with dilute hydrochloric acid, and purified by column chromatography on calcium carbonate and recrystallization from dioxane-water. About 6 mgm of the pure material were obtained from each 100 gm of the spines. The pigment forms dark red-brown needles, m.p. 214°-215° and shows absorption maxima at 255, 340, 467, 490, 527 mμ in chloroform solution. Ferric chloride reaction gives a dirty black-violet colour and a violet precipitate appears when it reacts with methanolic lead acetate. The percentage of C and H was 53.94 and 3.90 respectively (calc. for C₁₂H₁₀O₇: C, 54.14, H, 3.79). The trimethyl-derivative was obtained by methylation with diazo methane in ethereal solution, as long red needles which were crystallized from dioxane-water. It melts at 130°, is not soluble in sodium bicarbonate solution, but dissolves in dilute sodium hydroxide with a blue colour. Absorption maxima were at 323, 476, 502, 537 mμ in chloroform solution. The percentage of C and H was 58.85 and 5.17 respectively (calc. for C₁₂H₇O₄(OCH₃)₃: C, 58.35, H, 5.29). Treatment with zinc dust, pyridine and acetic anhydride gave the leucoacetyl derivative as colourless fine rods, m.p. 240° (decomp). The absorption maximum was at 295 mμ in methanol solution. The dehydro-derivative, formed by treatment with silver oxide, showed

absorption maxima at 260, 319, 392 mμ in methanol solution.

Mixed melting point determinations have been carried out with echinochrome A, trimethylechinochrome A and leucoacetylinochrome A (isolated from *E. mirabilis*)⁷, and in each case no depression of the mixed m.p. was observed. The infra-red spectrum of this pigment and echinochrome A⁷ was also fairly agreeable. Full details of this work will be published elsewhere.

I wish to express my gratitude to Prof. Y. Nakamura and Prof. T. Satto, of Hokkaido University for their encouragement and guidance. I am also grateful to Prof. R. Kamohara and Prof. T. Yatzuka of Kochi University for offering me every possible assistance in collecting samples and to Dr. M. Inoue of Takeda Research Laboratory for the elemental and infra-red analysis.

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Occurrence of 4-Hydroxypipicollic Acid in Acacia Species

EXTRACTION of *Acacia excelsa* heartwood gave an amino-acid (0.2 per cent), m.p. 294° (decomp.) [α]_D²⁰ -13.4° (1 per cent in water), characterized by an *N*-benzoyl derivative, m.p. 172°, and identified as *trans*-4-hydroxypipicollic acid. The acid was later isolated from the wood of other *Acacia* species, and was more conveniently obtained from the fresh leaves of *A. osualldi* (0.25 per cent yield). The imino acid fraction, isolated by means of the *N*-nitroso derivatives¹, consisted almost entirely of proline, pipicollic acid, and the hydroxypipicollic acid, which crystallized readily from aqueous ethanol. The naturally occurring *trans* isomer was epimerized by aqueous barium hydroxide (155°, 12 hr) to a mixture of *cis*- and *trans*-4-hydroxypipicollic acid, and on paper chromatograms developed with butanol-acetic acid-water (4:1:5) the *cis*-acid (*R_F* 0.17) was indistinguishable from an authentic specimen, but was clearly separated from *cis*-3-hydroxypipicollic acid (*R_F* 0.24). A further distinction between the 3- and 4-hydroxypipicollic acids is that the former acid is decomposed when heated with alkali under conditions that cause epimerization of 4-hydroxypipicollic acid, and 3-hydroxypipicollic acid therefore resembles other β-hydroxy-α-amino-acids in its alkali-lability². The naturally occurring *trans*-4-hydroxypipicollic acid ran in butanol-acetic acid-water with the same *R_F* (0.21) as 5-hydroxypipicollic acid from dates¹, but the two acids were separated on paper chromatograms developed with water-saturated phenol, and the 4-hydroxypipicollic acids were also distinguished by giving with ninhydrin a characteristic grey colour which showed deep red fluorescence under ultra-violet light.

Isolation of 4-hydroxypipicollic acid was first reported by Virtanen and Kari³, and the same acid was isolated from *Armeria maritima* by Fowden⁴ who tentatively revised its structure to 3-hydroxypipicollic acid. It now appears that 4-hydroxypipicollic acid is the true structure of the acid isolated by Virtanen and Kari and by Fowden as a

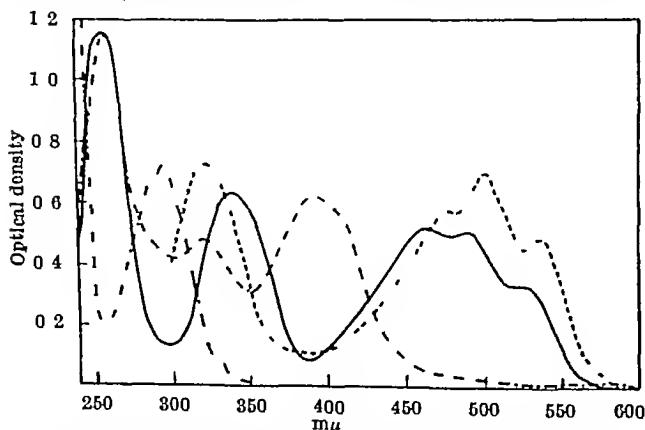


Fig. 1. Absorption spectra of echinochrome A of *Diadema setosum*. —, Free pigment in chloroform solution, ---, trimethyl derivative in chloroform solution, ·····, dehydro-derivative in methanol solution, — · — · —, leucoacetyl derivative in methanol solution.

sample provided by Dr Fowden proved chromatographically indistinguishable from our *trans*-4 hydroxy pipercolic acid, and its was similarly epimerized by hot baryta. Structural and stereochemical investigation of the *trans*-4 hydroxypipercolic acid from *Acacia* species is continuing and details will be published elsewhere.

We thank Dr L Fowden for a sample of the acid from thirt and for comparing it with our imino acid, and we are grateful to Dr H Pfenninger and Dr H Vanderhaeghe respectively for samples of *cis* 3 and *trans*-4-hydroxypipercolic acids. This work was carried out during tenure of a General Motors Holden Fellowship (by P I M).

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ANIMAL PHYSIOLOGY

Increase by Chlorothiazide of the Paralyzing Activity of *d*-Tubocurarine Chloride

It is a well-established fact that chlorothiazide potentiates the hypotensive effects of ganglion blocking agents.¹⁻³ However the way this potentiation is brought about is not clear. It has been thought that chlorothiazide acts either by a direct hypotensive action² or by sodium depletion³, or by reduction in plasma volume⁴, or as in the case of mecamylamine and possibly of pempidine, by a reduction in renal excretion⁵ of the ganglion blocking agents. From a pharmacological view point there is a good deal of similarity between the neuromuscular junction and the ganglionsynapses.

We have therefore investigated whether the paralyzing activity in a rabbit, treated with *d*-tubocurarine chloride, could be modified by a previous intravenous injection of chlorothiazide.

In evaluating the paralyzing activity of *d*-tubocurarine we have taken into account: (a) the appearance of muscular insufficiency that allows the animal, when set in a lateral position quickly to resume its normal stand up position (partial paralysis), (b) the appearance of a muscular insufficiency that deprives the animal of its ability to resume its stand up position (total paralysis), (c) the animal's death owing to a respiratory insufficiency.

We have summarized our results in Table I.

It is evident that chlorothiazide pretreatment potentiates the neuromuscular blocking activity of *d*-tubocurarine. Hydrochlorothiazide, on the other hand, is ineffective in 10-100 mgm/kgm dose intravenously in increasing *d*-tubocurarine paralysis.

The mechanism of chlorothiazide action is not clear as yet.

Our results will be published elsewhere in detail.

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Are Mucosal Nerve Fibres Essential for the Peristaltic Reflex?

RECENTLY Bulbring and co workers^{1,2} abolished the peristaltic reflex in an isolated piece of intestine by scraping off its mucous membrane and assigned an essential role in the initiation of the reflex to processes of sensory neurones which are distributed to the intestinal mucosa.

In the experiments reported here, an attempt was made to destroy the mucous membrane selectively by local administration of a protein precipitating chemical. Silver nitrate and tannic acid were chosen as suitable chemical agents.

The method of eliciting the peristaltic reflex in an excised loop of guinea pig ileum mounted in an organ bath³, was modified so that the output of each peristaltic wave could be directly measured. This permitted to distinguish unequivocally between peristalsis which propelled fluid in a cephalocaudal direction, and pendular activity which did not. In order to avoid formation of silver chloride, the tubings and the intestinal lumen were thoroughly flushed with distilled water before and after the administration of silver nitrate.

Among various concentrations tried, a 30 per cent silver nitrate and a 20 per cent tannic acid solution proved suitable when left in contact with the mucosal surface for about 10 and 30 sec respectively. After such treatment peristaltic activity continued in its normal pattern of co-ordinated contractions of the longitudinal and circular muscle layers. The amount of fluid expelled was generally slightly reduced and so was the size of the longitudinal contractions and at the same time the response of the longitudinal muscle to acetylcholine indicating that some damage had occurred to all layers of the intestinal wall. As controls revealed part of this could be accounted for by the mechanical strain exerted on the wall by forcing the solutions and wash fluid through the lumen in a specified time. However in two experiments, peristaltic activity was even increased after treatment with 30 per cent silver nitrate solution.

Histological investigation of these preparations, carried out by Dr M R Crompton of the Department of Histology, showed that most of the mucous membrane and parts of the muscularis mucosae were destroyed.

Table I PARALYSING ACTIVITY OF *d*-TUBOCURARINE CHLORIDE IN RABBITS TREATED WITH CHLOROTHIAZIDE AND HYDROCHLOROTHIAZIDE

| Pretreatment | mgm./kgm. i.v. | <i>d</i> -tubocurarine mgm./kgm. i.v. | Interval between the two treatments min. | Animals with partial paralysis/ treated animals | Animals with total paralysis/ treated animals | Dead animals/ treated animals |
|---------------------|-------------------|---|---|---|---|-------------------------------------|
| Chlorothiazide | — | 125 | — | 11/18 | 0/18 | 0/18 |
| " | 100 | 125 | 10 | 7/7 | 0/7 | 2/7 |
| " | " | 125 | 15 | 2/2 | 0/2 | 0/2 |
| " | " | 125 | 30 | 3/3 | 0/3 | 0/3 |
| Hydrochlorothiazide | 100 | 125 | 1-14 | 7/9 | 2/9 | 0/9 |
| " | 10 | 125 | 0-13 | 4/6 | 2/6 | 0/6 |

There was only little variation between different preparations and different sections of the same preparation. The demarcation line between necrotic and normal tissue lay in the neighbourhood of ganglion cells of Meissner's plexus and was particularly conspicuous in preparations treated with silver nitrate where deposits of free silver developed if the preparation was exposed to light during fixation. Thus the damage reached approximately the same depth of the intestinal wall as in the experiments of Bulbring *et al* after the mechanical removal of the mucosa.

The findings therefore permit the conclusion that the mucosa and the nerve fibres situated there, do not play an indispensable role in the peristaltic reflex of the guinea pig ileum.

A detailed description of these findings and the methods used will be published elsewhere.

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Extrahepatic Metabolism of Ethanol in Man

It is generally assumed that only small amounts of ethanol are metabolized outside the liver in man^{1,2}. The results obtained when working at very low concentrations of ethanol, where the metabolic capacity of the liver is no longer fully saturated, are not consistent with this view. When the concentration of ethanol in the blood reaching the liver is below 50-60 mgm/l, the concentration in the liver vein, obtained by catheterization, has been found to be zero. If extrahepatic metabolism can be excluded the amount metabolized at these levels of ethanol must be proportional to the liver blood flow and to the concentration in the blood. Measurements of the liver blood flow by means of ethanol and bromsulphalein have shown, that the blood flow during experiments at periods similar to those mentioned below, is almost constant^{3,4}. The amounts of ethanol metabolized can therefore be proportional only to the concentration in the blood.

If ethanol is infused intravenously at a constant rate the concentration in the blood will be constant after 60 minutes and the amount metabolized will then be identical to the amount infused. The metabolism of ethanol has been investigated in 10 apparently healthy students by this technique and the rate of

TABLE 1

| Case | mgm ethanol oxidized per min | mgm ethanol/l blood | Liver blood flow (ml/min) | Ethanol oxidized extra hepatically (mgm/min) |
|------|------------------------------|---------------------|---------------------------|--|
| 3 | 34 | 19 | 1770 | 14 |
| | 47 | 31 | 1520 | |
| 4 | 29 | 14 | 2070 | 17 |
| | 53 | 42 | 1260 | |
| 5 | 26 | 8 | 3250 | 17 |
| | 40 | 25 | 1810 | |
| 12 | 54 | 21 | 2570 | 20 |
| | 76 | 34 | 2240 | |
| 15 | 48 | 21 | 2290 | 27 |
| | 67 | 40 | 1680 | |
| 16 | 46 | 15 | 1070 | 20 |
| | 64 | 25 | 2500 | |
| 9 | 35 | 9 | 3800 | 21 |
| | 49 | 16 | 3060 | |
| 10 | 64 | 28 | 2250 | 19 |
| | 30 | 11 | 3270 | |
| 11 | 50 | 23 | 2170 | 23 |
| | 65 | 30 | 2170 | |
| 13 | 37 | 9 | 4110 | 26 |
| | 52 | 17 | 3060 | |
| 13 | 67 | 27 | 2480 | 26 |
| | 45 | 20 | 2250 | |
| | 63 | 40 | 1575 | |
| | 81 | 58 | 1400 | |

infusion was changed two to three times during the same experiment. If the ethanol was only metabolized in the liver a strictly proportionality was to be expected between the amount infused and the concentration in the blood. By plotting the results in a graph with ethanol metabolized per minute for the abscissa and the concentration in the blood for the ordinate, a straight line passing through the origin should be obtained. As will be seen from Fig. 1, a straight line was obtained, but in all cases it passed to the right of the origin.

The best explanation for this result seems to be extrahepatic metabolism of ethanol. The point where the line crosses the abscissa indicates the amount of ethanol metabolized outside the liver with a mean value (Table 1) from 10 experiments of 20.5 mgm per minute (standard deviation 4.2). The constancy of the extrahepatic metabolism down to very low concentrations in the blood seems to indicate an organ, or organs, with a low concentration of alcohol dehydrogenase and a high blood flow, but no information is at present available on this location.

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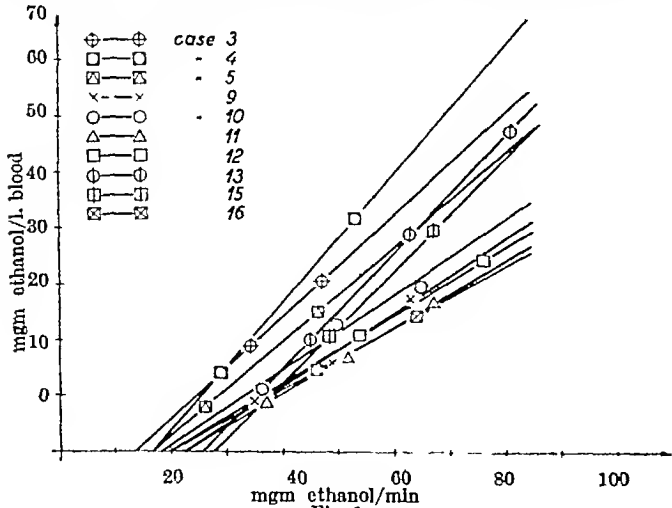
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Natriferin: A New Hormonal Principle in the Neurohypophysis of Certain Vertebrates

THE active transport of sodium is an important function of the amphibian skin, this transport can be increased by extracts of mammalian neurohypophysis¹. In *Rana esculenta*, oxytocin alone is active, vasopressin having only a small effect corresponding to its intrinsic oxytocic activity. On the other hand, neurohypophyseal extracts of Amphibia and fish influence this transport at such low concentrations, that it would seem reasonable to postulate that their action is due to an unknown principle, more specific to sodium transport than is oxytocin itself^{2,3}.

Acetic extracts were prepared from acetonic powders of entire hypophysis or neurohypophysis from various aquatic vertebrates (elasmobranchs, marine and freshwater teleosts, amphibians) and from mammals. The oxytocic activity of these extracts was



measured by their effects on rat uterus contractions⁴ and their natriuretic⁵ (that is, sodium transporting) activity, by their effects on the net flux of sodium produced by *Rana esculenta* skins, as measured by the short-circuited current⁶ (Ussing's technique modified by Morol *et al.*⁷). As a standard of reference for both these biological activities, synthetic oxytocin ('Syntocinon', Sandoz) was used, permitting the activities to be expressed quantitatively in terms of mU/mgm dry powder

Table 1 OXYTOCIC AND NATRIURETIC ACTIVITIES OF THE ENTIRE HYPOTHALAMUS (H) OR NEUROHYPOPHYSIS (N) IN DIFFERENT VERTEBRATES

| Species | Oxytocic activity* (± 8 E.L.) | Natriuretic activity* (± 8 E.L.) |
|-------------------------------------|---------------------------------------|--|
| <i>Herichthys griseus</i> (H) | 3.0 \pm 0.25 | 4.6 \pm 0.4 |
| <i>Scyllorhynchus caeruleus</i> (H) | 6.8 \pm 1.0 | 15.1 \pm 1.8 |
| <i>Scomber scombrus</i> (H) | 450 \pm 35 | 4560 \pm 120 |
| <i>Gerrhonotus</i> (H) | 595 \pm 45 | 5610 \pm 1550 |
| <i>Blennius gottorpius</i> (H) | 108 \pm 11 | 1030 \pm 138 |
| <i>Trutta trutta</i> (H) | 45.5 \pm 6.0 | 443 \pm 110 |
| <i>Rana esculenta</i> (N) | 1066 \pm 170 | 12800 \pm 1180 |
| <i>Bufo bufo</i> (N) | 1000 \pm 16 | 12050 \pm 1165 |
| <i>Salmo gairdneri</i> (N) | 1950 \pm 46 | 1990 \pm 47 |
| Ox (N) | 909 \pm 63 | 1356 \pm 92 |
| Pig (N) | 1460 \pm 117 | 1610 \pm 70 |

*Both activities expressed in mU oxytocin/mgm dry powder

Table 1 shows the results of this investigation: the elasmobranch extracts have a very low biological activity, the mammalian extracts, a natriuretic activity more or less equal to their oxytocic activity, whereas the teleostean and amphibian extracts exhibit a far greater natriuretic than oxytocic activity. Fig. 1 represents these results in terms of the ratio of natriuretic to oxytocic activity in the various species studied. This ratio is approximately 1 in the mammals, indicating that oxytocin alone is the active principle in both tests. The teleosteans and amphibians show ratios of roughly 10. In other words, their oxytocic activity cannot account for their natriuretic activity. Further experiments were performed to test whether the discrepancy between the two activities could in fact be due to antihypophyseal hormones, intermediate or vasopressins. All these substances were found to be devoid of natriuretic activity. Furthermore, the oxytocic and natriuretic activities of the hypothalamus of *Rana esculenta* were measured and found to be 5.0 ± 0.4 mU and 52.7 ± 4.5 mU respectively, giving a ratio of 10.5, comparable with that found for the neurohypophysis. The above experiments thus indicate the existence of a new factor in amphibians and teleosts, probably of hypothalamic origin, and responsible for the natriuretic

activity. The term 'natriuretin' has been proposed to designate this principle.⁸

There is evidence to support the hormonal nature of natriuretin. Thus it acts *in vitro* at very low concentrations (1/10,000 of a neurohypophysis of *Bufo*, that is, 0.0125 μ gm. of dry powder per ml.) Neurohypophyseal extracts injected *in vivo*, into normal individuals of *Bufo* and *Rana* (that is, kept in tap water) have also a far greater effect on the active sodium uptake than would be expected from their actual oxytocic contents. Furthermore, in individuals of *Rana esculenta* adapted to a high salinity in the external medium, there is a diminution of active transport of sodium by the skin and a corresponding reduction in the oxytocic and natriuretic activities of the neurohypophysis whereas the antidiuretic activity of the gland remains unchanged.⁹

The physiological role of natriuretin would seem to lie in relation to osmoregulation. Such a function is indicated by its specificity of action on the active transport of sodium and also by its ecological distribution within the aquatic vertebrates. Its absence in elasmobranchs may be explained by their very special solution of osmoregulatory problems.¹⁰ One fact should be stressed: the ratio between natriuretic and oxytocic activities remains constant throughout the amphibian and teleostean species studied despite considerable variation in absolute concentration of active principle in the glands. This points in favour of the hypothesis that a single substance, common to all these animals, is responsible for both natriuretic and oxytocic activities. Natriuretin *in fact*, would appear to be a substance closely related to oxytocin. Its relationship with the water balance principle¹¹ remains to be studied.

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Vagal Afferents in the Monkey

VAGAL afferents in several vertebrate species have been extensively described¹, but we are unaware of any previous recording of afferent activity in the vagus nerve of a primate. The opportunity arose to study these in the monkey *Macaca mulatta*.

In the supine animal, anesthetized with 'Nembutal' the left cervical vagus was exposed. Under paraffin oil the sheath was opened and individual fine strands of nerve were sectioned, separated peripherally and subdivided and the resulting filaments were laid across a pair of silver recording electrodes. The electrical activity in such filaments was displayed with one beam of a dual beam oscilloscope. The electrocardiogram and usually arterial central venous and intrapleural pressures, registered with strain gauge manometers, were displayed with the second beam by the use of a multichannel beam splitter. The

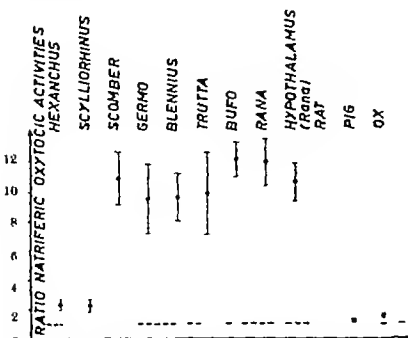


Fig. 1 The ratio natriuretic/oxytocic activities (± 8 E.L.) in different vertebrates

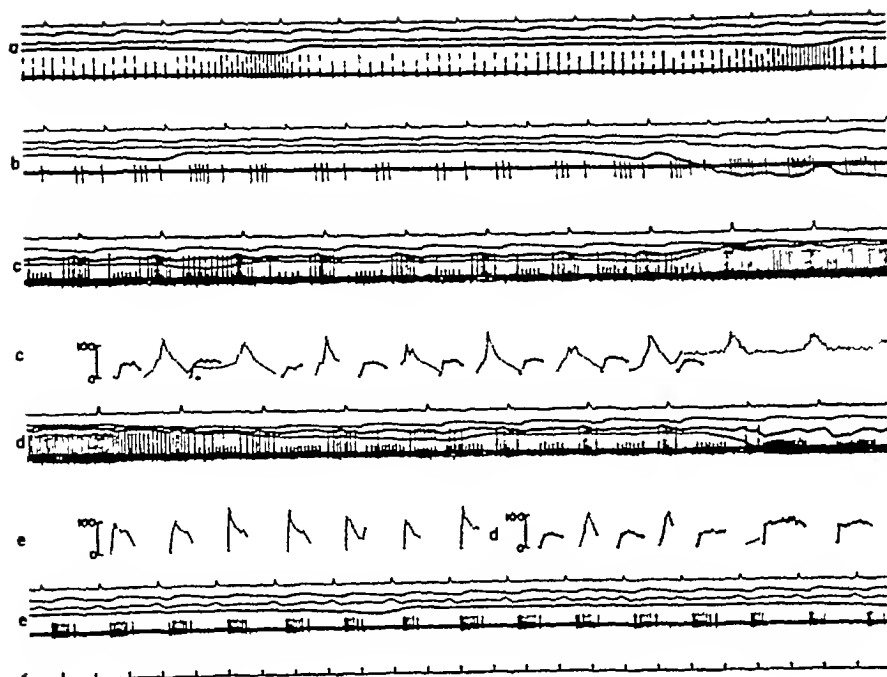


Fig 1 Each oscilloscope record, top to bottom: electrocardiogram, aortic pressure, central venous pressure, intrapleural pressure (inspiration downwards), afferent vagal impulses. Graphs: impulse frequency per sec, on same time-scale as oscilloscope records. *a*, discharge characteristic of continuously firing pulmonary stretch receptor during two normal respirations, *b*, discharge characteristic of single atrial stretch receptor during normal respiration and with application of negative pressure to the trachea, *c*, largest spikes: discharge characteristic of pulmonary stretch receptor with pronounced cardiac rhythm persisting during application of positive pressure to trachea. Also prominent is the discharge of an atrial stretch receptor. Discharge frequencies for the two receptors noted are plotted below, *d*, shortly after record *c*, comparing effects on the same two receptors of applications of positive, then negative, intratracheal pressure, discharge frequencies during the latter manoeuvre plotted below, *e*, discharge characteristic of arterial baroreceptor with frequency plotted above, *f*, 60 cps time marker and 0.2 sec lines.

graphic records were obtained using moving paper. Nerve impulse frequencies were plotted from the records using a miniature direct-plotting nomogram².

In six monkeys, afferent discharges were recorded from about forty individual receptors. The temporal features of their discharge patterns and their responses to respiratory manoeuvres were generally characteristic of types of receptors described in other mammals. Easily recognized were the discharges of pulmonary stretch receptors of several kinds, arterial baroreceptors and cardiac atrial receptors. No attempt was made to identify the exact site of the receptors by manipulation of the viscera. Two types of pulmonary stretch receptor behaviour were commonly encountered, the first (Fig 1 *a*) showed a continuous discharge with the usual respiratory modulation, while the second (Fig 1 *c*, *d*) possessed an adventitious cardiac rhythm. The prominence of the latter type of discharge, although observed in experimental circumstances, leads one to speculate that the cardiac component, usually associated with systole, may represent physiologically significant information. In nine atrial receptors, the main pattern of discharge was diastolic in timing (Fig 1 *b*, *c*, *d*), indicating their sensitivity to distension but not to pressure, one atrial receptor only was encountered with a pronounced atrial systolic discharge, but with a diastolic component as well. Arterial baroreceptor fibres were found in four of the monkeys (Fig 1 *e*) and unlike the atrial receptor fibres, these appeared to travel together in a discrete region within the main trunk of the vagus, as they do in the dog.

The demonstration in the monkey of the usual vagal afferents was not unexpected. Of special interest,

however, in view of their proposed role as thoracic blood volume receptors^{3,4}, is the occurrence of atrial stretch receptors in a primate which, like man, spends much of its time in the upright position.

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Prevention of Foetal Development by Enzyme Inhibition

It has been shown recently that foetuses of rats and humans at a definite phase of development produce histamine at a very high rate¹⁻³. Towards the end of pregnancy an average sized set of rat foetuses produces about ten times more histamine than the mother in a given time and about fifty times more per unit weight. The foetal histamine enters the mother's circulation and is then in part destroyed, in part excreted in the urine. Foetal tissues bind histamine only loosely, they thus contain little, and produce it at a high rate³. As a working hypothesis it would seem that the striking histamine-forming capacity of the foetus might be related to growth in general. To test this hypothesis we have investigated histamine formation in the regenerating liver.

In the rat, the median and left lateral lobes of the liver, amounting to about two-thirds of the whole, can be removed without difficulty⁴. The remnant grows and reaches the size of the normal liver within about 20 days. In partially hepatectomized rats it was found that the rate of histamine formation, as reflected in the urinary excretion of the amine, is considerably increased during liver regeneration. Also, when radioactive histidine was injected and histamine formation followed, it was seen that decarboxylation took place at a higher rate during liver regeneration than before the operation. In the foetus, as in the regenerating liver, rapid histamine formation is not due to mast cells since such cells have only been found in foetal skin where the histamine-forming capacity is rather low.

These observations encouraged us to study the effect of inhibition of histamine formation on foetal development. First, we had to discover a suitable way of producing this inhibition. To this end we made use of two new methods for the determination of the rate of endogenous histamine formation. One depends on the fact that in the female rat fed on a specially compounded histamine free diet, the amount of free histamine excreted in the urine parallels the amount of endogenously formed histamine⁵. The other method, introduced by Schayer, measures the amount of radioactive histamine formed and excreted

following subcutaneous injection of radioactive histidine. Because a specific inhibitor of histidine decarboxylase has not yet been found, we used semicarbazide, the least toxic among known inhibitors of amino acid decarboxylases. On omitting the coenzyme of histidine decarboxylase, pyridoxine, from the diet semicarbazide in fairly small doses inhibited the rate of histamine formation by as much as 85 per cent. Under this treatment the rats fared reasonably well as regards appetite, exercise and maintenance of body weight.

In the rat the effect on foetal development of enzyme inhibition due to semicarbazide superimposed on a pyridoxine-deficient diet has been studied. Procedures and doses were such as to reduce the rate of histamine formation to about 15 per cent of normal. In one group of rats fed on the pyridoxine deficient diet, semicarbazide was given for eight days from the seventh day of pregnancy onwards that is from about the day of implantation of the ovum. At the nineteenth day, when the weight of the normal foetus is about 2 gm., there were only tiny remnants of foetuses in the form of plaques of disintegrated maternal, whilst the placentae were small and appeared to be in a state of regression (Fig. 1). In another group fed on the pyridoxine-deficient diet semicarbazide was given for eight days from the fifteenth day of pregnancy. On killing the animals at the 22nd day the findings were largely the same as in the other group. The foetuses were dead and mummified and their growth appeared to have been arrested at about the seventeenth day that is the day when enzyme inhibition became maximal. In controls fed for the same period of time on the pyridoxine deficient diet or simply injected with semicarbazide no abnormalities in the course of pregnancy and foetal development were noted.

We have not yet investigated to what extent other enzymes besides histidine decarboxylase are inhibited by the measures which in these experiments prevent foetal development. Inhibition of histamine formation appears to be involved for the following reasons. Of the substances the formation of which is known to be inhibited by semicarbazide only histamine has so far been found to be specifically related to foetal development. It has been shown by G. B. West as well as by our colleague H. Westling that the formation of 5-hydroxytryptamine is not

increased in rat pregnancy (personal communications). Further semicarbazide in doses larger than the ones used in our experiments did not inhibit the endogenous formation of 5-hydroxytryptamine in the guinea pig.⁴ Diamine oxidase (histaminase) is known to be inhibited by semicarbazide. It has however, been shown that complete inhibition of this enzyme by aminoguanidine has no detectable effect on the course of pregnancy or the fitness of the newborn.⁵ Nevertheless final proof of the dependence of foetal development on a high rate of histamine formation will have to wait until a specific non-toxic inhibitor of histidine decarboxylase becomes available. The recent discovery of a rich source of this enzyme foetal rat liver,⁶ is likely to encourage the search for a specific inhibitor.

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Effect of Sexual Maturation and Castration on the Sex Chromatin Pattern in the Male Rat

The nucleolar satellite described by Barr and Bertram¹ is generally considered to be of chromosomal origin and is, therefore, determined genetically. That is why, theoretically the incidence of sex chromatin bodies is not influenced by age or oestrogen and endogenous factors. Davidson and Smith² recognizing the sexual dimorphism of leukocytes thought that the drumstick form which is characteristic of females represented a fusion of the heterochromatic segments of two paired X chromosomes. However certain signs would seem to indicate that the chromatin condensations in leukocytes do not show in every respect the properties of the nucleolar satellites. In addition to the female drumstick³ several authors⁴ have observed so-called pseudo forms, the occurrence of which is also related to actual sex. At the same time it cannot be unambiguously explained how it is possible that chromosome pairs have so many variegated and yet nonspecific morphological equivalents. The foregoing facts and the presumptive relationship between sexual hormones and leukocytes has tempted us to study in leukocytes the hormonal relations of the sex chromatin especially those of the pseudo forms.

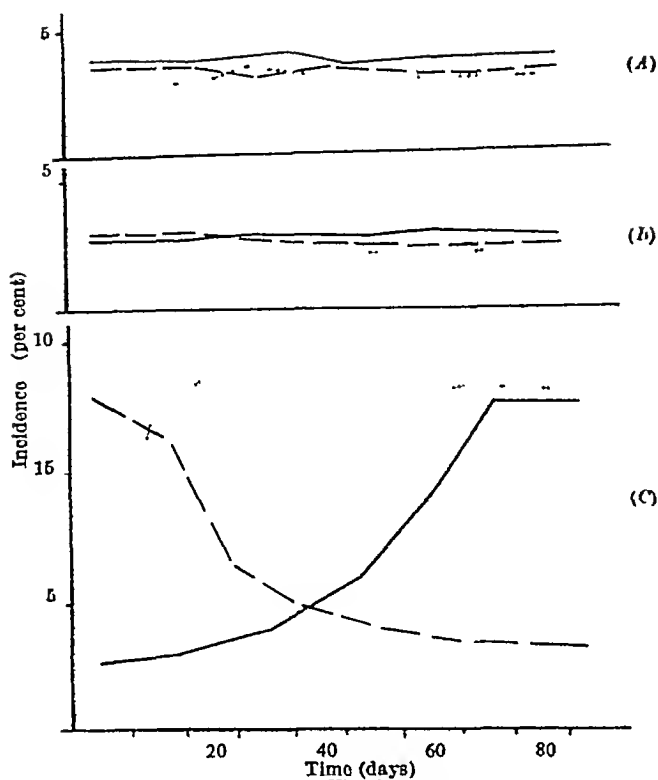
In this work Kosenow's method was applied, which uses the equation $Q = A + B/C$ where A represents drumsticks⁵ and B and C pseudoforms. Thus the numerical changes in the different types are made conspicuous.

64 male albino rats of a Wistar strain and of known age were divided into four groups of 16. Blood smears were taken weekly, the slides fixed with methanol and stained with a Giemsa solution. 500 neutrophil leukocytes were counted and the quotient Q , which in the mature male rats was less than 0.0 determined.

In the first group of animals counts were made from the 2nd to the 12th week of life (Fig. 1).



Fig. 1. The uterine contents of two rats at the nineteenth day of pregnancy. Left: undisturbed pregnancy; right: after enzyme inhibition. The latter animal was fed a pyridoxine-deficient diet from the first day of pregnancy onwards, semicarbazide was injected between the seventh and fifteenth days starting with 50 mgm/kgm twice daily on the seventh day followed by 75 mgm/kgm twice daily. On discontinuing semicarbazide a normal diet was given.



In the second group, mature males were castrated and observed for 10 weeks

The two groups, consistently and regardless of age, showed the same values for forms A and B (3.5 and 2.5 per cent on an average). At the same time, there was a considerable difference in the incidence of form C, its frequency, about 2-3 per cent at birth, gradually increased with age (full line), reaching about 12 per cent at sexual maturity, which is characteristic of mature males. On the other hand, after castration form C decreased in number (dashed line) and, within a month, approached the percentage for the newly born male rats. These results suggest that the incidence of form C is in relation with the actual androgen-level. To elucidate the question, a new experiment was carried out with a third group of animals.

A dose of 1 mgm/day (altogether 36 mgm) of a testosterone-propionate ('Androfort', Kőbányai Gyógyszerárnyár, Budapest) was injected into young male rats of 3 weeks of age. As early as by the 10th day sex chromatin form C was found to have reached a frequency characteristic of mature animals (dotted line), which had been expected to occur only six or eight weeks later, as seen in the first group under physiological conditions.

To exclude a possible aspecific steroid effect, 2 mgm of an oily cholesterol suspension were administered to the fourth group, which, however, failed to influence the sex chromatin pattern.

It should be emphasized that, as has been reported by other workers^{5,6}, after administration of testosterone no changes whatever were seen in the sex chromatin pattern of the epithelial cells of skin.

These findings indicate that the incidence of form C—in contrast to A and B—is influenced by age and androgen. This has led to the conclusion that form C in neutrophil leukocytes should not be regarded as a real sex chromatin body. The incidence of form C being an important factor in Kosenow's formula, it would seem that his method for the determination of

sex by blood smears cannot always be relied upon to demonstrate the real genotype in the rat. This view has been supported by our observations upon female animals, the results of which will be reported at a later date.

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A Peripheral Effect of the Bromide Ion on the Contraction of Striated Muscle

ACCORDING to current literature, the main effects of the bromide ion are on the central nervous system. We have observed a hitherto undescribed but well-defined effect upon striated muscle in the following circumstances.

The diaphragm-phrenic nerve preparation in the rat described by Bulbring¹ was modified so as to use it for alternative supramaximal direct and indirect stimulation.² Upon replacement of normal Tyrode solution by Tyrode solution in which an equimolar concentration of sodium bromide was substituted for sodium chloride, both types of contractions were enhanced (see Fig. 1). The effect could be repeated

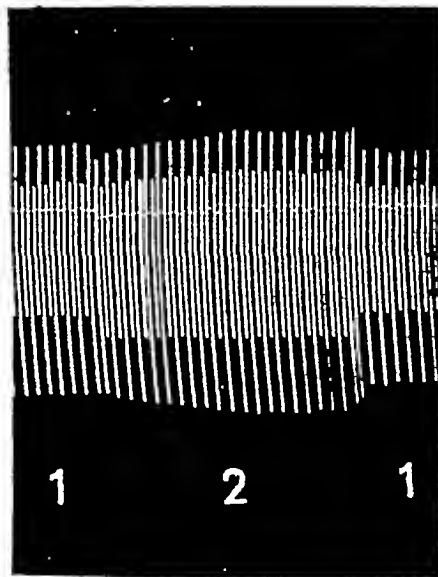


Fig. 1. Diaphragm-phrenic preparation in the rat with alternatively direct and indirect stimulation. 1, normal Tyrode solution; 2, Tyrode solution with sodium bromide.

several times on one and the same preparation. The bromide effect disappeared on continued exposure to the bromide Tyrode solution. It was also observed with preparations in which indirect excitability was completely inhibited by a high concentration of d-tubocurarine.

Experiments designed to analyse this phenomenon in more detail are in progress. They will be reported upon elsewhere.

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Sodium Chloride Intake and Urinary Histamine in Adrenalectomized Rats

It has been found by Schayer and his co-workers that adrenalectomy induces an increase in the rate of histamine formation in some tissues of the rat.^{1,2} This increase may be due to the cause of the increased tissue histamine content.³⁻⁵ Hicks and West pointed out that the tissue histamine content in adrenalectomized rats could be kept at a normal level by giving 0.9 per cent sodium chloride as drinking fluid.⁶ A similar effect was observed by Roso and Browne.⁷ During experiments on the effect of the adrenocortical hormones on the urinary excretion of histamine in normal and pregnant rats we made an observation which is of interest in this connexion.

White female rats were kept in metabolism cages and fed a dry cake diet *ad libitum*. The diet had a low histamine content (less than 0.8 µgm/gm) and contained about 0.4 per cent sodium chloride and about 0.7 per cent potassium chloride. The rats were allowed to drink either distilled water or a 0.9 per cent sodium chloride solution *ad libitum*. Urine was collected in 24 hr specimens and its histamine content estimated on the guinea pig ileum. In most cases the rats were given a daily subcutaneous injection of aminoguanidine sulphate (20 mgm/kgm) to prevent destruction of histamine by histaminase (for example ref. 7). The urinary excretion of histamine was followed before and after adrenalectomy and the following changes were observed:

- (1) In animals drinking water there was no or a small increase after removing the adrenal glands.
- (2) In animals drinking 0.9 per cent sodium chloride there was a progressive and distinct increase of the histamine excretion.
- (3) In adrenalectomized rats kept on water for 6-8 days after the operation the substitution of sodium chloride for water as drinking fluid caused an immediate increase in urinary histamine (Fig. 1). The high urinary histamine of adrenalectomized rats kept on saline could be lowered by changing over to water (Fig. 1).
- (4) Mock-adrenalectomized rats showed no significant changes in the levels of urinary histamine.

From these observations and those of the other workers it seems probable that there is an increased formation of histamine in the adrenalectomized rat regardless of whether it is allowed to drink water or 0.9 per cent sodium chloride. In animals kept on

water the formed histamine accumulates in the tissues and little is excreted. In animals kept on sodium chloride the histamine does not accumulate to the same extent but is excreted in the urine.

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Effect of Sulphonamides on the Phagocytic Activity of the Reticulo-Endothelial System

The effect of various steroids stilbenes antibiotics and other substances on the phagocytic activity of the reticulo-endothelial system has been reported previously by Nicol and his co-workers.^{1,2} It was shown that some of these substances stimulate the reticulo-endothelial phagocytes some have little or no effect, and some are active depressants. So far, diethylstilbestrol has been found to be the strongest stimulant and cortisone the most powerful depressant. Florey³ has stated that it is possible that some chemotherapeutic agents depend for their complete effectiveness on the action of phagocytes. In this connexion it may be stated that our results with antibiotics⁴ showed that these substances have little or no effect on the phagocytosis of particulate carbon.

The following work was designed to study the effect of sulphonamides on the phagocytic activity of the reticulo-endothelial system to find out whether or not these compounds depend for their effectiveness on the action of the reticulo-endothelial phagocytes.

The present experiments were carried out on 188 male white mice (TO Swiss strain) of 18-25 gm body weight. Thirteen sulphonamide compounds were investigated. The drugs were taken up in propylene glycol and the dose of sulphonamide given was 1 mgm in 0.05 ml propylene glycol once daily for 6 days. Twelve animals were used to investigate each compound, six receiving the drug orally and the other six subcutaneously. On the 8th day after the commencement of sulphonamide treatment the phagocytic activity was assessed by the rate of disappearance of a known amount of carbon from the circulating blood⁵, the procedure used being that described in previous communications.⁶

Thirty of the animals were used as controls. They were given 0.05 ml propylene glycol once daily for 6 days and on the 8th day the phagocytic activity was assessed by the carbon method.⁷ Half of the control animals received the propylene glycol orally, the other half subcutaneously.

The results are shown in Table 1. The control animals showed an average phagocytic index or K value of 16 ± 4 after oral administration of propylene glycol and 18 ± 4 after subcutaneous administration. Compared with the control values it can be seen that the sulphonamides used, with the exception of sulphadiazine, have little or no effect on the phagocytic activity of the reticulo-endothelial system and there is no significant difference between the results

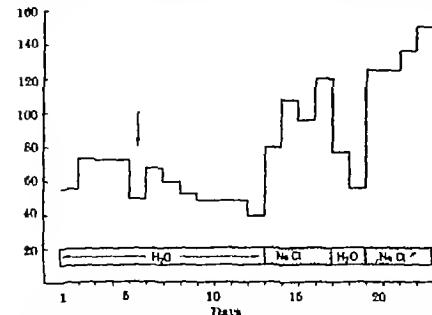


Fig. 1. Urinary histamine in µgm base per 24 hr (vertical axis) in female rat before and after adrenalectomy (at arrow). The drinking fluid was distilled water or 0.9 per cent sodium chloride as indicated. The rat was injected with 20 mgm/kgm of aminoguanidine sulphate once daily under the skin.

Table 1 EFFECT OF VARIOUS SULPHONAMIDES ON THE PHAGOCYTIC ACTIVITY OF THE RETICULO-ENDOTHELIAL SYSTEM

| Sulphonamide used | Phagocytic Index (K value) after oral administration | Phagocytic Index (K value) after subcutaneous administration |
|---|--|--|
| Sulphaguanidine | 20 ± 0.3 | 15 ± 3.1 |
| Sulphamethoxypyridazine | 19 ± 4.5 | 13 ± 2.2 |
| Sulphamerazine | 18 ± 3.7 | 13 ± 3.6 |
| Acetazolamide | 18 ± 2.0 | 15 ± 4.9 |
| Sulphanilamide | 10 ± 5.2 | 9 ± 4.5 |
| Sulphadimidine | 15 ± 2.0 | 10 ± 2.2 |
| Sulphathiazole | 15 ± 4.8 | 13 ± 3.0 |
| Phthalylsulphathiazole | 15 ± 1.4 | 15 ± 3.3 |
| Succinyl sulphathiazole | 14 ± 4.0 | 15 ± 3.3 |
| 6-sulphonilamido-2,4-dimethylpyrimidine | 13 ± 1.7 | 14 ± 3.1 |
| Sulphapyridine | 13 ± 1.4 | 10 ± 3.0 |
| Sulphisoxazole | 11 ± 2.4 | 13 ± 2.5 |
| Sulphadiazine | 10 ± 1.4 | 10 ± 1.0 |
| Propylene glycol controls | 16 ± 2.4 | 18 ± 4.4 |

of oral and subcutaneous administration. The low K values for sulphadiazine and sulphisoxazole and the absence of toxic symptoms suggest that these two compounds are mild depressants. These results resemble closely those recorded for antibiotics³ and suggest that the phagocytes do not play an important part in the action of these drugs. It is more likely that both antibiotics and sulphonamides act directly on invading organisms.

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Effect of Cobaltic Oxide Pellets on the Vitamin B₁₂ Content of Ewes' Milk

EVIDENCE that the provision of cobalt containing supplements to ruminants will increase the vitamin B₁₂ content of their milk is conflicting. Harper *et al*¹ and Momuddin *et al*² found that cobaltized mineral mixtures given to ewes fed on dry rations significantly increased vitamin B₁₂ levels in the milk. Other workers³, however, have reported that supplementary feeding with cobalt-containing trace element mixtures had no effect on the vitamin B₁₂ content of cows' milk when the animals were either stall-fed or grazed on pasture. According to Shrimpton and Duckworth⁴ extra cobalt given to grazing ewes either as a drench or in a mineral supplement failed to increase the vitamin B₁₂ content of the milk, but it seems doubtful whether any response would have been expected under the particular conditions of their trials.

In the work reported here a flock of pregnant ewes, grazing pastures marginally cobalt-deficient for lambs, was divided into two groups. Ewes in one group were each given a pellet containing 90 per cent cobaltic oxide (described by Dewey *et al*⁵). Ewes in the second group served as controls. Lambing commenced 3 weeks later and continued for a further 3 weeks. When the lambs were approximately 3 months old and averaged about 50 lb body-weight, and 5 weeks before weaning, milk samples were drawn from each group of ewes, extracted with

cyanide⁶, and assayed for vitamin B₁₂ using *Lactobacillus leichmannii*⁷. Results are shown in Table 1.

TABLE 1

| Group | No of Ewes | Vitamin B ₁₂ (μgm / l) | |
|------------------------|------------|------------------------------------|------|
| | | Range | Mean |
| Cobaltic Oxide Pellets | 15 | 4.3-10.1 | 10.3 |
| Control | 12 | 1.0-4.6 | 2.5 |

The mean result for milk from pellet-treated sheep is comparable with mean values found by Harper *et al*¹ for their cobalt-supplemented groups. Australian workers (O'Halloran, M W, and Skerman, K D, private communication) have also examined the effect of pellets on the vitamin B₁₂ content of milk from pasture-fed ewes. Their results are similar to ours. It is concluded that continuous supplies of cobalt given in the form of cobaltic oxide pellets to grazing ewes will increase the vitamin B₁₂ content of the milk several-fold.

According to Gregory⁸, the vitamin B₁₂ activity of milk is due almost entirely to cyanocobalamin, a form biologically active for higher animals. Hence it is of interest to consider to what extent ewe's milk will meet the lamb's requirement for the vitamin. On the basis of calculations made by Smith and Loosli⁹, the daily requirement of a 50 lb lamb for vitamin B₁₂ given parenterally is about 9 μgm. But for crystalline vitamin B₁₂ given orally existing evidence suggests that the daily requirement would not be less than 100 μgm^{8,9} and could be of the order of 300 μgm⁸. Lambs will drink about a litre of milk each day¹⁰. Thus assuming that there is no great difference in availability to the animal between crystalline vitamin B₁₂ and the bound form occurring in milk⁸, it is evident that milk from the cobalt supplemented ewe will provide only a small fraction of the lamb's total daily requirement for vitamin B₁₂.

The technical assistance of Messrs A J Poole and B J Stephenson is acknowledged.

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Effects of Carbon Tetrachloride on Kidney and Liver Function in the Sheep

CARBON tetrachloride is often taken as a classical example of a hepatotoxin. However, there is some suggestion¹ that its lethal effect should be attributed to its action on the kidneys.

Five Corriedale adult wethers, between 35 and 42 kgm body-weight, were drenched with a mixture of 50 ml carbon tetrachloride and 100 ml liquid paraffin. Estimations were made of bromsulphthalein clearance, *p* aminohippurate synthesis from *p* aminobenzoate and plasma concentrations of bilirubin and glutamate oxalacetate transaminase as indications of liver function, and *p*-aminohippurate clearance and plasma concentrations of creatinine and urea as indications of kidney function. Methods used are described elsewhere.²

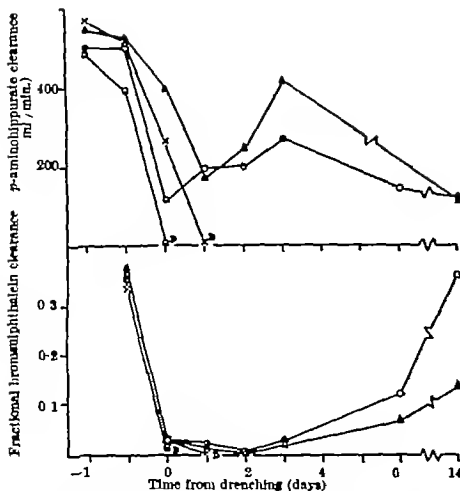


Fig. 1. Assessments of liver and kidney function in sheep after drenching with carbon tetrachloride. Each symbol (\times , \circ , \square and Δ) refers to the same sheep throughout.

Two of the sheep remained clinically normal and three of the sheep died. One was found in extremis about 18 hr after drenching, one died about 24 hr and one 48 hr after drenching. Symptoms noticed were progressive dullness and unwillingness to stand. Death occurred within 5 hr of development of symptoms.

It will be seen from Fig. 1 that 18 hr after drenching there was as expected in all sheep a severe degree of liver dysfunction as judged by fractional bromsulphthalein clearance. The other tests for liver function, plasma glutamate oxalacetate transaminase, plasma bilirubin concentration and p-aminohippurate synthesis from p-aminobenzoate also showed evidence of severe liver dysfunction. The maximum changes were found between two and three days after drenching (depending on the test) but function had returned virtually to normal by 14 days. In none of these tests was there any correlation between the severity of the dysfunction and the appearance of symptoms. There was also a decrease in p-aminohippurate clearance 18 hr after drenching which persisted for the 14 days of the experiment. In those sheep which died the p-aminohippurate clearance had fallen to very low values before death. In these sheep there was also a rise in plasma urea and creatinine concentrations before death, but little change in the unaffected sheep.

These findings suggest that clinical symptoms and death were associated with almost complete cessation of kidney function in the presence of a severe degree of liver dysfunction. A similar degree of liver dysfunction with only a moderate degree of kidney dysfunction was not associated with clinical symptoms.

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Cartilage Homografts in Papain-Injected Rabbits

CRUDE papain administered intravenously to young rabbits brings about ear collapse within 24 hours¹⁻⁴ and there is a concomitant loss of metachromasia of the ear cartilage⁵. A return to normal after a single dose occurs within a few days but can be delayed for about 28 days by the administration of cortisone¹. Biochemical studies have shown that there is release of chondromucoprotein from the ear cartilage and a reduction of chondroitin sulphate content in the chondromucoprotein that remains in the cartilage⁶; there is also liberation into the blood and urine, of a mucopolysaccharide resembling⁶ in chemical and physical properties chondroitin sulphates A and C. Cartilage homograft survival is held by some workers to be attributable to the mucopolysaccharide nature of the cartilage matrix^{7,8}. Hence it was of interest to test survival of homografts of cartilage the matrix of which had been degraded by papain.

The papain sample used was found to produce ear collapse within 24 hours in each of three rabbits given 3 ml. of a 2 per cent aqueous solution intravenously. The ear cartilage from all three rabbits exhibited metachromasia which was however more alcohol labile than that of normal ear cartilage. In the experiments to be described the papain effect was extended by administering cortisone to the recipients. As, however, cortisone has been shown to prolong survival of homografts^{9,10,11,12} it was thought advisable, in order to counteract the latter property of cortisone, to use as hosts rabbits sensitized by skin homografts from the prospective cartilage donors (It should be noted that these skin grafts were rejected by all the hosts in due course).

Sixteen rabbits of under 1 kgm. body weight were used, eight as donors and eight as recipients. Each of four control recipients received a large homograft of ear skin. 14 days later a subcutaneous implant of a large piece of ear cartilage from the skin donor and then a daily intramuscular injection of 5 mgm. of cortisone for 28 days. The experimental group was dealt with in similar fashion with this difference that (a) the donor had papain induced ear collapse when the cartilage was taken from its ear and (b) the recipient was given a dose of crude papain inducing ear collapse after implantation of the cartilage homograft. The cartilage homografts, sought after three months, were found to be rolled up but otherwise unchanged macroscopically in seven of the eight recipients. In the remaining rabbit which was an experimental one, only a small hard nodule was recovered. The recovered material was fixed in Bouin's fluid and embedded in paraffin. Sections were stained by (1) hematoxylin and eosin (2) toluidin blue and (3) the periodic acid Schiff reaction.

Microscopically it was found that the fibrous nodule actually contained some small pieces of cartilage, and it is thought that in this instance infection had supervened. These cartilage remnants, and all other seven cartilage homografts recovered generally showed normal histological and histo-chemical staining properties.

These findings show that cartilage homografts the matrix of which had been degraded by papain at the time of transplantation and maintained in this condition for some time thereafter persisted in sensitized hosts. The results are still reconcilable with the matrix theory of cartilage homograft survival for although much of the mucopolysac-

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charide is removed by papain, the residual chondro mucoprotein could well be sufficient to give protection to the graft

I wish to express my thanks to Charles Zimmermann and Co Ltd, Perivale, Middlesex, for their generous donation of the papain used in these experiments

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Electrical Activity in the Muscle Cells of *Ascaris lumbricoides*

If a fresh specimen of *Ascaris* is opened by a longitudinal incision and pinned out under 30 per cent sea water at 37°C, fluctuating intracellular potentials can be recorded, using relatively large 3 μ potassium chloride microelectrodes inserted into the swollen bodies of the large muscle cells

Superimposed on the resting potential is a sequence of simple or complex depolarizing spikes normally of magnitude less than that of the resting potential

If concurrent recordings are made of the potentials in two muscle cells, one of which is in the dorsal field and the other in the ventral, no correlation is found in the timing of the two sets of pulses (Fig 1) if recordings are taken from two cells, a few mm apart, in the same field, a definite correlation between the two records can be seen (Fig 2) Each pulse in one record has its counterpart in the other. If the muscle cells concerned are at the same antero-posterior level, but at different distances from the nerve cord, the cell nearer the nerve cord gives the first pulse. If the cells are on a line parallel to the nerve cord, the anterior cell gives the first pulse

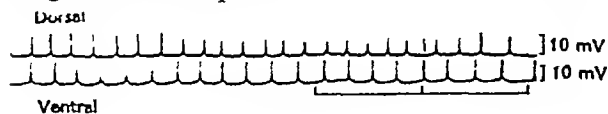


Fig 1

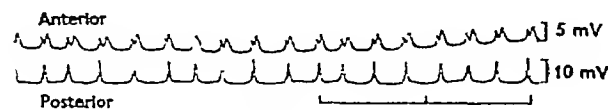


Fig 2

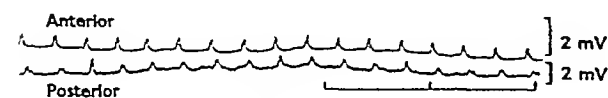


Fig 3

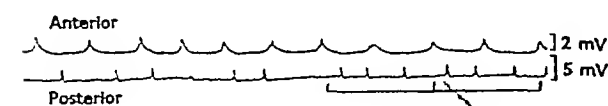


Fig 4

Experiments involving transverse cuts made between an anterior and a posterior muscle cell have demonstrated two significant features

(a) A transverse cut between the two cells, through the muscle column, hypodermis and cuticle of the worm, provided it does not sever the nerve cord, does not destroy the correlation between the pulses (Fig 3).

(b) Cutting the nerve cord between the two cells, with or without an extension of the cut through the muscle column, abolishes the correlation, and independent sequences of impulses are then recorded from the two cells (Fig 4)

Correlated pulses are therefore obtained so long as the nerve cord between the two cells is intact

The origin of these depolarizing pulses and their relations to the membrane potential and tension in the muscle fibre are being investigated, but the results outlined above indicate the interesting possibilities of this material for neuro-physiological work

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Distribution in the Mouse of Lethal and Sub-lethal Doses of Cottonmouth Moccasin Venom labelled with Iodine-131

THOUGH disease and death from the bite of the poisonous snake is considered not unusual, and treatment has become more or less standardized, little is actually known about the site of action of snake venom *in vivo*. The value of a radioactive tag for studies of this sort is evident, and therefore, an attempt was made to label the whole dried venom of the cottonmouth moccasin (*Ancistrodon p piscivorus*) with iodine 131, evaluate its toxicity relative to the original venom preparation, and chart its distribution in the mouse after injection of lethal or sublethal doses

50 μ gm of whole dried venom, dissolved in physiological saline and buffered to a pH of 9, was labelled by alkaline extraction of cold carbon tetrachloride to which sodium iodide carrier and 3 me of iodine-131 had been added^{1,2}. The extraction mixture was relieved of excess uncombined iodide and buffer by dialysis against dibasic potassium phosphate ($10^{-2}M$) at 34 C for 48 hr. The resultant radioactivity of the labelled protein preparation was 117 c/m/ μ gm (thin window Geiger-Muller counter)

Although the iodinated dialyzed venom was somewhat less toxic than whole venom, it was equally as toxic as whole venom which had been dialyzed but not iodinated (Fig 1). This loss of toxicity of snake venom during dialysis has already been described by Goncalves³, and is attributable to the loss of small molecules of toxic materials. A comparison between the toxic effects produced by the dialyzed venom and those caused by the non-haemolytic toxins which are separable from the whole by ammonium sulphate precipitation indicates that enough of the hemorrhage-producing material is present in the dialyzed venom for it to contribute appreciably to the total effect

| | DOSE (μ g/gm MOUSE) | | | | | | | | | | |
|---------------------------------|--------------------------|----|----|----|---|---|---|---|---|---|---|
| | 13 | 12 | 11 | 10 | 9 | 8 | 7 | 6 | 5 | 4 | 3 |
| ¹³¹ I-LABELLED VENOM | | | | | | | | | | | |
| DIALYZED VENOM | | | | | | | | | | | |
| WHOLE DRIED VENOM | | | | | | | | | | | |

Fig 1 The toxicity of *Ancistrodon p piscivorus* venom labelled with iodine 131 compared with dialyzed venom and dried whole venom from the same sample. Black, complete lethal dose (100) hatched, minimum lethal dose, white, sub-lethal dose (0)

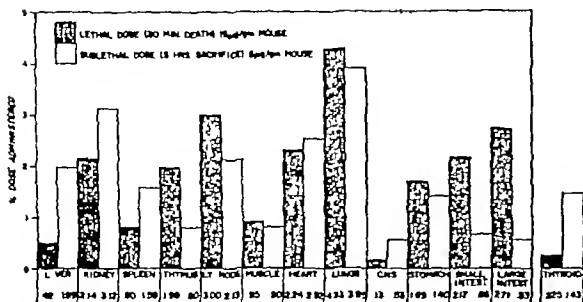


Fig. 2. The distribution of venom labelled with iodine-131 of the cottonmouth moccasin (*Anacrotodon p. pictiventris*) in the mouse. Most mice injected intraperitoneally with 10–20 μ gm of iodinated-dialyzed toxin per gram of mouse died within 18 hr and the remainder, which appeared in poor condition, died within 3 days following treatment. This is unlike the effect produced in the groups injected with the non hemolytic fractions in which the animals died within 24 hr or not at all. Further, the gross pathological changes produced by injection of the labelled venom were those which followed injection of the whole dried poison, namely, generalized hemorrhage and edema. The abdominal cavity and small gut were filled with serosanguineous fluid and the urine was bloody. All organs and tissues exhibited hemorrhagic changes, most large vessels were thrombosed and the heart had stopped in systole.

The distribution of the labelled venom was observed after intravenous injection of mice at 2 dose levels. The first 15 μ gm/gm, when injected into 20 gm male Swiss mice caused death within 30 min in all individuals, the second 5 μ gm/gm, when injected intravenously into 8 similar animals produced disease but no deaths, and within 5 hr all showed significant improvement. Distribution of the radioactivity in pooled organ homogenates can be seen in Fig. 2. Before death the lethal dose did not accumulate to any great extent in the liver or spleen, organs in which collection or detoxification of venom might be expected to occur, even though some radioactive material presumably a metabolite is present in the kidneys at this time. Relatively large quantities, however were concentrated in the thymus and lymph nodes (mesenteric) but most striking was the large concentration of radioactivity in the lung. Though radiolabelled venom was not accumulated greatly by the skeletal musculature, a considerable quantity was found in the heart. Similar amounts were also found in the gastro-intestinal tract, especially in the colon. Only very small amounts of radioisotope were detected in tissues of the central nervous system.

The low thyroid radioiodide level after 30 min was interpreted as indicative of the integrity of the labelled venom protein.

It may be that the different distribution of radioactivity in tissues of animals which received a sublethal dose are due to the detoxification and/or excretion of the labelled protein in the period after administration. In support of this was the considerable increase in these animals of what was probably free radioiodide (thyroid) presumably accumulating as a result of the metabolism of the labelled venom protein. That the toxic properties of the latter have been reduced at this time was emphasized by the improved condition of the animal and its ultimate recovery. Concentration of the radioactivity in the

lung had diminished and though it had increased in the heart it is difficult to say whether the slight change is significant. The increase in the radioactivity of the central nervous system, interpreted in the light of the complete absence of neurotoxic sign in the animal, is thought simply to be due to an accumulation of circulating radioiodide which has been shown to localize here. If this were the case it might be indicative of a peripheral site for neurotoxic action. It is thought that the concentration in the lung and possibly the heart may be associated with the lethal effect of the venom. Further studies now under way seem to reinforce these preliminary data.

We are indebted to the Ross Allen Reptile Institute, Silver Springs, Florida, for the venoms used in this work and to H. P. Hall for assistance with the technical procedures.

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Passage of Insulin Through the Wall of the Gastro-intestinal Tract of the Infant Rat

It is well known that protein molecules can pass through the wall of the gastro-intestinal tract into the blood in new born animals¹. The possibility, therefore, exists that hormones which might be present in milk also are absorbed by infant animals. To test this hypothesis, insulin, which is ineffective when given *per os* to adult animals, was administered to infant rats by a stomach tube. Regular insulin was used in a dose of 40 units/ml, 1 ml/100 gm body weight. Rats were starved for 16–18 hours at 30° C environmental temperature before the start of the experiment. Control animals received an equivalent dose of saline. All rats were killed two hours after insulin administration and blood glucose levels were determined by a modification of the Somogyi-Nelson method².

It is evident from Table 1 that in 2 and 8 day-old animals insulin causes a large drop in blood glucose levels when administered *per os*, whereas in 21 and 30-day-old animals this is no longer the case. This change in the hypoglycaemic effect of insulin occurs at the same postnatal period as the change in permeability to antibodies³. At this period alkaline phosphatase activity in the duodenum⁴ and the whole intestine⁵ increases and glucose absorption is also raised⁶. It is evident from Table 1 and has already been shown by others⁷ that peptic activity in the stomach rises enormously between the 8th and 21st

Table 1 HYPOLYCEMIC EFFECT OF INSULIN ADMINISTERED BY STOMACH TUBE AND PROTEOLYTIC ACTIVITY* OF THE GASTRO INTESTINAL TRACT

| Age (days) | Weight (gm) | Insulin (U) | Blood sugar level (mgm per cent) | | Proteolytic activity | |
|---------------|----------------|----------------|----------------------------------|-----------------|----------------------|---------------------------------------|
| | | | saline | Insulin | stomach (units)† | intestine + pancreas (units + + +) |
| 2 | 4.5 | 2 | 39.3 ± 2.4 (8) | 25.1 ± 2.1 (11) | 0.01 (6 pooled) | 0.81 (6 pooled) |
| 8 | 10.3 | 4 | 75.0 ± 2.5 (10) | 28.0 ± 2.5 (4) | 0.00 (6) | 0.23 ± 0.07 (8) |
| 21 | 25.2 | 10 | 91.0 ± 4.5 (6) | 95.0 ± 2.4 (6) | 0.53 ± 0.15 (7) | 2.10 ± 0.18 (7) |
| 30 | 43.0 | 20 | 118.0 ± 9.8 (4) | 136.0 ± 2.2 (5) | 1.23 ± 0.16 (6) | 4.00 ± 0.10 (6) |

Values are given ± standard error of the mean. Figures in brackets are the numbers of animals.
 * Proteolytic activity in the stomach was determined using biuret reaction at pH 2.1 (ref. 6). In the intestine and pancreas the amino-groups released at pH 9.2 were determined (ref. 7).
 † 1 unit = 1 mgm. pepsin Organofarma (1:10,000).
 ‡ 1 unit = 1 mgm. pancreatin Organofarma (1:100).
 Decrease of blood sugar level after insulin administration in 2 and 8-day-old animals is significant ($P < 0.01$).

day. Tryptic activity of the intestine and pancreas also increases, but this increase is much less pronounced.

It was also tested whether insulin given subcutaneously to lactating rats would produce hypoglycaemia in the sucking infant animals. This could not be demonstrated. It was found, however, that lactating rats are very resistant to high doses of regular insulin (80–120 units per rat). Seven animals out of seven survived such a dose while 4 non-lactating female rats succumbed within 3 hr. of the injection.

It is also of interest that infant rats aged 2 and 8 days never had seizures when blood glucose levels were depressed, whereas it is reported that piglets do have seizures under such conditions⁵.

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PLANT PHYSIOLOGY

Changes in Adenosine Di- and Tri-phosphate Concentrations in the Early Stages of the Action of Yeast on Glucose

In a previous communication¹ we reported attempts to measure the concentrations of adenosine diphosphate and triphosphate in yeast fermenting or respiring in the presence of glucose, in the steady state of these processes. We concluded that there was little difference in the concentration of adenosine diphosphate under anaerobic or aerobic conditions, while the concentration of adenosine triphosphate was slightly higher aerobically. Propionitrile at a concentration sufficient to inhibit the Pasteur effect had no effect aerobically on the concentration of either substance.

A small technical improvement has now enabled us to identify with greater certainty the material in the ion-exchange chromatographic fractions which we had used to estimate adenosine di- and tri-phosphates, and we have applied this method to follow the changes in concentration of these substances in the early stages of fermentation and respiration in yeast.

25 ml. samples of a 30 per cent suspension (fresh weight/vol.) of bakers' yeast in *M/40 tris* buffer at pH 6.5 were bubbled at room temperature (approx.

20°) with purified nitrogen or with a vigorous stream of oxygen, and glucose solution added to give a final concentration of 1.2 per cent. After the appropriate time, with continuous gassing, 5 ml. of 50 per cent trichloroacetic were added. After they had stood at room temperature for 1 hr., the suspensions were centrifuged and the yeast residue washed once with 20 ml. of 5 per cent trichloroacetic acid. The combined extracts were treated with 2 gm. of barium acetate, the pH adjusted to 8.5, and the precipitate removed and dried.

The water-insoluble barium salt fractions were freed from barium by treatment with the ion-exchange resin 'Amberlite CG-120', neutralized with

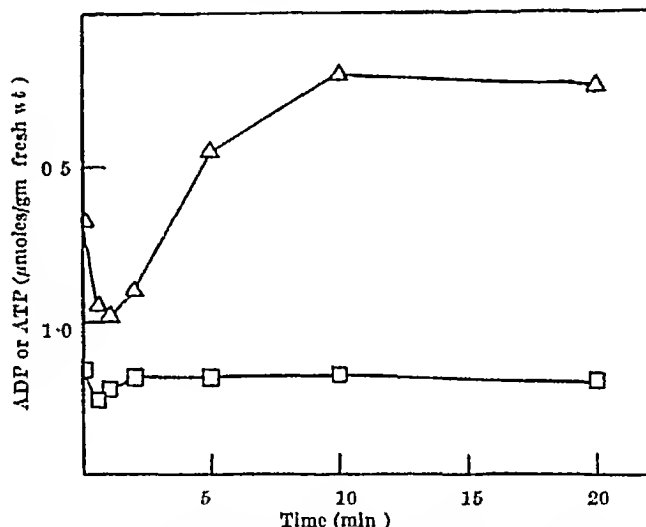


Fig. 1. Changes in adenosine diphosphate (ADP), □—□, and in adenosine triphosphate (ATP), Δ—Δ, in yeast in nitrogen. Glucose added at zero time.

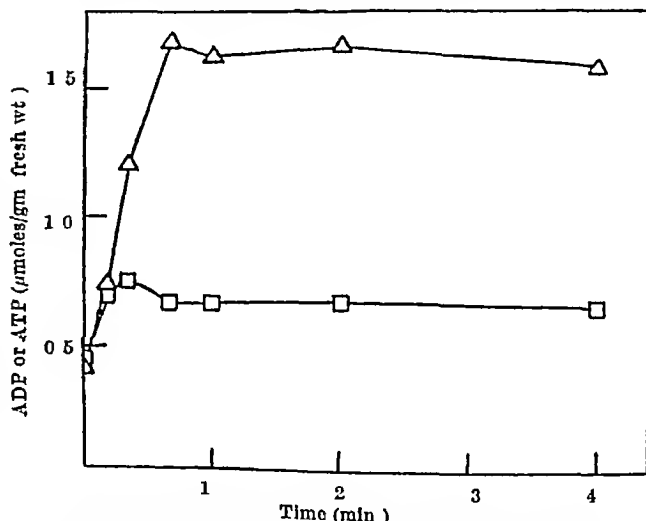


Fig. 2. Changes in adenosine diphosphate (ADP), □—□, and in adenosine triphosphate (ATP), Δ—Δ, in yeast in oxygen. Glucose added at zero time.

ammonia, and applied to a column of the anion exchange resin 'Amberlite CG 400'. The solutions used for elution from the resin column were hydrochloric acid 0.01 N + sodium chloride 0.002 N (X), hydrochloric acid 0.01 N + sodium chloride 0.02 N (Y), and hydrochloric acid 0.01 N + sodium chloride 0.2 N (D). (X) removed the inorganic phosphate and much organic phosphate of a non nucleotide nature which had previously interfered with the analysis of the adenosine di and tri phosphates, (Y) removed adenosine diphosphate, and (D) adenosine triphosphate. The adenosine di and tri phosphate fractions obtained in this way gave molar ratios of adenine ribose phosphorus closely approximating to 1:1:2 and 1:1:3, respectively.

The result of a typical anaerobic experiment is shown in Fig. 1, and of a typical aerobic experiment in Fig. 2. Anaerobically, adenosine diphosphate fell to a minimum value after 1 min then rose and reached its final steady value after 2 min. Adenosine triphosphate also fell initially, then rose more slowly and reached its steady high value in about 10 min. Aerobically, adenosine diphosphate rose to a small peak in 20 sec, and fell slightly to a steady value after 40 sec. Adenosine triphosphate rose steeply and reached its high steady value in 40 sec.

The final concentrations of both adenosine di and tri phosphates were practically identical, whether conditions were anaerobic or aerobic (average adenosine diphosphate, in nitrogen 0.31 μ moles/gm fresh weight in oxygen 0.27 μ moles, adenosine triphosphate, in nitrogen 1.26 μ moles, in oxygen 1.22 μ moles). This was found in three experiments with three different samples of yeast though the steady state concentrations of both nucleotides varied somewhat in the different experiments, as can be seen in the examples plotted in Figs 1 and 2.

In all our experiments there was a large increase in the sum of adenosine di plus tri phosphate. The obvious source of this increase would be adenylic acid in the resting yeast but our previous experiments¹ indicated that very little adenylic acid was present in the initial samples. We now find that adenylic acid, when in the presence of large amounts of other water soluble alcohol insoluble barium salts, does not behave normally on the ion-exchange column. Pure adenylic acid is completely eluted by 0.003 N hydrochloric acid (eluent B of Cohn and Carter)² but if adenylic acid is added to the alcohol insoluble barium salts from a sample of yeast, and the mixture placed on the column, eluent B does not elute it. Instead, it appears in the eluate with eluent X, mixed with a number of other nucleotides which we have not been able to separate. However the total quantity of this mixture, estimated in experiments with yeast such as those described above, shows a fall approximating to the rise in the sum of adenosine di and tri phosphates, so there is little doubt that the sum of adenylic acid, adenosine di and tri phosphates remains, as would be expected, roughly constant.

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Response of *Sequoia sempervirens* (D Don) Endl and *Pseudotsuga menziesii* (Mirb.) Franco Seedlings to Temperature

CONIFEROUS species show marked differences in their temperature requirements for seedling growth. These differences are connected with not only mean temperature but also with response to fluctuations in day, night and diurnal temperatures.

Kramer¹, working with *Pinus taeda* (L.) found that the plants made the maximum growth when the day temperature was 12 deg C or 13 deg C higher than the night temperature. Growth decreased as day and night temperatures approached equality regardless of the absolute level.

To determine if such diurnal temperature fluctuation is required by other conifers we have grown redwood (*Sequoia sempervirens* (D Don)) and Douglas fir (*Pseudotsuga menziesii* (Mirb.) Franco) both from the northern coast of California, under a series of temperature conditions. One month-old seedlings were grown for an additional 6 months in the Earhart Plant Research Laboratory under 16 hr days of approximately 600 ft candles intensity.² Twenty four plants were grown per treatment.

We have found that the top growth of redwood seedlings responds significantly to day temperature (Fig. 1). Only when day temperature was low (7° C) did increased night temperature significantly increase top growth. Root growth is, however, less responsive and is essentially not influenced over most of the range of temperature used. Cool nights (7° C) with 23° C day temperatures favoured root growth whereas cool days (7° C) with nights of 7° C depressed root growth.

In contrast to the redwood Douglas fir from the same region shows a marked optimum for top growth within the range of temperatures studied. This optimum was a 17° C day temperature (Fig. 2) with both 7° C and 23° C night temperatures. Root growth exhibited the same optimum as well as better growth at a night temperature of 7° C.

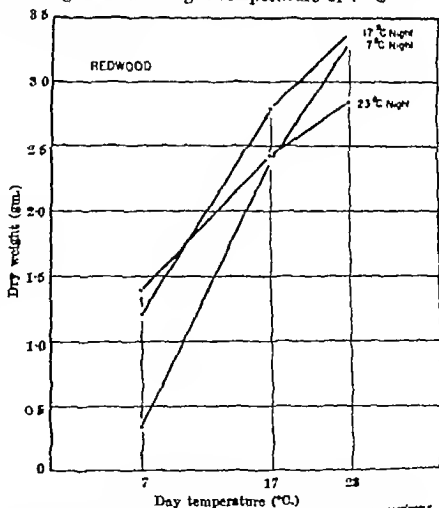


Fig. 1. Average top growth per plant of *Sequoia sempervirens* seedlings grown under nine different day/night temperature conditions.

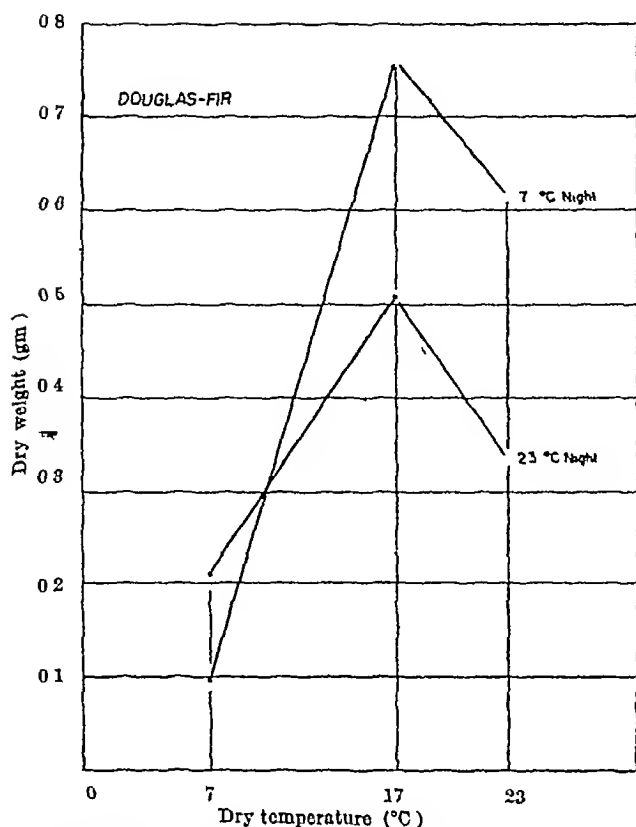


Fig. 2. Average top growth per plant of *Pseudotsuga menziesii* seedlings grown under six different day-night temperature conditions.

Thus, these results show that a diurnal temperature variation is not required for the maximum growth of redwood. The case is not so clear for Douglas fir, this plant makes optimum growth with a 10 deg. C diurnal variation, but a diurnal variation of 16 deg. C inhibits growth.

The fact that redwood initially grows much faster than Douglas fir (Figs. 1, 2) has been noted by others working with these species⁴.

Further studies are being conducted with extended temperature ranges to obtain additional information on the relative effects of temperature of the growth of these and other conifers. More detailed reports will be presented elsewhere as the individual studies are completed.

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PLANT PATHOLOGY

Some New Specific Bacteriophages for Plant Pathogenic *Xanthomonas* spp.

THE study of phages from the point of view of plant pathology has practical applications besides being of theoretical interest. By the use of specific phages the

detection of plant pathogenic bacteria was possible in infected seeds and tissues. Furthermore, using phages, slight biological differences were demonstrated between pathogens otherwise hardly distinguishable from each other. Therefore, the detection and isolation of new specific phages has considerable interest. The present communication will deal with the isolation of some new phages for *Xanthomonas* spp.

Xanthomonas carotae (Kendrick) Dowson was first described as a pathogen damaging the leaves and inflorescences of carrot in Europe³. Heavily infected leaves and inflorescences were ground and from the ground material a bacteriophage, specific for *X. carotae*, was isolated. On agar plates the phage for *X. carotae* forms plaques of 1–2 mm in diameter. Of the 30 *Xanthomonas* species tested only strains of *X. carotae* were lysed by the phage, which indicates a high specificity (Table 1).

Table 1. SPECIFICITY OF PHAGES FOR *X. carotae* AND *X. vesicatoria* FROM TOMATO AND PEPPER

| Organism tested | Phage for | | <i>X. carotae</i> |
|----------------------------------|-----------------------------------|-----------------------------------|-------------------|
| | <i>X. vesicatoria</i> from tomato | <i>X. vesicatoria</i> from pepper | |
| <i>X. vesicatoria</i> | | | |
| (1588) from pepper | — | + | — |
| (1590) " | — | + | — |
| (1608) " | — | + | — |
| (S01) from tomato | — | — | — |
| (S02) " | — | — | — |
| (S03) " | — | — | — |
| (S04) " | — | — | — |
| (S06) " | + | — | — |
| (S07) " | + | — | — |
| (S08) " | + | — | — |
| (S09) " | + | — | — |
| (S10) " | + | — | — |
| (424) " | + | — | — |
| <i>X. carotae</i> (No. 16) | — | — | + |
| (No. 60) | — | — | + |
| (No. 78) | — | — | + |
| <i>X. begonia</i> (A.B. 10)† | — | — | — |
| <i>X. campestris</i> (A.C. 107)† | — | — | — |
| <i>X. citri</i> (407)† | — | — | — |
| <i>P. gardneri</i> ‡ | — | — | — |
| <i>X. hyacinthi</i> (A.H. 104)† | — | — | — |
| <i>X. maltaceticum</i> | — | — | — |
| <i>X. pelargonii</i> (A.P. 130)† | — | — | — |
| <i>X. phaseoli</i> (L1388) | — | — | — |
| var. <i>fusca</i> (L1200) | — | — | — |
| <i>X. ricinicola</i> (113)† | — | — | — |
| <i>X. stewartii</i> (440)† | — | — | — |
| <i>X. translucens</i> (A.T. 19)† | — | — | — |
| <i>X. uredoformis</i> (O 040) | — | — | — |
| <i>X. vascularium</i> (181)† | — | — | — |

* The strains S2 and S03 also differ in their other biological properties from the other strains isolated from tomato.

Strains supplied by

† National Collection of Plant Pathogenic Bacteria, England

‡ M. P. Starr, Univ. of California, Davis

§ D. Sutic, Institut for Plant Protection, Beograd, Yugoslavia

Xanthomonas vesicatoria (Doidge) Dowson is a pathogen of tomato and pepper (*Capsicum annum*) widespread in Hungary². Hitherto the bacteria isolated from the diseased tomato and pepper plants have been regarded as a uniform species. Only a recent study by Sutic⁴ revealed the differences between the pathogens concerned. By the use of specific phages we also were successful in proving the differences between the two bacteria isolated from tomato and pepper.

The phage isolated from infected tomato fruits lysed exclusively the bacteria deriving from tomato, without affecting the pathogens of pepper. The clear plaques formed by this phage are 1.5–2 mm in diameter.

Similarly, strongly infected pepper leaves contained another phage which lysed only the pathogens deriving from pepper. The bacteria isolated from tomatoes were resistant to it. This phage formed plaques of varying diameter (1–3 mm).

The two phages were assayed for eventual infectivity against 19 *Xanthomonas* species. All of these proved to be resistant (Table 1).

The conclusion can be drawn that all the three phages exhibit a high degree of specificity. The last two make it possible to detect variants within the *X. vesicatoria* species.

It has thus been demonstrated that the species *X. vesicatoria* is not really uniform, that is, the pathogen isolated from the tomato plant is not identical with that occurring on pepper. The work carried out with the two specific phages justifies the conclusion of Burkholder and Li¹ and Suttie², based on slight biochemical differences, as to the different nature of pathogens damaging tomato and pepper.

Further studies on the biological properties and mutual relations of various pathogens belonging to *X. vesicatoria* group will be published elsewhere.

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ANIMAL PATHOLOGY

Urinary β -Glucuronidase Activity in Patients with Bone Fractures

DURING an investigation into the urinary β glucuronidase activity of patients with cancer of the bladder a substantial number of controls was investigated. These controls were grouped into normal adults and patients with pathological conditions other than cancer of the bladder. Among them was a group in hospital with fractures of bone.

24 hr specimens of urine were collected and the method of estimating the β glucuronidase activity was a slight modification of that used by Boyland, Gasson and Williams¹. The results were expressed as units of activity per ml of urine and from this was calculated the enzyme excretion per day. Results from the following groups of patients are summarized in Table 1.

- Group 1 Normal control subjects
Group 2 A 'miscellaneous' group of patients excluding those with genito urinary diseases
Group 3 Patients who within the past eight days had undergone minor surgery
Group 4 Patients who within the previous eight days had undergone major surgery in which some trauma and subsequent repair might be expected
Group 5 Patients who within the previous fourteen days had suffered bone fractures

In these five groups only those results were included in which the pH of the urine was within normal limits

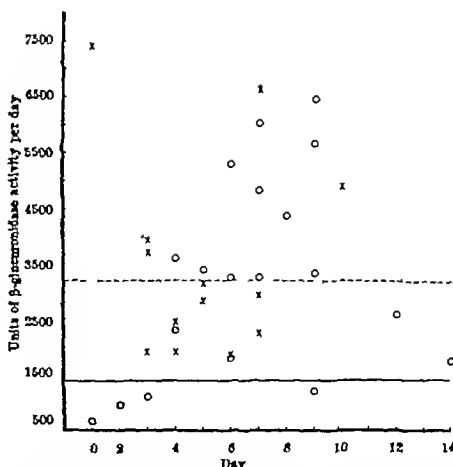


Fig. 1. Daily excretion of β -glucuronidase in patients after fractures or the leg or after major operations. The average value for normal subjects is ——— with twice the standard deviation ———. O patients with fractures, x patients after a major operation.

and the patient was not pyrexial during the urine collection.

The results indicated that the urinary β glucuronidase activity was significantly raised after major operations. This is in accord with the observation² that the urinary enzyme activity is increased immediately after operations. On the other hand, minor operations did not result in any such elevation. In the group of patients with fractures the urinary β glucuronidase activity was also significantly increased.

This fracture group included eighteen patients with fractured lower limbs and only four with fractured arms. It is interesting, though not statistically significant, that in these four, although serious enough to be kept in hospital, the enzyme activity was not increased to the level of those with fractured legs. Fig. 1 demonstrates that in lower limb fractures, the urinary β glucuronidase reached a peak 6-8 days after the accident and then fell.

The apparent relationship between the height of the β -glucuronidase activity and the degree of trauma and subsequent repair may be more than coincidental and is being investigated more fully. It is possible that this activity may be associated not only with hydrolysis of chondroitin³ but also with active formation of new bone.

Table 1. URINARY β -GLUCURONIDASE ACTIVITY

| Group | n | β -glucuronidase activity—units/ml. of urine | | | t test against normal subjects | β -glucuronidase activity—units/day | | | t test against normal subjects |
|--------------------------|----|--|------|--------------|--------------------------------|---|------|--------------|--------------------------------|
| | | mean | S.D. | S.E. of mean | | mean | S.D. | S.E. of mean | |
| 1 Normal Subjects | 24 | 1.05 | 0.55 | 0.098 | — | 1405 | 803 | 160 | — |
| 2 Miscellaneous diseases | 55 | 1.16 | 0.62 | 0.084 | 0.82 | 1719 | 1047 | 141 | 1.40 |
| 3 After minor surgery | 20 | 1.19 | 0.39 | 0.088 | 0.98 | 1523 | 589 | 127 | 0.52 |
| 4 After major surgery | 13 | 8.72 | 1.66 | 0.466 | 5.08 | 3534 | 1750 | 480 | 5.37 |
| 5 After bone fractures | 27 | 2.85 | 1.24 | 0.239 | 6.14 | 2990 | 1740 | 323 | 4.48 |

This work was supported by a British Empire Cancer Campaign Grant. We wish to thank Prof G Gordon Lennan, University Department of Obstetrics and Gynaecology, Southmead Hospital, for provision of laboratory space and we would particularly like to thank Dr G Herdan for help with the statistical analysis.

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Production of an Agglutinating Auto-Antibody (Panagglutinin) Active upon Tanned Erythrocytes in the Rabbit

P LEVINE *et al*¹ demonstrated the positive immune response of the rabbit to the injection of tanned *hetero-* or *iso-*erythrocytes coated with *P*-reactive material obtained from hydatiform cysts. This response is rapid and vigorous, contrasting with the slow or negative result when the same material was injected by other routes, even with the use of adjuvants.

We used this technique for the introduction of several soluble antigens into the rabbit, especially human gamma-globulin plasma fraction and thyroglobulin obtained from fresh human thyroids.² The results collected to date show that the intravenous injection in a rabbit, of iso-specific tanned erythrocytes coated with the desired antigen often leads quickly to a very spectacular immune responses. For example, the production of specific anti-human globulin by this method was found to be the most satisfactory of all the methods in our experience.

Blood was obtained from the ear vein of a group of three 'donors' (Nos 15-17). The erythrocytes were, washed three times in phosphate in phosphate-

Table 1 NEUTRALIZATION STUDY OF THE RABBIT SERUM T_γ III*

| Test cells | Original serum | | | | | Serum neutralized with human gamma-globulin | | | | |
|---|----------------|-----|-----|-----|-----|---|-----|-----|-----|----|
| | 2 | 4 | 8 | 16 | 32 | 2 | 4 | 8 | 16 | 32 |
| Rh positive human red cells | — | — | — | — | — | — | — | — | — | — |
| Normal cells | (3)† | (4) | (5) | (5) | (6) | — | — | — | — | — |
| Tanned auto-erythrocytes coated with human γ globulin | (2) | (2) | (4) | (4) | (4) | (2) | (3) | (2) | (1) | — |
| Tanned auto erythrocytes | (3) | (3) | (2) | (1) | — | (3) | (2) | (2) | + | — |

* One part of the serum was neutralized with one part of 0.4 per cent human gamma globulin

† (3) = + + +, (4) = + + + +, etc

buffered saline at pH 7.2, resuspended to a concentration of 4 per cent, mixed with one volume of a 1/20,000 tannic acid solution in buffered saline, shaken gently at room temperature for 10 minutes, washed once and re-suspended to a concentration of 2 per cent in physiological buffer to which 1 per cent of normal rabbit serum had been added. One volume of this suspension was mixed with one volume of a 0.4 per cent solution of human gamma globulin and allowed to stand for 30 minutes. The erythrocytes coated with human γ-globulin were then washed free from any excess of γ globulin and readjusted to a concentration of 2 per cent in physiological buffer containing 1 per cent normal rabbit serum.

A group of three rabbits were injected intravenously, twice weekly, with 2 ml of this suspension. After four injections (on the fourteenth day of immunization) the titre of the agglutinin was well above 1/2,000 against rabbit erythrocytes coated with γ-globulin and against human Rh-positive sensitized cells.

After twelve intravenous injections of the same material (that is, at the end of the sixth week), the sera of all three rabbits exhibited prozones and reached an anti-globulin agglutination titre above 1/16,000. In addition, the three rabbits had developed specific iso agglutinins against blood groups present in some of the 'donors' and absent on their own erythrocytes.

Finally, one of the rabbits (T_γ III) had developed an agglutinin active on all tanned red cells of the

Table 2 ABSORPTION STUDY OF THE RABBIT SERUM T_γ III d*

| Test cells | Unabsorbed | | | | | Absorbed with γ-globulin coated erythrocytes | | | | | Absorbed with pooled normal iso-erythrocytes (No 16 and No 17) | | | | | Absorbed with tanned auto-erythrocytes (T _γ III) | | | | | Antibody tested |
|---|------------|-----|-----|-----|-----|--|-----|-----|-----|----|--|-----|-----|-----|-----|---|-----|-----|-----|-----|--|
| | 2 | 4 | 8 | 16 | 32 | 2 | 4 | 8 | 16 | 32 | 2 | 4 | 8 | 16 | 32 | 2 | 4 | 8 | 16 | 32 | |
| Normal Rh positive human red cells | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | Anti human β-globulin |
| Sensitized† | (3)† | (4) | (5) | (5) | (5) | — | — | — | — | — | (3) | (4) | (4) | (4) | (4) | (3) | (4) | (4) | (4) | (4) | |
| Normal iso-erythrocytes (No 16) | (2) | + | ± | — | — | (2) | + | ± | — | — | ± | — | — | — | — | (3) | (2) | + | — | — | Iso-antibody |
| (No 17) | (4) | (2) | (2) | ± | — | (4) | (2) | (2) | + | ? | ± | — | — | — | — | (3) | (2) | (2) | ± | — | |
| (No 15) | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | |
| Normal auto-erythrocytes (T _γ III) | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | 'Auto-antibody against tanned erythrocytes |
| Tanned iso-erythrocytes (No 16) | (4) | (3) | + | + | — | (4) | (3) | + | ± | + | — | (4) | (4) | (2) | + | ± | — | — | — | — | |
| (No 17) | (5) | (4) | (4) | (2) | + | (4) | (4) | (4) | (2) | ± | (4) | (4) | (3) | + | ± | (2) | + | — | — | — | |
| (No 15) | (3) | (3) | (3) | + | — | (4) | (4) | (3) | + | — | (4) | (4) | (3) | + | — | ± | — | — | — | — | |
| Tanned auto-erythrocytes (T _γ III) | (3) | (3) | + | ± | ± | — | (3) | (3) | + | ± | + | — | (4) | (3) | + | ± | — | — | — | — | Anti human γ-globulin |
| Tanned auto-erythrocytes coated with human γ globulin | (4) | (4) | (4) | (4) | (4) | (3) | (2) | + | + | — | (4) | (4) | (4) | (4) | (4) | (4) | (4) | (4) | (4) | (4) | |

* Absorption was performed with 1 vol of packed cells for 3 vol of serum, at 37° C for 20 minutes

† Rh positive human red cells of genotype CDe/CDe were sensitized by 5 volumes of very potent anti C + D and washed six times in buffered saline

‡ (3) = + + +, (4) = + + + +, etc

rabbit, including auto-erythrocytes, up to a titre of 1/16—1/32. Neutralisation with human gamma globulin showed that the auto antibody was independent (Table 1).

Suitable absorption experiments (Table 2) with erythrocytes coated with human gamma globulin with heterospecific iso erythrocytes, and with tanned auto-erythrocytes eventually showed that three distinct and independent antibodies were present in this particular serum (T γ III) (1) a high titre anti human γ globulin, (2) an iso agglutinin active on a rabbit blood group antigen, (3) an auto agglutinin (pan agglutinin) active on tanned rabbit erythrocytes.

A curious phenomenon may be observed when the serum has been absorbed with tanned auto-erythrocytes (Table 2) tannic acid appears to destroy or inhibit the agglutination of iso erythrocytes No 16 and No 17 by the iso antibody, although it apparently had no effect on their antigenicity, as shown by the iso-immune response in rabbit T γ III into which they were injected.

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BIOLOGY

Endogenous Rhythms of Body Temperature in Hibernating Bats

ENDOGENOUS rhythms of motivity with periods close to 24 hr have been described previously in the two most common bats of the north eastern United States *Myotis lucifugus* and *Eptesicus fuscus*^{1, 2}. Rawson has shown that this periodic motivity persists for at least several weeks under conditions of constant darkness and temperature. Folk³ has suggested that the endogenous "clock" may control the timing of the periodic arousals of bats during their winter hibernation.

Recent experiments in this laboratory have demonstrated that the endogenous clock of both *Myotis lucifugus* and *Eptesicus fuscus* continues to function, with a period in the neighbourhood of 24 hr while the animals are in hibernation in constant darkness and at various constant ambient temperatures of 3°–10°C.

Bats were taken from an abandoned mine in Hibernia, New Jersey, in which they were hibernating and kept with drinking water but no food, in an ordinary refrigerator at about 8°C. Under these conditions, they returned quickly to hibernation. For the experiments the bats were removed from the refrigerator, their feet were held in a felt lined clamp, a rectal thermocouple was inserted, and they were placed in a moist chamber. The moist chamber was then placed in a precision temperature-controlled cabinet in constant darkness. A sensitive Brown recording potentiometer (full scale=80 μ V) was used to record the difference between the bat's rectal temperature and that of a reference junction in the air of the moist chamber. The temperature of the moist chamber was also monitored independently on another channel.

Figs 1 and 2 show the kinds of rhythmic fluctuations in body temperature obtained from bats in constant darkness and at constant ambient temperatures of 8° to 10°C. The bat the record of which is

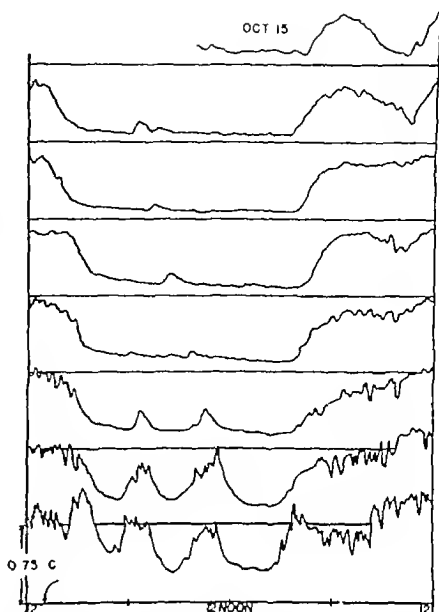


Fig. 1. Continuous record of the rectal temperature of a female *Myotis lucifugus* in constant darkness and at an ambient temperature of 10°C. The height of the temperature record above the base line is a measure of the difference in temperature between the bat and its environment. Successive days are plotted under each other.

shown in Fig. 1 was collected on October 7 and the experiment began on October 15. As is shown in Fig. 1, its body temperature never rises more than 1° above the ambient and there are several distinct features of the curve which recur with somewhat different periods. The bats, the records of which are shown in Fig. 2 were collected on January 28 and placed in the experimental apparatus on February 3 and 6. The extreme sensitivity of the recording potentiometer did not permit following the body temperature further than 1½ deg above ambient temperature. However, measurements made with a potentiometer of lower sensitivity on other bats indicate that when the body temperature rises quickly and smoothly as in Fig. 2A and on 5 of the days shown in Fig. 2B, a body temperature rise of at least 15°C and more often 20°–25°C is indicated. The differences in form and amplitude between the temperature record shown in Fig. 1 and those shown in Fig. 2A and B seem to be dependent on the length of time the animals have been in hibernation and not on the sex or species. Autumn animals (those collected soon after entering hibernation in the autumn) always show temperature records similar to Fig. 1, whereas winter bats, which have been in hibernation a month or more, show records similar to those in Fig. 2. It is possible to obtain records similar to those of autumn animals by arousing a bat in February, keeping it in a warm room feeding it for several weeks, and then measuring its body temperature after returning it to hibernation.

A consistent feature of the temperature records of winter bats (such as those in Fig. 2) is that on some days the temperature elevation is large on other days

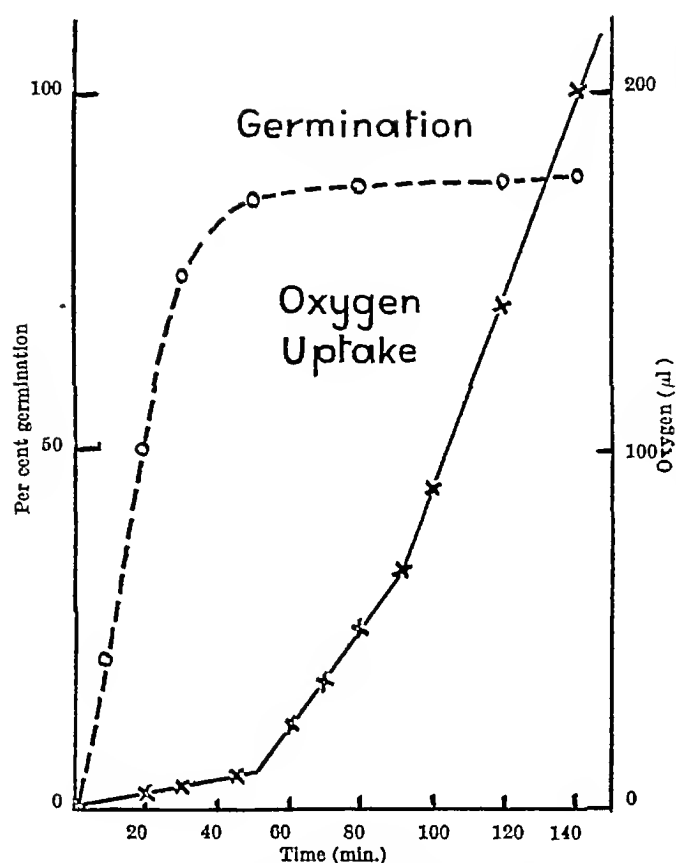


Fig. 2. Oxygen uptake during germination of heated spores of *B. coagulans* var. *thermoacidurans*. Warburg flasks contained 20 μ M glucose and spores (equivalent to 10 mgm. of dry weight) suspended in 2 ml of M/40 phosphate buffer (pH 7.0).

phosphate dehydrogenase are present in the spores.

Details of these results obtained will be published elsewhere. The work was supported by a grant from the Ministry of Education, for which we wish to express our gratitude. We also express our thanks to Dr. Z. John Ordal, University of Illinois, for his generosity in supplying the strain and some chemicals used in this study.

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Antibiotic Production as a Function of Spore Formation in *Bacillus licheniformis*

ELABORATION of antibiotics by postlog-phase cells of several different micro-organisms has been emphasized recently. Conditions required for optimum production of penicillin,¹ synnematin,² chlortetracycline,³ erythromycin,⁴ streptomycin,⁵ and neomycin⁶ all provide for a fast growth period followed by a period of fermentation involving slow growth or no growth at all.

During an investigation on the biosynthesis of bacitracin by *Bacillus licheniformis*, we observed that the antibiotic is produced only after growth on glucose is complete. A microscopic examination of the culture during the time of appearance of the antibiotic indicated active spore formation, and

prompted a more intensive investigation of this observation. Bacitracin is produced only under cultural conditions that support spore formation. Sporulation and antibiotic release can be inhibited by several different methods designed to prevent a rise in pH above 6.5, for example, glucose addition, buffer regulation, or intermittent titration. Bacitracin is not produced when sporulation is completely inhibited with ethyl malonate, whereas vegetative cell growth and pH are not affected. Production of this polypeptide seems to be related in some way to the spore-forming metabolism of *B. licheniformis*.

A spore suspension of *B. licheniformis*, A-5, was germinated by overnight incubation in a water-bath shaker in a modified medium of Hills *et al.*⁷ This medium contains per litre: glucose, 3.6 gm.; ammonium lactate, 5.35 gm.; citric acid, 312.0 mgm.; crystalline magnesium sulphate, 1.0 gm.; ferrous ammonium sulphate, 25.0 mgm.; crystalline magnesium sulphate, 6.0 mgm.; sodium chloride, 400.0 mgm.; potassium chloride, 400.0 mgm.; and orthophosphoric acid, 450.0 mgm. The pH of the salts mixture was adjusted to 7.4 with potassium hydroxide and sterilized independently from the carbohydrate. Growth of the cells and antibiotic production were observed in the same medium when an 8 per cent inoculum of the germinated spore culture was used. Conditions for fast growth and slow fermentation, considered optimum for the production of other antibiotics, are provided by this medium. Fig. 1 shows the time course of growth, pH change, bacitracin production, and spore formation. Initially, growth at the expense of glucose is rapid, with the concomitant formation of acid. The pH drops, but rises after the glucose has been exhausted, usually 7 hr. after inoculation. After this time, the cells begin to utilize lactic acid, and growth progresses at a much slower rate. Bacitracin production is first observed at 8 hr., and its release into the medium continues for about 20 hr. Sporulation begins in about 10 hr., with the first free spores appearing after 20 hr., and sporulation is essentially complete in 36 hr. The medium of Hills *et al.*⁷ contains much higher concentration of glucose and ammonium ions, and provides for erratic and incomplete sporulation, even after 7 days.

Strange and his coworkers⁸⁻¹⁰ and Greenberg and Halvorson¹¹ isolated and characterized several enzymes from sporulating cultures of *Bacillus* sp. The activity of these enzymes is directed toward cell walls and seems to be responsible for the release of polypeptides into the medium. It is interesting that the composition of bacitracin includes four D-amino acids and ϵ -aspartyl-lysine residue, found in the cell

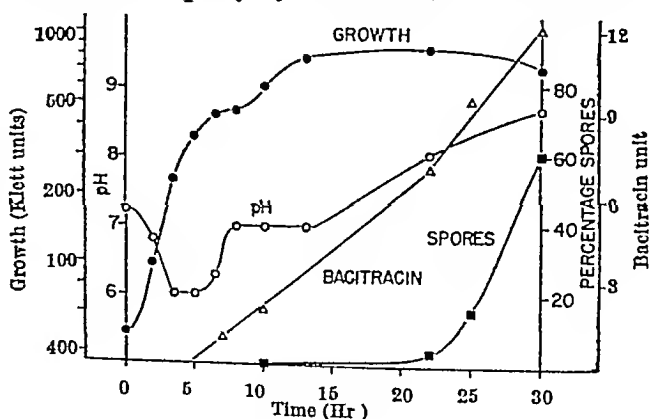


Fig. 1. Production of bacitracin and spores by *B. licheniformis*.

walls of several lactobacilli, *Actinomyces bovis*, and probably in *Bacillus sphaericus*¹²

The possibility exists, therefore, that this polypeptide antibiotic is part of the cell wall of *B. licheniformis* and is released by the activity of a lytic enzyme produced by the cell as part of its spore forming metabolism

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CYTOLOGY AND GENETICS

Glass Micro-Electrodes for Measuring Intracellular Activities of Sodium and Potassium

RECENTLY, Eisenman, Rudin and Casby¹ reported on the preparation of cation-sensitive glasses and indicated their potential usefulness as electrodes for biological studies. Friedman *et al.*² adapted such electrodes for measuring continuously the plasma sodium of a rabbit and dog. Caldwell³ demonstrated that pH glass electrodes can be constructed on a microscale for measuring intracellular pH. The present report concerns construction of micro-electrodes for intracellular measurement of sodium and potassium activities

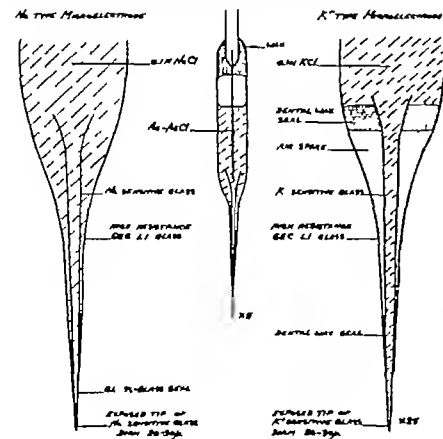


Fig. 1

Cation sensitive glasses were supplied by Friedman and behaved similarly to Eisenman's *NAS₁₁₋₁₁* (sodium selective) and *NAS₁₁₋₁₁* (potassium selective) glass. Fig. 1 illustrates the design of the micro-electrodes. Note that a glass to glass seal was made between the *L-I* and *NAS₁₁₋₁₁* glass. This simplified its construction and produced a very durable and stable electrode. Since *NAS₁₁₋₁₁* did not fuse to *L-I*, the glasses were sealed with dental wax as shown. The trapped air prevented shorting between the inside and outside solutions when the lower wax seal broke down. No insulation other than the lead glass jacket was required. The exposed tip of cation sensitive glass was $20\mu \times 150\mu$ with a $1-4\mu$ wall thickness. Conventional micro-electrodes filled with 2*N* ammonium chloride were used as reference electrodes. Potential recordings were made with a 'Vibron' electrometer model 33B (Electronic Instruments Limited, Richmond, Surrey, England) since the glass electrode resistance ranged between 10^{10} and 10^{11} ohms.

Over the biological electrolyte range the sodium electrode behaved according to the empirical equation⁴

$$E = E^0 + \frac{RT}{F} \ln (a_{Na} + k_{NaK} a_K)$$

where E , measured o.m.f., E^0 , standard potential, R , ideal gas equation constant, T , temperature (absolute), F , Faraday constant, a_{Na} and a_K , activity of sodium and potassium ions; k_{NaK} , empirical constant for a given glass composition.

Since $k_{NaK} = 0.005$ the equation could be simplified to

$$E = E^0 + \frac{RT}{F} \ln a_{Na}$$

with no appreciable error as long as pH was not less than 6.5 and a_K not greater than 0.15. The potassium electrode varied but could be calibrated daily to fit a curve:

$$E = E^0 + s \ln (a_K + k_{KNa} a_{Na})$$

where s = slope or mV per unit log change. E^0 was 3-6 mV less than the expected 58 mV at 20°, E^0 also varied by $\pm 3-5$ mV but k_{KNa} (0.1) remained relatively stable.

Muscle cells from the propodite of crab and lobster (*Callinectes sapidus* and *Homarus vulgaris*) were chosen because of their size (200-500 μ diameter). The preparation consisted of a row of intact fibres mounted vertically in a bath containing (mM/l) sodium, 51; potassium, 12.0; calcium, 11.8; magnesium, 23.6; bicarbonate, 2.6; chloride, 50.4. The glass electrodes were manipulated so as to pierce the membrane at an acute angle and guided along the fibre axis until the sensitive tip was about 100 μ from the puncture site. The membrane potential was measured between an internal and external ammonium chloride filled capillary micro-electrode. The internal capillary was used as reference electrode in measuring the cation activity. For a chemical check, carapodite muscles kept under similar experimental conditions were analysed for total sodium and potassium content by flame photometry. Shaw's method of dissection was followed. The intact muscle was then allowed to equilibrate for 1 hr. in the artificial bathing solution before it was rinsed for 1 min. in iso-osmotic dextrose.

Table 1 summarizes the activities calculated from six preparations (3 of the crab and 3 of the lobster with the potassium electrodes used the last).

Table 1 INTRACELLULAR ACTIVITIES OF SODIUM AND POTASSIUM OF MUSCLE CELLS


| No of Cells | Range of Membrane potential | Activity $\pm S.E$ |
|-------------|---|--|
| 20 | 30-55 mV (<i>Carcinus maenas</i>) | $a_{Na} = 0.0135 \pm 0.0008$ |
| 10 | 30-40 mV (<i>Homarus vulgaris</i>) | $a_{Na} = 0.016 \pm 0.001$ |
| 10 | 31-39 mV | $a_{Na} = 0.012 \pm 0.0004$ |
| 12 | 31-52 mV | $a_{K} = 0.034 \pm 0.0015$ $a_{Na} = 0.015$ |

Table 2. TOTAL CONCENTRATIONS OF SODIUM AND POTASSIUM OF MUSCLE UNDER SIMILAR CONDITIONS AS IN TABLE 1

| No of muscles | [Na ⁺] $\pm S.E$ moles/kgm H ₂ O (<i>Carcinus maenas</i>) | [K ⁺] $\pm S.E$ moles/kgm H ₂ O (<i>Homarus vulgaris</i>) |
|---------------|--|--|
| 12 | 0.0516 ± 0.0033 | 0.160 ± 0.0025 |
| 6 | 0.055 ± 0.0043 | 0.153 ± 0.0026 |

Values were accepted from cells if the membrane potential was higher than 30 mV. The standard errors are given to indicate the small variation from cell to cell despite the wide range of membrane potentials. The sodium activity is virtually the same in crab and lobster muscle. Comparison with the concentrations per litre of tissue water (Table 2) shows that concentration of sodium is at least three times greater than the measured activity of sodium, and concentration of potassium is twice as great as activity of potassium.

The experiments are of a preliminary kind and will have to be repeated under different experimental conditions and on other material. Nevertheless, they show the practicability of using these glass electrodes on a micro scale and of measuring activities of sodium and potassium in the interior of the cell.

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Production of a Perfect Stage in a Nutritionally Deficient Mutant of Pathogenic *Fusarium oxysporum* after Ultra-violet Irradiation

THE genus *Fusarium* has 16 sections, many of which have a sexual stage, belonging to such Ascomycete genera as *Nectria*, *Calonectria*, *Hypomyces* and *Gibberella*. *Fusarium oxysporum*, the form species of the section *Elegans*, is a widely distributed soil-borne fungus that causes wilt in many economically important crops. It has no known perfect analogue, although it can achieve genetic variation through sexual methods of recombination.^{1,2}

During experimental production by ultra-violet irradiation of nutritionally deficient mutants in the a wilt fungus, *Fusarium oxysporum* f. *pisi*, many different wild-type isolates of its physiological races have been genetically marked in this laboratory. Any such mutants retain their wild-type morphology, but others are considerably altered, usually producing more spores per amount of mycelium and, as frequently, spores of different shape from the wild-type.

One of many isolates that have been repeatedly used for artificial inoculation tests was irradiated in October 1954 and found to be deficient in its methionine and arginine synthesis. In June 1955, further

irradiation of this mutant resulted in additional deficiencies in cystine and vitamin B₁ synthesis. It can grow only slowly on non-supplemented agar media.

This isolate, together with many other mutant strains, was used extensively in genetical work, which entailed repeated subculturing from single spores, both on a 'minimal' and 'complete' agar medium.² It retained its capacity to wilt peas throughout several experiments and readily formed heterokaryons with other marked strains of *F. oxysporum* f. *pisi*. It would not, however, form stable heterokaryons with isolates of *Fusarium solani* f. *pisi*, a soil-borne fungus that causes foot-rot in peas. Since March 1956, all the mutant strains have been retained by subculturing every 3 months on 'complete' medium.

In late 1956 the mutant strain produced a few bright red very small perithecia, which remained immature and blind, with no discernible ascus. In the summer of 1957 the perithecia were again examined but still showed no sign of ascus development. After repeated examinations of the cultures, mature perithecia were finally seen in February 1959, when ascospores were observed in the abundant extruded ascus.

After tentatively identifying the isolate as a *Hypomyces* sp., it was sent to the Commonwealth Mycological Institute, Kew, where Mr C Booth kindly identified it as *Nectria* (*Hypomyces*) *haematococca* Berk and Br. This fungus, well known in the tropics, where it can damage citrus, cocoa and other crops, has not previously been recorded in this country. The perithecial wall is coarsely cellular and the ascus are extruded from a short ostiolar neck. Each ascus contains eight two-celled hyaline ascospores which have longitudinal striae. A fuller account of the taxonomic features will be published elsewhere.

Both micro-manipulated single ascospores and single *Fusarium* stage conidia readily produce cultures with perithecia and *Fusarium* conidia. The *Fusarium*, which is morphologically indistinguishable from *Fusarium oxysporum* f. *pisi* and from the parent un-irradiated colonies, causes typical wilt of pea, with symptoms indistinguishable from those caused by all previous parent colonies during the past 5 years. Perithecia occur on the fungus that has been re-isolated from the reddened vascular tracts of the wilted plants. There can, therefore, be little doubt that this homothallic *Nectria* is the perfect stage of this particular wilt-inducing *Fusarium* isolate. Because of its peculiar mode of origin, it cannot yet be considered the perfect analogue of other members of the *Fusarium* section *Elegans*. Whether it arose as a direct result of ultra-violet irradiation or came indirectly from the altered nutritional needs of the mutant is an open question, but it may be that the genotypic mechanism governing perithecial formation in this particular isolate was unmasked by irradiation damage to nuclear material that previously suppressed the formation of perithecia. Further work on the ability of this particular isolate to hybridize with wild-type isolates of pathogenic *F. oxysporum* should show whether it represents a more general perfect analogue of the wilt-causing *Fusaria*.

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ORGANIZATION OF SCIENTIFIC AND TECHNOLOGICAL RESEARCH IN BRITAIN

IN the election manifesto of the Conservative Party released on September 11 it was stated that, as the first of five measures to promote technological advance in Britain and to translate this into productive capacity with a high and rising rate of investment, one Cabinet Minister would be given the task of promoting scientific and technological development. "While it would be wrong to concentrate all Government scientific work into a single Ministry this Minister for Science will have responsibility for the Department of Scientific and Industrial Research, the Medical and Agricultural Research Councils, the Nature Conservancy, the atomic energy programme, and the United Kingdom contribution to space research." The manifesto added that the development of nuclear energy for peaceful purposes would be pressed ahead, a conference called for those concerned in industry and education to forward the spread and understanding of automation, while besides encouraging new inventions and the development of new techniques, further changes would be made from time to time in the functions of Ministers as might be necessary to meet modern needs.

Thus emphasis on the importance of science in the national welfare and the need to adapt administration to ensure that due account is taken of scientific and technological advance, was followed on September 17 by a special statement from the Labour Party entitled "A New Deal for Science". This statement proposed the appointment as "Minister of Science" of a senior Minister with general responsibility for scientific affairs and the authority to perfect and carry out by and through the various Ministries concerned a carefully planned programme to use modern science to the full. This programme would include a further expansion of scientific and technological education, more scientific training in the schools, and consequently more science teachers; a substantial increase in the number of research and development contracts and Government grants to individual firms for approved long term research projects, and the establishment under the Minister of a scientific and technical planning board to advise on the direction of industrial research and development, on the awards of research contracts and on the grants to individual firms.

Both major political parties of Britain have thus committed themselves to some modification of the organization of research and development in the country, and of the means by which scientific and technical advice is presented at the highest level. Neither statement gave sufficient information to allow a sound judgment as to which is the more promising proposal, but now that Mr Macmillan has been returned to power he has lost no time in making the promised appointment. The Cabinet changes announced on October 14 included the appointment of Lord Hailsham as Lord Privy Seal with the general

duty of promoting scientific and technological advance in consultation with the departmental Ministers. No Ministry of Science is to be created. Indeed, it is pertinent to observe that Lord Hailsham gave last April a reasoned argument against the practicability of any such appointment, and it is clear that Ministers will retain executive responsibility for scientific matters within their own departments and that no attempt will be made to limit the freedom and initiative of universities or industry in determining the content of scientific education or the direction of research.

Lord Hailsham, who relinquishes the chairmanship of the Conservative Party, takes with him from the Lord Presidency of the Council ministerial responsibility for the work of the Department of Scientific and Industrial Research, the Medical Research Council, the Agricultural Research Council and the Nature Conservancy: this constitutes a definite break with the structure built up in the past forty years and more. He will also assume responsibility for the work of the Atomic Energy Authority, the Atomic Energy Office, the Overseas Research Council and supervision of the British contribution to space research. At a Press conference on October 14, Lord Hailsham indicated that his task would be to do some fundamental thinking on the relations between Government and science, and he stressed his anxiety to do nothing to interfere with the independence of the Government financed scientific bodies. Essentially he confirmed the views he expressed last April to the Institution of Chemical Engineers, and indicated that the appointment was only likely to show results after a long period and that its terms were not such as could easily be put down on paper.

It is thus unlikely that Lord Hailsham's appointment contributes anything material at the moment to the formal organization of the scientific effort of Great Britain either in research and development or in other fields. Lord Hailsham's addressee to the Institution of Chemical Engineers and the Institute of Physics last year showed how well aware he is of the dependence of our scientific and technical effort not merely on the resources allocated for such work, but also on education and the interlocking of problems of application with those of defence as well as of industry. Equally he recognizes that if educational and scientific institutions are to function efficiently, they must retain complete integrity, and accordingly a high degree of independence. His conception of a scientific policy—and presumably in this he includes technological policy—is of a partnership in which Government, teaching institutions, research institutions and industry all play important and inter-related parts. It could well be that Lord Hailsham was selected for his new office because he has publicly stressed the need for a more intelligent understanding of the forces at work and has indicated that he was

already thinking deeply about the relations between Government and science

There can be little doubt that Lord Hailsham intends to consider whether the new arrangements are adequate, and whether they can be improved, but there seems little reason to fear that new administrative arrangements will be created without due forethought and consultation, or new policies concerted and applied unimaginatively or without due regard to the essential conditions for scientific work. It may be expected that Lord Hailsham's inquiries and thinking will lead to the elimination of some of the duplication of effort that can be found, though it is improbable that he will fail to recognize that there are occasions when such duplication is an advantage and an asset rather than waste. What is important is that Lord Hailsham appears to be bringing to his task the breadth of vision, the imagination and something of the understanding of the mind of the scientist that are essential for success.

What is more important, perhaps, is that Lord Hailsham himself recognizes that the task of Minister of Science or for Science is inherently impossible for any one man to discharge, and he is likely to look rather for the administrative arrangements which may best permit the Government as a whole to take full account of the scientific and technical factors involved in its decisions on policy, and to ensure an adequate and balanced apportionment of our resources in man-power, in finance and in materials for scientific and technical work generally. If also he examines the question whether, as has been alleged, the authority of scientists in the key Departments of State is really being dangerously eroded, he will have done as much as can fairly be expected of any one man.

The statement, "The First Minister for Science", which Lord Hailsham has since issued (see p. 1263) of this issue of *Nature* confirms all this. He emphasizes the need for other Ministers in the Government to be scientifically minded if his work is not to be incomplete, and he stresses again that his appointment should impel scientists themselves to take a share in thought about scientific policy. Such a policy, he reiterates, cannot be the product of Government thinking alone.

Several specific points in this statement should also be noted. Lord Hailsham believes that Government science, and perhaps all British science, is at present too parochially minded, too departmentalized and lacking in broad vision. He believes also that the Advisory Council on Scientific Policy holds the key to the situation, and announces his intention of relying more upon this Advisory Council for general advice on questions of scientific policy. With this welcome indication that the Advisory Council's authority is to be restored comes the admission at last that the office of the Lord President of the Council has been under-staffed, and the warm welcome which scientists generally will extend to the whole tenure of Lord Hailsham's statement will be accompanied by greater confidence in that he is now likely to enjoy the services of a larger and more flexible office staff. Lord

Hailsham's efforts to tackle such questions as the general balance of scientific effort, to forge closer ties between Government research stations and institutes and the universities, and to foster alike applied research and increased benefactions for universities and colleges, will carry the greater conviction in this context, and it should also assist to enlist the support of scientists and technologists generally, for which he pleads.

Above all, it is important that Lord Hailsham's appointment should be regarded as a challenge to scientists and technologists generally to think deeply about the issues displayed in this statement, many of which were set forth earlier by Lord Hailsham and Sir Hugh Beaver in their addresses to the Institution of Chemical Engineers. It should not be forgotten that, however admirably an administrative structure may be devised and established, its effectiveness will always largely depend on the men who use it. Apart, too, from the perennial temptation to look for rapid political returns rather than the long-term gains which a sound scientific policy would offer, the penetration of science into the more backward industries and into some Departments of State is a matter both of education and of personal influence. Personalities again may play a vital part, especially when it is a matter of securing co-operation.

It is accordingly worth while to look carefully at the way previous arrangements have functioned before deciding on further changes. Valuable clues may well be found as to the essential conditions, and even in the context of the new responsibilities which Mr. Macmillan has entrusted to the office of Lord Privy Seal, Lord Hailsham will not find it easy to give better services to science than have been rendered by some of his predecessors as Lord President of the Council, notably Lord Balfour and Lord Waverley. The late Sir Walter Morley Fletcher has written of Lord Balfour's deep interest in the work of the Medical Research Council, the chairmanship of which he retained when he became Lord President in spite of the anomaly. Lord Balfour was no less interested, however, in the work of the Department of Scientific and Industrial Research, and sought strenuously to increase effective contact between scientists themselves and also between them and the administrative departments, promoting for this purpose the establishment of the Committee of Civil Research, the counterpart of the Committee of Imperial Defence.

Besides the testimony of members of these Councils and Committees to the encouragement and inspiration derived from the experience of encountering a statesman who possessed both the power to help research and the imagination to understand its value to the State, there is on record the further services to science which Lord Balfour rendered at the Imperial Conference of 1926. Balfour said at the time that he regarded the work of the Research Sub-Committee of the latter Conference, over which he presided, as only second in importance to that of the Committee on Inter-Imperial Relations, and in its proposals for co-ordinating research he sought to

forge new cultural links between all parts of the Commonwealth, through the departments and individuals engaged in scientific work in every field. The recently formed Overseas Research Council owes something to the foundations thus laid, and it might well be worth re-examining the circumstances which have held back for a generation such a promising start.

If there is thus on record how much can be achieved by a Minister with vision and imaginative understanding of the needs of the scientist, there is also testimony to the value of a Cabinet Minister himself trained as a scientist. Such tribute has been paid in regard to both Sir Stafford Cripps and Lord Waverley, notably in regard to the latter by Earl Attlee and also by Lord Winster, who during the Second World War had been given responsibility as a Cabinet Minister for the promotion of science and was for a time a member of the Cabinet's scientific advisory committee (out of which the Advisory Council for Scientific Policy later developed) when Lord Waverley was Lord President of the Council. Lord Hailsham himself has stressed the authority which Lord Waverley could derive in scientific matters from being able to speak as a science graduate. Lord Bridges has testified to the outstanding quality of Lord Waverley's work as Lord President of the Council, not only to his capacity for understanding and sound judgment, but also to the way in which he worked so far as possible through departmental staffs without building up any large organization of his own, and also to the importance of the complete confidence which existed between the Lord President and the Prime Minister.

Lord Bridges, in his Royal Society memoir, referred particularly to Lord Waverley's services to science both while he was Lord President during 1940-43 and afterwards, particularly in what might be called the scientific administration of the development of nuclear energy. It is too early yet to expect the critical biography of Lord Waverley which might illuminate these arrangements more fully, but it is important that they should be examined as fully as possible in the light they could throw on the kind of arrangements which are desirable to day. They suggest, for example, that any constructive thinking should include a careful appraisal of the functioning of both the Advisory Council for Scientific Policy and the Research Defence Policy Committee.

Even this cursory review indicates the critical importance of personal factors, and there is a further reason for looking closely into this aspect. The late Sir Henry Tizard, who has claims to be considered as a military scientific genius, was very successful in his joint chairmanship of the Advisory Council for Scientific Policy and the Research Defence Policy Committee during 1946-52. Nevertheless, in spite of the conspicuous services he had rendered even before the Second World War in developing defence research policy and later in encouraging the development of operational research, in 1942 he suddenly resigned from most of his official appointments to become president of Magdalen College, Oxford. Sir Henry was one of the easiest of colleagues, so any admini-

strative structure which led to such a decision is *ipso facto* suspect. Incidentally, in their Romanes and Haldane Memorial Lectures respectively, both Lord Waverley and Sir Henry Tizard have recorded considered opinions and constructive proposals for providing the Government with more authoritative guidance in technical matters.

It may be hoped that Lord Birkenhead's official biography of Lord Cherwell will in due course throw some light on these matters. Sir George Thomson in his Royal Society memoir refers briefly to the existence of conflicts of opinion between Cherwell and Tizard which were well known in the scientific world, but no light is thrown on this by Sir Roy Harrod's more recent personal memoir, "The Prof". He does, however, indicate another aspect of some interest in considering the functions of a Minister of Science. It is the personal relations between Lord Cherwell and Sir Winston Churchill, first as First Lord of the Admiralty and later as Prime Minister rather than Lord Cherwell's own subsequent position in the Cabinet as Paymaster General that are of primary interest. Lord Cherwell was able to render his great contribution to the national war effort because of the extent to which he possessed Mr Churchill's confidence and understanding.

What Sir Roy Harrod writes of this relationship will bear pondering. Where such confidence and understanding can be established, from whatever beginning, the outcome may well be as effective for the promotion of science and technology as when the Cabinet Minister concerned has himself been trained in science. It might possibly be a waste of scarce and highly trained manpower, even if it were possible, to provide every Cabinet Minister carrying departmental responsibilities involving highly technical and scientific matters or research with a scientific adviser of Cherwell's quality for his personal assistant. The results in any event would depend alike on the quality of that adviser's mind and on the personality of the Minister, as well as on the intimacy of the relations between him and his adviser, but it should be clear enough that it is not sufficient for scientific and technical advice to be presented at one point alone. The effective formulation of policy where science and technology are concerned will come when such factors are accurately assessed, not by one Minister only, but all the Ministers concerned.

There could well be found here the reason why the single handed efforts of Lord Balfour a generation ago and the advocacy of such men as Lord Samuel have hitherto failed of full fruition. For that reason alone the functioning of the advisory committee compared with that of the personal assistant or adviser requires further examination. Moreover, in Sir Roy Harrod's memoir of Lord Cherwell the emphasis is on the contribution which Lord Cherwell and his statistical section made to quantitative thinking about the conduct of the War, and Sir George Thomson's memoir appears to confirm that this was the most important characteristic of Lord Cherwell's contribution. This again suggests that there is something to be learned from the functioning

of this section and the work of the Central Statistical Office established in 1941

There can be no doubt as to the immensity of the task which Lord Hailsham has undertaken, and the diversity of problems he will need to consider. Now that he has divested himself of his party political responsibilities as chairman of the Conservative party, he appears to be as good a choice as could have been made. His experience as Lord President of the Council has already given him a close insight into some of the problems involved and his speeches have shown both that he is thinking deeply about the real issues and that he is averse to hasty and unilateral decisions.

If it should be reiterated that Lord Hailsham's appointment represents no essentially new departure, similar positions having been occupied by Lord Balfour more than thirty years ago and by Lord Winster and possibly Lord Waverley in the Second World War, the scale and range of problems now confronting him cannot be compared with those presented to any predecessor in peace-time. He will doubtless examine the functioning of the Advisory Council for Scientific Policy and its interrelations with the Defence Research Policy Committee, as well as the specific problems and relations of the several research councils and organizations for which he is specifically responsible. There is the question of departmental research as against centralized research, for example, under the Council for Scientific and Industrial Research. There is a whole range of problems presented by the industrial research associations and the stimulation of research and its exploitation in industry. There is the matter of the balance of our research effort generally and the place of the universities and the independent research institutions and the resources at their disposal and the way in which Government policy can best strengthen such resources without infringing academic or professional autonomy. There are problems which will lead Lord Hailsham into the educational field, as when he considers our resources in scientific and technical man-power and their expansion, as well as their most effective deployment.

Nor are all these problems sharply separated. The support, for example, which the Department of Industrial and Scientific Research already gives to the universities, both by way of grants to individuals for postgraduate study and to university departments in support of specific research projects, already takes it within the orbit of the University Grants Committee, and this holds in varying degrees for the other research councils also. It is arguable that nowhere below the level of the Prime Minister himself can all the responsibilities involved rest in one man, if indeed the task is not too immense for any person to discharge it alone. There, of course, we touch the question of Cabinet responsibility, but without entering on any such discussion it might be observed that the Cherwell-Churchill relation seems at least to support the view that a Minister who carried general responsibility for scientific (and presumably also technological) matters might be able to

give the Cabinet sufficient detailed advice to clarify and facilitate decisions either in the Cabinet or by the Prime Minister himself. Lord Hailsham is obviously approaching these questions without preconceived ideas as to whether changes are required in our present arrangements, and if so, what changes for the better are possible, and he has at his disposal much valuable evidence not merely from Lord Waverley, Lord Bridges and Sir Henry Tizard, but also from others like Lord Hankey, Lord Ismay and Sir Henry Dale. Whatever the administrative structure may be, there is one essential condition if it is to function smoothly: effective measures must be taken to eliminate or bridge the gap between what Sir Charles Snow has described so vividly as the two cultures. The effective use of science and technology for the public welfare and in the affairs of State will not be ensured by establishing a Ministry of Science or appointing a special Minister. It will be secured in the measure, and only in that measure, in which Ministers and administrators, the Departments of State, the public corporations, industry and the public generally are aware of the conditions and nature of scientific work, understand in some degree what science is doing and are prepared to provide the necessary support.

THE PRINCIPLES AND PRACTICE OF CROP PROTECTION

The Scientific Principles of Crop Protection

By Hubert Martin. Fourth edition. Pp viii+359 (London: Edward Arnold (Publishers), Ltd., 1959) 65s net.

Advances in Pest Control Research

Vol. 2. Edited by R. L. Metcalfe. Pp vii+426 (New York: Interscience Publishers, Inc., London: Interscience Publishers, Ltd., 1958) 94s.

Recognition of Diseases and Pests of Farm Crops

By Ernst Gram, Prosper Bovien and Chr. Stapel (Danish Agricultural Information and Advisory Aids Service). Pp 128+112 colour plates (Cambridge: W. Heffer and Sons, Ltd., 1958) 35s net.

The Control of Pests and Diseases in Agricultural and Horticultural Crops

By G. L. Hey and K. Marshall (Agricultural and Horticultural Students Series). Pp 172 (London: Vinton and Co., Ltd., 1958) 12s 6d net.

TO say that, nuclear wars apart, the greatest problem of the future will be to feed the rapidly increasing human population is none the less true for being trite. Happily there is no need to think it is insoluble. Average crop yields are so low that the scope for improvement is enormous, and starvation can be avoided for a long time simply by improving the health of crops. Over much of the world most crops are left to fend for themselves, unaided in their struggle with pests and diseases. What annual toll these predators take cannot be estimated at all accurately, but there is little doubt that human beings will have at least twice as much to eat when they stop sharing their crops with pests and diseases.

The four books listed above differ greatly in content and immediate purpose, but all have the same ultimate aim of increasing yields by protecting plants against

their pests and diseases. They make it clear that many of the losses now suffered are legitimately described as avoidable in the sense that they could be avoided by applying existing knowledge more widely, but it is also clear that much new knowledge will be needed before all losses come into this category. Between them the books also show how complex and varied are the problems entailed in improving the health of crops. First, there are the research problems, diagnosis of the cause, the histological study of the pest or pathogen to find where it comes from, how it spreads and whether there is a stage in its life history at which it is especially open to attack, and this to be followed by tests of pesticides, of variations in cultural practices or of seemingly resistant varieties. Secondly, when research has produced a control method, there still remains what is often the more difficult task of getting it established in practice, and even with this achieved the position must be closely watched to ensure that the method remains effective and has no undesirable side effects.

"The Scientific Principles of Crop Protection" is one of the few books that attempt to cover the whole subject, and a new edition was long over-due, for most of the insecticides currently used have been discovered since the third edition was published in 1940. The title has been changed to the extent that 'plant protection' has become 'crop protection', but the presentation and approach are as before. The new edition might have been even more welcome had the changes been greater, for it is now more difficult than twenty years ago to contain the subject in a single volume and some parts get scant attention considering their recent growth. Whether the parts briefly mentioned should have been omitted in favour of more detail on those in which the author is most authoritative, however, is a moot point, for in these days of increasingly narrow specialization it is certainly refreshing to find someone willing to look at the subject broadly, even though the looks in some directions may be only glances.

Review journals are necessarily complementary to standard texts. They are better able to keep up with advances in the subject and they provide opportunities for specialists to present detail inappropriate in a general book. The eight articles in volume 2 of "Advances in Pest Control Research" cover a wide range of subjects and some authors have undoubtedly made full use of the opportunity to be detailed. Here the contents can only be indicated by summarizing the titles and naming the authors: fluid kinetics of sprays (R. P. Fraser, 108 pp), toxicity of fungicides (S. E. A. McCollan and L. P. Miller, 28 pp), seed and soil treatments with insecticides (H. T. Reynolds, 48 pp), the use of isotopes to measure spray residues (C. T. Redeman and R. W. Meikle, 24 pp), wool digestion and moth proofing (D. F. Wetherhouse, 56 pp), the relation of chemical structure to herbicidal activity (R. L. Wain, 44 pp), chemical structure and activity of DDT analogues (R. Riemschneider, 44 pp), the spread of resistance to insecticides in pests (A. W. A. Brown, 64 pp). It is to the credit of the authors that most have accepted the editor's invitation to evaluate their subjects critically and have not simply summarized published work.

The other two books are for the grower of crops rather than the research worker. "Recognition of Diseases and Pests of Farm Crops" is a most welcome and most unusual book. The text consists simply of captions to the 112 magnificent colour plates containing more than 700 beautiful water colour paintings

by I. Frederiksen and E. Olsen. The sole purpose is to aid diagnosis, which the book will do permanently and everywhere, and methods for controlling the pests and diseases so accurately portrayed are deliberately omitted because they often change and may differ in different countries. The book by G. L. Hey and K. Marshall complements the work of art from Denmark and contrasts strikingly with it. It is most valuable for its succinct recommendations for controlling specific pests and diseases, is least satisfactory for diagnosis, and its pictures are neither beautiful nor very helpful. With both books, the farmer or gardener is well equipped to avoid much loss, and it is no mean testimonial to the achievements of plant pathologists that growers now have reliable methods to control so many pests and diseases.

F. C. BAWDEN

FREE RADICALS

Free Radicals as Studied by Electron Spin Resonance By Dr D. J. E. Ingram. Pp ix+274. (London: Butterworths Scientific Publications, New York: Academic Press, Inc., 1958.) 50s. 0.50 dollars.

Free Radicals

An Introduction By A. F. Trotman-Dickenson (Methuen's Monographs on Chemical Subjects). Pp viii+142. (London: Methuen and Co. Ltd., New York: John Wiley and Sons, Inc., 1959.) 12s. 6d. net.

MOST free atoms are associated with one or more unpaired electrons, and the formation of compounds generally involves the complete pairing of such electrons in molecular orbitals. Nevertheless many molecules, of widely varying degrees of structural complexity, have a single unpaired electron. These bodies, known as monoradicals, comprise the most important group of free radicals and it is with them that the greater part of both of these books is concerned.

The unpaired electron confers two important properties on the monoradical. In the first place the electron spin is associated with a magnetic moment, which may align itself in one of two ways with respect to an applied magnetic field. Transitions between the energy levels corresponding with these two alignments can be made to fall conveniently in the microwave region, giving the phenomenon known as electron spin resonance. The transition will be associated with hyperfine structure resulting from the interaction of the electron spin with the various nuclear spins if any in the radical. This hyperfine structure may then be used to 'locate' the electron within the molecule, and hence to obtain information about the orbital, and about the structure of the molecule. In the second place, the presence of an unpaired spin within a molecule makes it more reactive, and free radicals often play important parts in chemical reactions, since their reactions can provide convenient paths by which the final products may be produced most easily. Dr Ingram's book is concerned with the first of these aspects of free radical behaviour and Dr Trotman-Dickenson's with the second, in particular with the elementary reactions of free radicals, while avoiding chain reactions and oxidation processes.

The overlap between the books is very small, and it is a pity that they have effectively the same title differing only in subtitle. In both cases the contents are excellent, and may be recommended to all workers in the field of free radicals.

Dr Ingram's work falls into two main sections, the first being concerned with the techniques of electron resonance, and with those parts of the theoretical background necessary for the interpretation of the spectra of free radicals. The 'experimental' part will be a most valuable guide to those contemplating work in this field, to many of whom microwave methods will be unfamiliar. The various types of spectrometer are clearly explained, and their relative merits discussed. The appendix, dealing with sources of equipment, is a worthwhile addition. A pleasing account of the sources of hyperfine structure follows. The rest of the book is a sectionalized review, with useful explanations, of work up to the present. There are chapters on stable free radicals (mostly fairly elaborate organic molecules or ions), on 'trapped' radicals produced by irradiation of solids or materials in glasses, and on the radicals formed in the course of polymerization and of pyrolysis (of solids). All are interesting, and suggest future applications. Dr Ingram's field defines itself well without the rather odd definition of a free radical which he gives (p. 2), in which reference is made to 'normal chemical bonding', all free radicals are held together by normal chemical bonding.

The book by Trotman-Dickenson is, in effect, an extended and intelligently written review covering a field of chemistry with a much longer history. It is of great value in so far as it ignores the artificial boundaries which appear to have arisen in chemistry, and because of its systematized account and assessment of a very large amount of material. It is not the author's fault if the available matter for some of the sections is inconclusive. The book will prove useful to those connected in any way with this amorphous field.

Both books attempt short treatments of 'biradicals', from very different points of view. This topic holds much for the future.

T. M. SUGDEN

THE IMPORTANCE OF NEW DETECTORS

Čerenkov Radiation and Its Applications

By Dr J. V. Jelley. Pp. x+304. (London and New York: Pergamon Press, 1958.) 65s. net.

IT is seldom that the first book to appear on any topic is so thorough as this work by Dr. Jelley. The treatment of the largely new subject of Čerenkov radiation is very complete in its scope and the many workers in the field, whether they are engaged in fundamental studies of this form of radiation or in some relatively straightforward application of a tool based on the phenomenon, owe a debt of gratitude to the author for this comprehensive study. Those who heard the evening discourse by Academician Tamm at Geneva in 1958 were given a clear picture of the rather intriguing history of the subject and the relatively sudden introduction of practical detectors, based on the Čerenkov effect, seemed the more surprising.

Jelley has gleaned his material from many rather scattered sources and presented it here in a well-integrated form. The rather extensive theory is well supported by his clear expositions of the experimental work in the field and in this he shows the skill of one who has personally made considerable contributions to the subject. The author makes it obvious that the subject is likely to produce more surprises in the

future and those interested will find much to stimulate their thought in this volume. Many fruitful researches can be expected in this field and Jelley himself indicates some of these. Modern physics perhaps owes its rapid progress more to the introduction of novel detectors than to any other successes. We need but mention the Geiger and proportional counters, the Wilson cloud-chamber, the nuclear emulsion-plate, the scintillation counter, the Čerenkov detector and the bubble chamber to realize the fundamental nature of the contribution that stems from the study and perfection of these devices. Moreover, their value extends to many fields beyond that of pure physics.

The volume can be very highly commended as a most readable, careful and thoroughly up-to-date account of the subject.

THE VERY COLD WORLD

Experimental Techniques in Low-Temperature Physics

By Guy Kendall White. (Monographs on the Physics and Chemistry of Materials.) Pp. viii+328. (Oxford: Clarendon Press, London: Oxford University Press, 1959.) 45s. net.

ABOUT a quarter of a century ago, all low-temperature physicists (and there were not many of them) knew each other, and picked each others' brains fairly regularly, so that the dissemination of cryogenic techniques was rapid and satisfactory. To-day, however, when every well equipped physics laboratory has or should have its cryogenic facility, the older method of communication is no longer adequate. Many physicists all over the world now want to be able to handle cryogenic liquids safely and efficiently, hence the timely appearance of this useful book on cryogenics, the first for nearly twenty years and the first in the English language.

A wholly satisfactory book on techniques is a difficult thing to achieve, probably because a technique is part of a craft and the communication of a craft is not easily done by the printed word. In spite of this difficulty, here is a book which will be of very great assistance to new hands at the low-temperature game, and of not inconsiderable value to the old hands as well. An especially good feature is the 'feel' it gives for cryogenic physics, which will be appreciated by its practitioners.

There are faults, of course. The book strays too frequently into theory. No one is seriously going to read this book to find out how electron spins align themselves in an external magnetic field, or to study the formal derivation of the absolute thermodynamic scale of temperatures. But there are excellent chapters on heat exchangers and their calculation, on mechanical thermal contact, and on thermometry. The important methods of cryostat temperature control are well described, although it would have been valuable to have included some of the electronic circuit diagrams with magnitudes of quantities to give any desired sensitivity of control.

The chapter on vacuum techniques, soldering and sealing is good so far as it goes, but there is no mention of how to make a soft soldered joint that (a) will be mechanically strong, (b) will never leak, and (c) can be non-destructively unsoldered. Further, there is no mention of leak-hunting, that grimmest of pursuits, or of real or virtual leaks, or indeed of whether or

not the author personally believes in such things as low temperature leaks. The diagrams of actual apparatus are often too schematic to be of great use, for example, the transfer tube and valve on pages 53 and 55, of the design of both of which I disapprove. There is a mention of the use of spontaneous oscillations as a means of liquid level indication, but no description of this odd phenomenon nor any warning of its often annoying and occasionally horrifying effects.

All of these are, however, minor criticisms. The book contains a mass of useful cryogenic information. Generally it gives highly commendable critical comparisons of various experimental methods such as those used in calorimetry, and for the first time collects really valuable critical data on onisativities and on total thermal conduction and expansion coefficients between room temperature and 1°K.

J F ALLEN

A BIOCHEMIST'S GUIDE TO THE NERVOUS SYSTEM

Biochemistry and the Central Nervous System

By Prof Henry Mellin. Second edition. Pp vii+288 (London: J and A. Churchill Ltd, 1959) 45s.

IT is a considerable achievement for Prof Mellin to have produced a second edition of his book (already translated into Spanish and Japanese) in such a relatively short time. The need for a new edition is some indication of the rapid increase in our knowledge of the biochemistry of the nervous system to which the author and his colleagues at the Maudsley Hospital have made valuable contributions.

The layout of this book follows the previous pattern though there have been extensive revisions and additions. There is, for example a new chapter, which is very much to the point, on the relation of the brain to the body as a whole, and the section on brain lipids has been considerably modified in the light of recent observations. Knowledge of the metabolism and functions of proteins in the brain is still somewhat limited, but until Table 6 on the chemical nature and diversity of brain proteins can be extended it is likely that progress on this particular aspect will be slow. I was again impressed by details given about the rates of chemical reactions in brain and their relation to the speed of cerebral processes information which is becoming more valuable as it becomes more extensive.

Much useful information is summarized in diagrams and tables (Fig 34 and Table 28 are instances of this). It is perhaps significant that one of the column headings in Tables 8 and 9 has been changed from 'acid labile phosphate of adenosine triphosphate' to 'acid labile phosphate of purine nucleotides' in the second edition, thus indicating that the free nucleotide content of cerebral tissues is more complex than had previously been indicated.

The chapter on chemical factors in nervous transmission is an extremely able résumé of a mass of information, and some indication of the speed at which this subject is developing can be deduced from the fact that references to the possible role of γ amino butyric acid as a pharmacologically active agent are all dated 1955 or later. Biochemical aspects of the action of depressants and excitants receive their due and in view of the current multiplication of drugs this

summary is of some considerable value. Perhaps the one surprising omission in the book is an appraisal of the extensive work of Geiger and his colleagues on the metabolism of the isolated perfused brain *in situ*.

Elsewhere the author of this volume has remarked, 'Until the central problems of neurochemistry have been successfully tackled and we see more clearly how the nervous system utilizes its large energy supply in nervous transmission and in maintaining the system in a state of readiness to react, and how the brain is moulded to an animal's experience chemical aspects of most of the neurological sciences—and above all material approaches to nervous mental and emotional diseases—remain as empirical as was organic chemistry before the advent of structural formulae. If this book promotes further studies on this intriguing but complex subject then we shall all have been well served. Indeed, it can be recommended to anyone who wishes to learn something of the biochemical processes underlying nervous activity and the relevance of these processes to a study of mental diseases. A comprehensive bibliography at the end of each chapter and for a book of its size, a monumental index make it an extremely useful handbook in a field where suitable handmaidens are hard to come by.'

G B ANSELL

FAUNA OF NETHERLANDS NEW GUINEA

The Animal World of Netherlands New Guinea
By Dr L D Brongersma. Pp 71 (Groningen: J B Wolters, 1958) n.p.

THE island of New Guinea remains little known to the majority even to-day, and its fauna has received little attention through television or in popular published work. It is one of the remaining major areas in which new zoological discoveries are likely to be made and is a region as yet little touched by commercial development. Its animals, despite their affinities with Australia, are unique and much work remains to be done before they are fully surveyed. Geographically the island and its outcrops form the most western extension of the Sahul shelf, and the study of the fauna is vital to the zoogeography of Australasia. For these reasons the publication of a semi popular account of the fauna of New Guinea is both timely and welcome. Dr L D Brongersma has produced an interesting and factual book, based on his radio talks on the subject. Written for the layman, the book is concerned with the novel and unusual, but also contains much of interest to the specialist. Notable peculiarities among mammals, birds, reptiles, amphibians, fish and crustaceans are described, with notes on their habits, ecology, economic value and sometimes history. The text is overlaid by field observations, line drawings and photographs. The author stresses the need for nature conservation in New Guinea, with emphasis on the dangers of uncontrolled commercial development and ill-considered introduction. A short chapter and a map of the Sunda and Sahul shelves give a background to the origin of the fauna, and the book concludes with a useful account of the zoological exploration of New Guinea. The author whose aim was to encourage interest in the fauna of New Guinea and its conservation, has written a thoroughly readable account of the novelties and notable animals of the island.

7 F HILL

Mineralogy and Geology of Radioactive Raw Materials

By Prof. H. Wm. Heinrich. Pp vii + 454 (London: McGraw-Hill Publishing Company, Ltd., 1958, 112s. 6d.)

IN recent years more geologists have been engaged in explorations for radioactive ore than in any other hard-rock phase of the mineral industry, and since the lifting of security restrictions many thousands of research papers on radiogeology have been brought to the light of day. Prof. Heinrich has set himself the task of evaluating and summarizing this vast literature, and the result of his labours is the most outstanding monograph on uranium and thorium mineralization that has yet appeared in any language. The work begins with approximately 150 pages on systematic mineralogy, continues for 400 pages with a lucid and descriptive classification of the world's radioactive ore deposits, and ends with 100 pages of bibliography (1,000 items) and comprehensive indexes. Not all his views are uncontroversial: for example, the designation of the Witwatersrand and Blind River ore-fields as respectively mesothermal and hypothermal epigenetic mineralizations will find little acceptance in the placerist schools of South Africa and Germany. But all geologists concerned with the radioactive elements, academic workers and prospectors alike, will find interest and inspiration in these pages. Nearly all the 200 text-figures are new to textbook literature. Some minor errors in placement, in the failure to recognize synonymous localities (for example, Kasolo and Shunkolobwe) and in the consistent misspelling of the mineral names blinobite and parsonite should be corrected in the second edition, which will doubtless be required as soon as the present glut of uranium is taken up by industry and geologists are once again called on to find new ore fields. C. F. DAVIDSON

Substitution at Elements other than Carbon

By C. K. Ingold (The Fifth Weizmann Memorial Lecture Series, May 1958) Pp viii + 52 (Jerusalem: The Weizmann Science Press of Israel, 1959. Distributed by the Weizmann Institute of Science, Rehovot.) n.p.

THIS little book is a record of four lectures and is divided into two chapters. The first of these discusses substitution in some co-ordination compounds, principally derivatives of cobalt (III). Attention is directed to the stereochemical course of substitution by the unimolecular and bimolecular mechanisms, and to the particular problems associated with group replacements in molecules of octahedral symmetry. An appendix is also provided to support further the theory of a direct S_N2 mechanism.

The second chapter is concerned with nitration and nitrosation at nitrogen and oxygen atoms. There is much more evidence available in this field and the author has surveyed it lucidly and succinctly. The various reagents and mechanistic ambiguities are well set out and some ingenious experiments which exclude many of these alternatives are carefully detailed.

The work is clearly printed and the diagrams are well produced. There is no index, but a generous bibliography at the end of each chapter which is of greater value in a book of this length. The only error noticed is the omission of the minus sign from NO_2^- in the last relevant equation on page 32.

This book is valuable both as a summary of the present position in this rather neglected study and

for the continuity of a mechanistic pattern, to quote the author's own words. In his preface Sir Christopher suggests that prospects are extensive and I feel that the analysis given in this work maps out the way well into a largely uncharted region. R. I. REEN

Contact Catalysis

By Dr R. H. Griffith and J. D. F. Marsh. Pp x + 300 (London: Oxford University Press, 1957) 50s. net

IN these days of many volume treatises on catalysis, the smaller book also has its place; and the publication of a third edition of Dr Griffith's well known text book on contact catalysis, now written with the collaboration of J. D. F. Marsh, is both timely and welcome. It continues to give a condensed and well planned survey of many of the more important classes of reactions involved in heterogeneous catalysis, together with an adequate treatment of the underlying theory.

In order to accommodate, in a condensed form the large amount of additional material which has resulted from the intense study which this subject is receiving, three new chapters have been added. These deal, respectively, with modern practice in the preparation and empirical evaluation of stable catalysts having a high specific surface, with the part played by electronic factors in determining the catalytic activity of metals, and with a number of reactions involving hydrocarbons. There has also been considerable rearrangement of the older sections of the book, and much of the descriptive matter on the promotion of catalysts by small amounts of subsidiary components and on the poisoning of catalysts has been revised and brought up to date. This applies also to the chapter on the part played by geometrical factors, and especially by interatomic distances, in accommodating without undue strain the reactive portions of catalysable substrates. The volume ends with a critical survey of modern progress in catalysis, with some forecasting of possible future developments. This book continues to form an excellent summary of modern trends in catalysis.

E. B. MAXTED

Practical Animal Ecology

By W. H. Dowdeswell. Pp 316 + 16 plates (London: Methuen and Co., Ltd., 1959) 32s. 6d. net

IN many British schools and universities lip-service is paid to the importance of field studies in zoology, whereas the actual practical effort is often limited to a few days at a field study centre or attendance at a single Easter-course in marine biology.

Here, almost for the first time, is a book which will really assist teachers and lecturers to introduce their students to modern animal ecology. The book lives up to its title. A wide range of methods and techniques is described which are applicable to the study of terrestrial, freshwater, marine and brackish water habitats. In some cases guidance is given on the construction of what would otherwise be expensive pieces of apparatus. To get the best out of this book, the student should be given considerable help by his teacher. So much is packed into it that many students let loose with it will suffer ecological indigestion.

On modern standards the price is reasonable, for in my opinion this book should have a major effect on the teaching of animal ecology in schools.

J. B. CRAGG

THE FIRST MINISTER FOR SCIENCE

By the RIGHT HON VISCOUNT HAILSHAM, Q.C., LORD PRIVY SEAL
AND MINISTER FOR SCIENCE

THE proposal for a Minister for Science was first talked about when the Conservative Manifesto was being prepared. I was myself at first very sceptical. It seemed to me that there were two very great pitfalls to be avoided. On one hand there was the danger that the scientific world—the Royal Society, the universities, the industrial scientists, the Atomic Energy Authority and the Research Councils—the Department of Scientific and Industrial Research, Medical Research Council and Agricultural Research Council, Overseas Research Council and Nature Conservancy (the governing boards of which are very largely manned by volunteers)—would think that too much was intended and that the new Minister would interfere with the independence and integrity of the scientist in his own sphere. If that danger were not avoided, I feel that I should lose the confidence of those on whom all else depends and whose co-operation I must win if I am to succeed at all. I hope and believe my appointment has allayed these fears. After all I am the same man who has been Lord President of the Council for the past two years. My general attitude to science and scientists has been made plain to those who were interested, and I believe has won confidence. No change in that general attitude is involved in the new appointment. I have no authority over the universities to compel them to do anything they do not wish to do. My authority over the Atomic Energy Authority and the Research Councils is no greater than my predecessors and I had before, and I have no intention of taking away from them the authority which Parliament has given to them or the freedom which they now enjoy to perform their functions without detailed interference. I am there to give them general guidance and to help them in their relations with Government, especially other Government departments.

But an equal and opposite danger is to be expected at this point. I can almost hear the cynical comment "New Presbyter is but Old Priest writ large. The Manifesto promise, the new Minister, is just a piece of political window dressing. Nothing more is to be expected and everything will go on exactly as it was before." I hope and believe this is a mistake, and I would not have accepted the appointment had I believed otherwise.

All the same, I would like to make it plain at the outset that this is a long range project. You must not expect clutches of satellites to be flung into orbit in a miraculously short space of time. Sponsors of ingenious inventions will be disappointed. The Minister is not a repository of brilliant new thoughts which have failed to appeal to any one else. He is not an overlord to the Minister of Education and will not therefore be able to create vast new academies of science and technology. He is not "Master of the Queen's Rockets" and will not therefore play a decisive part in the politics of guided missiles. He is not a super Minister of Power nor a Minister of Transport, Agriculture or Health. Indeed, I must

emphasize that unless all the other Ministers in the Government—I think without exception—are at least as scientifically minded as I ought to be myself my work will be frustrated—and until they are my work will be incomplete. I do not think it is necessarily a disadvantage that I am not a professional scientist. The First Lord of the Admiralty is not a naval officer, the Minister of Transport would not necessarily be better for being a railway man. In the main, parliamentary government is government by amateurs advised by experts. The one exception is the Lord Chancellor, and he has a technical legal job to do. In my own case I believe that the appointment of a non-scientist as the first Minister will compel scientists to do the most urgent thing that is, to share in the thought about scientific policy themselves.

For whether or not there is need for a Minister or a Ministry two years experience as Lord President has convinced me that there is need for a policy for science and that policy cannot be the product of Government thinking alone.

In describing my task I will start by one or two general propositions. Science in Great Britain increasingly touches life at every point. It is thus necessarily a partnership—and since Britain is a democracy, it is necessarily a partnership in which everyone is invited to play a part. But the indispensable partners are industry, agriculture, medicine, teaching, the universities and Government—and, of course, both the scientists and the non-scientists who play their part in the administration of the various branches of public and economic life. In all these spheres my task is to promote science. But only in part of one of these spheres of activity—that of Government—have I the power to achieve this by the use of authority as distinct from encouragement, diplomacy, enthusiasm, example, precept or advice.

Secondly, after two years as Lord President of the Council I would say that, if only because of the very multiplicity of scientific disciplines Government science, and perhaps all British science, is at the moment too parochially minded, too departmentalized and lacking in the broader vision. The Research Councils and the Atomic Energy Authority are by their very terms of reference limited in their spheres.

However a Minister for Science is bound to look for a more generalized philosophy and approach if he is to succeed. In some ways the focus of scientific opinion in Great Britain is the Royal Society. Long may it flourish. But for the purpose of advising the Government on scientific policy, the proper channel already exists in the form of the Advisory Council on Scientific Policy. I believe that this body provides one of the keys to the present situation composed as it is of a unique connexion of Government and non-Government scientists under an independent chairman with a vice-chairman who happens also to be the chairman of the Defence Research Policy Committee. I shall endeavour to rely more than

ever upon this Advisory Council for generalized advice on questions of scientific policy. My purpose is to make the voice of science coherent and articulate under Government encouragement, and in one real sense to make science self-governing under Government inspiration. For this purpose a greater use of the Advisory Council on Scientific Policy is inevitable. I had already begun to move in this direction in the last Parliament. I hope to go further now, and I feel I am going to be helped by the more flexible and numerous office staff (which supplies the secretariat of the Advisory Council) with which I shall be equipped as the result of the marriage between the Atomic Energy Office and the Lord President's Office. Thus assisted I shall try to tackle such questions as whether the general balance of scientific effort is right or could be better deployed, and other questions of a general nature as they emerge. Already in the last Parliament I had pressed forward an inquiry under the late Sir Claude Gibb (now chaired by Sir Solly Zuckerman) on techniques of management and control of Government financed research and development, and I look forward to a report from them, with positive suggestions, when they have completed their heavy task.

One of the matters I referred to the Advisory Council on Scientific Policy in the last Parliament was the question of space research, and it was as a result of its advice that the Steering Group under Sir Edward Bullard was set up and the group of scientists under Prof H. S. W. Massey paid their recent and successful visit to the United States. I am not sure that either the philosophy or scope of our policy on space research is yet fully understood, and I would welcome the opportunity of expounding it more fully should questions be directed to me.

I also have great hopes of the Overseas Research Council which I set up at the end of the last Parliament under the chairmanship of Dr R. S. Aitken. The object of this body is to act as a sort of clearing-house for our research effort overseas both separately and in co-operation with other countries.

I also hope to show a personal interest in the applied research which is very widely carried out by private industry and in industrial research associations under the general authority of the Department of Scientific and Industrial Research. But execution of all this work will continue to rest with the bodies entrusted by Parliament with those functions.

In many ways the clue to the picture of science in Britain lies with the universities—especially with those which have great potentialities for growth and indeed an increase in numbers. To explore this in any detail would be outside my present purpose and indeed outside my function as the Minister for Science. I have no authority over the universities nor over the University Grants Committee, and I

have no ambitions to obtain such authority. But I shall try to forge friendly links with both, both personally through individual contacts, and by discussions between officials. In particular, I have ideas for the forging of closer links between the Government research stations and institutes, and the universities, from which I believe both the Government stations (and the scientists who work there) and the universities would stand to gain in prestige and in effectiveness.

I also believe that the time has come for the purse strings of private munificence by industries and industrialists to be opened again for the benefit of universities and colleges and I will do all in my power to produce interest in this. My object here is not to limit the amount of Government help, but to widen the front of public interest, and increase academic independence and flexibility. It would be ungenerous and at this time insensitive not to point in this connexion to the gifts rightly described as princely—including one particularly welcome from the Transport and General Workers' Union, to Churchill College and to the project for St Catherine's reconstitution at Oxford. But, greatly daring, may I say that I do not see why gifts from individuals and institutions should be concentrated on Oxford and Cambridge or even London? The greatest scope for enlargement and improvement surely lies elsewhere, as other generous and far-sighted benefactors have recognized.

The teaching of science and mathematics in the schools is again not a matter for me but for the teaching profession, and my contact with that profession must be through the Minister of Education, but I hope to keep a close liaison with the Minister in this and other matters, and I shall also try to seek guidance from the representatives of independent schools.

It is clear, I think, that in a single term of office only the foundation can be laid of a genuinely scientific approach to the problems of the present day. I hope that my ambitions in this direction will not be despised as inadequate because they are realistic and long-term. My hope will be to engender in all a genuine enthusiasm for science, and respect for scientific work and scientists, not merely for their practical achievements, but also for the cultural values they represent. If I win their confidence, and also make clear to the public and to my colleagues the nature of their needs and their outlook, I will not have failed. Above all, I would like to say that I bring to this new and creative work all the enthusiasm and desire to serve of which I am capable, and a real determination to see that British science continues to be an instrument of peaceful progress and a means of enhancing British prestige in the world and British prosperity and culture.

ROCKET PROPULSION

AT the meeting of the British Association in York, one of the sessions in Section B (Chemistry), on September 8, was devoted to a series of papers and discussions about various aspects of rocket propulsion.

The subject was introduced by Dr W. B. Littler, director-general of Scientific Research (Munitions), Ministry of Supply, who outlined the history of

rocket development. He referred to the early use of gunpowder for rocket propulsion and the introduction in the Second World War of a variety of rocket weapons made possible by the development of new solid and liquid propellants. The German V2 rocket, with a range of 200 miles and a payload of 1 ton, was the outstanding technical

triumph of its day. Since the War, vast sums of money have been spent, particularly by the Americans and Russians on all forms of missile research and development. The all up weight of some rockets has surpassed the 100 ton level, and a range of 5,000-6,000 miles is claimed for some ballistic missiles. In relation to the resources and man power employed, some impressive successes have been achieved in the United Kingdom, and important developments have been pioneered with solid and liquid propellants and with the motors associated with them.

The Index of propellant performance most frequently quoted is the 'specific impulse'. The solid and liquid propellants now in common use have a specific impulse in the range 180-250, compared with the figure of only 60 for gunpowder. Substantial increases in specific impulse are possible by the use of uncommon fuels and oxidants (for example, hydrogen and fluorine) but most military applications can be met by the use of conventional propellants, and these are adequate for putting artificial satellites into orbit. The most spectacular advances in recent years have arisen from three developments: (1) the substantial increases in the size of the rockets and the weight of propellant carried, (2) the perfection of the multi stage rocket, whereby motors are discarded successively in flight, after all the propellant has been burnt, thus eliminating dead weight as quickly as possible, (3) the development of very large solid propellant motors containing up to ten or more tons of propellant.

Unlike liquid propellant motors the thrust of solid propellant motors cannot yet be controlled in flight, but they are basically simpler for many applications and can be more easily maintained in a state of readiness. As a result, their use has greatly extended in recent years, but there is a future role for both types of propellant. For controlled flight in outer space, much higher performances, not attainable with chemical systems, are required.

The first paper, "Thermodynamic Aspects of the Choice of Rocket Propellants", by Mr G K Adams, of the Explosives Research and Development Establishment, Waltham Abbey, discussed the relation between the thermodynamics of propellant ingredients and combustion products and the performance of rocket propulsion systems. Applying the principle of conservation of momentum to a rocket in a force free field, it can be shown that the velocity increment v is given by $v = \bar{V} \ln(M_1/M_2)$, where \bar{V} is exhaust velocity of the combustion products, M_1 is initial mass of rocket, and M_2 is mass of rocket after all the propellant has burnt. The exhaust velocity is used as an index of propellant performance. It is generally quoted in the form of the 'specific impulse', which is the quotient of the exhaust velocity and the force to mass conversion factor, and has the dimensions of time.

By applying the principle of conservation of energy, the square of the exhaust velocity can be shown to be proportional to the decrease in total enthalpy per unit mass on burning the propellant under rocket conditions. It depends, therefore, on the initial chemical energy of the propellant and on the efficiency with which this is converted into translational energy in the exhaust jet.

The demand for high chemical energy per unit mass suggests the choice of elements of low atomic weight suitable oxidation reduction reactions between these have energies in the range of 2-4 kcal/gm. The

energies of reactions between free atoms or radicals are much greater but owing to their high reactivity even at extremely low temperatures, there appears to be little hope of utilizing them in propulsion systems. Other factors in addition to those of energy must also be taken into account. Thus a propellant must have adequate chemical stability, its physical properties must be suitable for the particular application, and the materials used in the construction of the combustion chamber must be able to stand up to the temperatures attained. In practice, such factors tend to limit the range of useful chemical energies still further, and in these circumstances particular attention must be paid to achieving the most efficient conversion of chemical energy into translational energy of the rocket.

The efficiency of the expansion process is governed by a number of considerations. A low total heat capacity per unit volume of gaseous products is beneficial: this leads to a requirement that the gaseous products shall contain the minimum number of constituent atoms (for example, HF rather than H_2O), lower efficiencies result if solid products are formed. Energy released by shifts in chemical equilibria during expansion can be used less efficiently than that released in the chamber. Energy is lost through the non attainment of velocity and thermal equilibria in systems giving solid products. Chemical energy alone, therefore is not an adequate criterion for the choice of propellant systems. A change which increases the efficiency is often more useful than a mere increase in chemical energy. Additional factors which have to be taken into account are cost and availability.

Mr J E P Dunning, director of the Rocket Propulsion Establishment, Westcott then spoke about "The Application of Liquid Propellants to Rockets". He referred to some of the more important ballistic equations and described the physical processes involved in a rocket engine using a liquid fuel (for example, kerosene) and a liquid oxidant (for example, oxygen). A steady pressure is maintained in the combustion chamber by feeding in the liquids at the same mass flow rates as the gases are ejected from the nozzle. The propellants are pumped into the head of the combustion chamber through a multiplicity of orifices designed to establish as quickly as possible a uniform mixture of fuel and oxidant. Both liquids must be vaporized and this is brought about by atomization, initiated by the actual process of injection and accelerated by the combustion of preceding droplets. Once established, the combustion process is self supporting but has, however many tendencies to instability. Satisfactory geometry of the chamber and injection head is essential to reduce these irregularities to a minimum, but the nature of the problem is such that the empirical approach still has to be largely relied upon.

In the case of a liquid oxygen/kerosene motor developing 100 000 lb thrust, it is necessary to feed liquid into the chamber at a rate of about 400 lb/sec, of which 280 lb/sec will be liquid oxygen and 120 lb/sec will be kerosene. The injection head may have as many as 2 400 orifices each 0.1 in in diameter, from which the liquids emerge at about 100 ft/sec. Within an axial distance of about 1 ft and a time of 2-3 millice, the physical processes of atomization, vaporization and chemical reaction have to take place. In the combustion chamber the temperature attains 3 300° K and the pressure 500 lb/in.², and the gases emerge at a velocity of

around 8,000 ft/sec. The temperatures attained are such that the walls of the chamber and the nozzle have to be cooled, and either fuel or the oxidant is used for this purpose. To feed the liquids into the injector head two turbo-pumps are used, since the alternative system of pressurizing the tanks is ruled out by considerations of weight. The pumping power required is large, but is achieved with a propellant consumption of rather less than 2 per cent of that used in the combustion chamber.

In selecting possible fuel/oxidant combinations, performance merits may be over-ridden by criteria such as toxicity, availability and cost. A limit on overall performance may thus be imposed, but this can be countered by increasing the mass ratio (mass at launch/mass at 'all-burnt'), although with a single-stage rocket it is not practicable to exceed a ratio of about 14 to 1. Enhanced performance can then only be achieved by the use of multi-stage propulsion systems.

Dr G. H. S. Young, of the Explosives Research and Development Establishment, Waltham Abbey, then dealt with British solid propellants for rockets. He pointed out that all solid propellants are explosives and, under appropriate conditions, can be detonated. These conditions must be avoided during manufacture and use, and this consideration frequently limits what can be achieved practically.

The two main solid propellants in use in Britain are extruded cordite, sometimes called double-base propellant, and plastic propellant. The extruded cordites are similar chemically to gun propellants and are available in a wide range of sizes and burning-rates. In general, the burning-rate is adjusted by altering the calorimetric level, the more energetic the composition, the faster it burns. The size of charge which can be produced is limited by the size of the presses available and the hazards involved with large quantities. However, the double-base system has been recently extended by the exploitation of a casting process in which the nitrocellulose is gelatinized in a mould by desensitized nitroglycerine, the charge then being cured at 140° F for some days. In this way charges larger, and more complex in shape, than these capable of extrusion are being produced. Both extruded cordite and cast double-base are used as loose charges in the rocket motors.

Plastic propellant, however, being a putty-like material, is capable of case-bonding, since the material can accommodate the differential thermal expansion between the motor wall and the propellant itself. This type of propellant has been developed to make use of ammonium perchlorate as the oxidizer. Burning-rates are adjusted by the addition of ammonium picrate and, as with extruded cordite, the lower-energy compositions burn more slowly than those of high energy. This propellant has been successfully used in the largest British solid-propellant rocket to date, namely, that used in the *Skylark* in the International Geophysical Year experiments; this rocket has a charge of about 1,800 lb of propellant and is 17 in. in external diameter.

Another solid propellant being investigated is the so-called pressed charge, pioneered by Nobel Division of Imperial Chemical Industries, Ltd. In this propellant the ingredients are consolidated to rock-like form by powerful presses. Ammonium nitrate is the oxidizer, and propellants with low rates of burning, particularly suited for assisted take-off units and gas generators, are produced.

The present trend is for rockets to increase in size, and none of the propellants mentioned, with the possible exception of cast double-base, is altogether suitable for large missiles. Work is therefore proceeding on other castable composite propellants based on synthetic rubbers and, of these, polyurethanes appear to have many advantages. There is also a demand for higher performance and this can only be achieved by the introduction of novel ingredients, such as light metals, or new combustion systems which might, possibly, be based on fluorine compounds. In addition, if solid propellants are to be used in the larger missiles, then methods of thrust control and thrust termination will need to be developed and the reliability of operation will have to be very high.

Finally, Dr L. R. Shepherd, of the Atomic Energy Research Establishment, Harwell, and chairman of the British Inter-Planetary Society, spoke about propulsion for space travel. The equation mentioned earlier represents an idealized condition and in the actual case of a rocket accelerating from the surface of the Earth the actual velocity may be 1,000–2,000 metres/sec less than the value predicted by this equation on account of atmospheric resistance and other effects. For even the most modest excursion into space the limitations of conventional propellants demand the use of multi-stage rockets. Using available chemical propulsion systems in staged rockets, it should be possible to put 20-ton payloads into orbit around the Earth or to deposit 1–2 tons of instruments on the Moon. But for any more ambitious mission, propellant systems of much higher performance are required.

Dr Shepherd considered that the difficulties involved in the application of reactions between free atoms or radicals (mentioned by Mr Adams) made it seem unlikely that these can be successfully applied to a practical propulsion system.

Another possibility is the utilization of forbidden transitions between excited and ground states in the electron shells of certain atoms, for example, helium. If the active material can be stored and its energy released in the thrust chamber of a rocket engine, the potential usefulness of a small single stage vehicle is enormously extended. It may be that the storage of active helium at low temperatures is more feasible than that of atomic hydrogen.

Speculations on the application of nuclear power to rocket propulsion generally assume that the energy from a nuclear reactor can be transferred to a suitable working fluid, the optimum material being hydrogen. This might be achieved by heating the working fluid in a thrust chamber and allowing it to expand through a nozzle in a manner similar to conventional practice. Alternatively, the working fluid may be ionized and accelerated as a plasma in a magnetic field. There are many formidable technical problems to be overcome before such nuclear systems can be developed.

The use of electrical methods of propulsion has also been proposed. This would involve an arc discharge to heat a working fluid and expand it through a nozzle, or, to avoid excessive temperatures, the electrical acceleration of a working medium. It is generally assumed that this would be effected by ionizing the working fluid, extracting the positive ions, and accelerating them through an electrostatic field. Alternatively, a fully ionized plasma may be accelerated in an electromagnetic pump.

The working medium of such a system would probably be one of the alkali metals, possibly sodium. At a temperature of $3,500^\circ \text{K}$ and a pressure of 10^{-4} atmospheres, a sodium plasma is 95 per cent ionized, there should therefore be little difficulty in producing and maintaining such a plasma.

It is known that a great deal of development work on novel propulsion systems is being carried out in the United States and presumably also in the USSR.

In the discussion, Prof M. Stacey expressed interest in the possibility of using fluorine in propulsion systems. The high toxicity of the combustion products was cited as a fundamental difficulty, and costs would also be high. In reply to questions concerning the relative reliability of liquid and solid propellant motors, it was pointed out that there is

very little information to support an absolute comparison. A liquid propellant motor being more complex might be expected to have a greater rate of failure, but the opinion of many British workers is that, given adequate attention in the research and development phases, the reliability of liquid propellant motors should at least approach that of corresponding solid propellant motors. Questions were also raised regarding the role of solid cigarette burning charges in view of the desire for high loading densities for propellants. It was explained that the application of this type of charge to larger motors is limited by the need for high burning rates and the additional insulation necessary to protect the motor wall which is exposed to the hot combustion products as burning proceeds. These factors rob the 'cigarette burning' charge of its immediate attraction.

W B LITTLE

DENSITY OF THE UPPER ATMOSPHERE FROM ANALYSIS OF SATELLITE ORBITS FURTHER RESULTS

By D G KING-HELE

Royal Aircraft Establishment, Farnborough

IN an article on this topic in *Nature* some months ago¹ a new method of determining air density from the rate of contraction of satellite orbits was described and applied to the satellites launched during 1957 and 1958. In the present article the method has been refined by taking account of atmospheric rotation, and further results are given utilizing the satellites of 1959, for heights between 180 km and 700 km. The variation of density with latitude and season, and day to night changes, are also discussed.

The rate of decrease of the orbital period of a satellite, which can readily be measured, depends on the integrated effect of air drag around the orbit. The drag is greatest at perigee, and for a given satellite it is the air density at heights a little above that of perigee which chiefly controls the drag effects and which can best be estimated from the rate of change of period, dT/dt .

atmosphere (taken equal to that of the Earth) and its inclination of orbit to equator. For almost all the satellites so far launched F has been between 0.9 and 1.

The second assumption is that the density ρ at heights above that of perigee may be taken as varying exponentially with height y , so that

$$\rho = \rho_p \exp \{ - (y - y_p)/H \} \quad (3)$$

where H which is approximately equal to the scale height is taken as constant. The value of H is not known accurately at heights above 180 km but, if H^* is the best estimate of H the density at a height $\frac{1}{2}H^*$ above perigee, ρ^* , can be expressed in terms of dT/dt by the equation

$$\rho^* = - \frac{0.158}{\delta} \frac{dT}{dt} \sqrt{\frac{e}{aH^*}} \left\{ 1 - 2e - \frac{H^*}{8ae} + 0 \left(e^2, \frac{H^*}{a^2e^2} \right) \right\} \quad (4)$$

where $\delta = FSCD/m$, m is the mass of the satellite, a is the semi-major axis and e the eccentricity of the orbit. If $0.02 < e < 0.15$ and H^* , the best estimate of H , does not differ from the true value of H by a factor of more than 1.5, the maximum error in the expression (4) for ρ^* is less than 5 per cent. If e is increased to 0.2, the maximum error is 10 per cent. Equation 4 is the same as equation 5 of the previous article, except that SCD/m has been replaced by $FSCD/m$. The introduction of the factor F allowing for atmospheric rotation changes the resulting values of density by 5–10 per cent, and the change is always an increase, since no satellite has yet (September 1959) been launched against the rotation of the Earth.

When $e < 0.02$, equation 4 becomes less accurate and for $0.005 < e < 0.02$ can best be replaced by

$$\rho^* = - \frac{0.0044}{\delta a} \frac{dT}{dt} \frac{\exp(ae/H^*)}{I_0(ae/H^*)} \left\{ 1 + 0(e) + 0 \left(\frac{H^*}{a} \right) \right\} \quad (5)$$

Method of Analysis

It is assumed, first that the drag D acting on a satellite of mean cross-sectional area S , moving with velocity v relative to the centre of the Earth, in air of density ρ , may be expressed in terms of a drag coefficient C_D as

$$D = \frac{1}{2} \rho v^2 FSCD \quad (1)$$

where SCD may be taken as constant, and the factor F is included to allow for the fact that v differs from the velocity V of the satellite relative to the ambient air. F , which is equal to $(V/v)^2$, may be taken as

$$F = \left(1 - \frac{r_p \omega}{v_p} \cos i \right)^2 \quad (2)$$

where r is distance from the centre of the Earth, suffix p denotes perigee, ω is angular velocity of the

Table 1 VALUES OF $\delta = FSC_D/m$ FOR SATELLITES 1957a-1959c

| Satellite | Mass m (kgm) | m/SC_D (kgm/sq m) | δ (sq m./kgm) |
|--------------------------|-------------------|------------------------|-------------------------|
| <i>Sputnik 1</i> | 1957 α 2 | 83.6 | 0.0088 |
| <i>Sputnik 1 rocket</i> | 1957 α 1 | — | 0.015 |
| <i>Sputnik 2</i> | 1957 β | 50 | 0.016 |
| <i>Explorer 1</i> | 1958 α | 14.0 | 0.039 |
| <i>Vanguard 1</i> | 1958 β 2 | 1.47 | 0.040 |
| <i>Explorer 3</i> | 1958 γ | 14.1 | 0.039 |
| <i>Sputnik 3</i> | 1958 δ 2 | 1,327 | 0.0046 |
| <i>Sputnik 3 rocket</i> | 1958 δ 1 | — | 0.015 |
| <i>Explorer 4</i> | 1958 ϵ | 17.5 | 0.032 |
| <i>Atlas</i> | 1958 ζ | 3,960 | 0.032 |
| <i>Vanguard 2</i> | 1959 α 1 | 0.75 | 0.044 |
| <i>Vanguard 2 rocket</i> | 1959 α 2 | 23 | 0.050 |
| <i>Discoverer 2</i> | 1959 γ | 635 | 0.021 |
| <i>Discoverer 5</i> | 1959 ϵ | 635 | 0.021 |
| <i>Discoverer 6</i> | 1959 ζ | 635 | 0.021 |

where I_0 is the Bessel function of the first kind with imaginary argument, of order zero

Evaluation of δ

The main difficulty in applying equations 4 and 5 lies in the evaluation of $\delta (= FSC_D/m)$, and in particular of SC_D . It is assumed here, as in the previous article, that each satellite rotated about its axis of maximum moment of inertia. For satellites with length/diameter ratio greater than about 2, the extreme modes of rotation are then (a) travelling exactly like an aeroplane propeller, and (b) tumbling end over end. In (a), the axis of spin and the direction of motion are in line, in (b), the angle between them is 90° : in practice, the angle may be anywhere between these extremes, and the mean of the values of SC_D for all modes of motion between (a) and (b) has been taken, the drag coefficient being calculated for free-molecule flow with diffuse reflexion.

For near-cylindrical satellites such as *Explorers 1*, 3 and 4 and *Atlas* (1958 α , γ , ϵ and ζ), SC_D has been taken as $1.85 \gamma d$, where γ and d are the effective

length and diameter, the maximum possible error being 19 per cent. A recent study² has shown that a rotating cone of length γ and base diameter d , and of shape similar to *Sputnik 3* (1958 δ 2), has $SC_D = 1.43 \gamma d$ under mode of rotation (a), and $1.45 \gamma d$ under mode (b), corresponding to drag coefficients (based on the appropriate mean cross-section) of 2.18 under mode (a) and 2.09 under mode (b). A drag coefficient C_D of 2.15 based on the mean of the cross sections under modes (a) and (b) has been taken here. For the spherical satellites, *Sputnik 1* and *Vanguard 1* and 2 (1957 α 2, 1958 β 2 and 1959 α 1), C_D has, as before, been taken as 2.2, based on the mean cross section, including antennae. The values of δ for *Sputnik 2* and the rockets of *Sputniks 1* and 3 have been obtained by comparison with *Sputniks 1* and 3, as explained previously¹. For the *Discoverer* satellites, which are cone-cylinders, δ has been taken as the mean of the cross sections under modes (a) and (b), with $C_D = 2.2$.

Table 1 lists the values of δ obtained for all the satellites launched before September 1959 whose orbits are known, except *Explorer 6* (1959 δ), to which the theory is not applicable, since e is greater than 0.2. The values for the *Discoverers* apply during the period after the ejection of the re-entry capsule. If the assumptions already stated are justified, the error (standard deviation) in the tabulated values of δ will probably be rather less than 10 per cent.

Evaluation of Air Density

The air density at height $\frac{1}{2}H^*$ above perigee has been found for each of the satellites listed in Table 1 from equation 4 (or, for *Discoverer 2*, equation 5), the values of H^* chosen being consistent with those given later in this article. For the Russian satellites, values of dT/dt , a and e have been taken from orbital

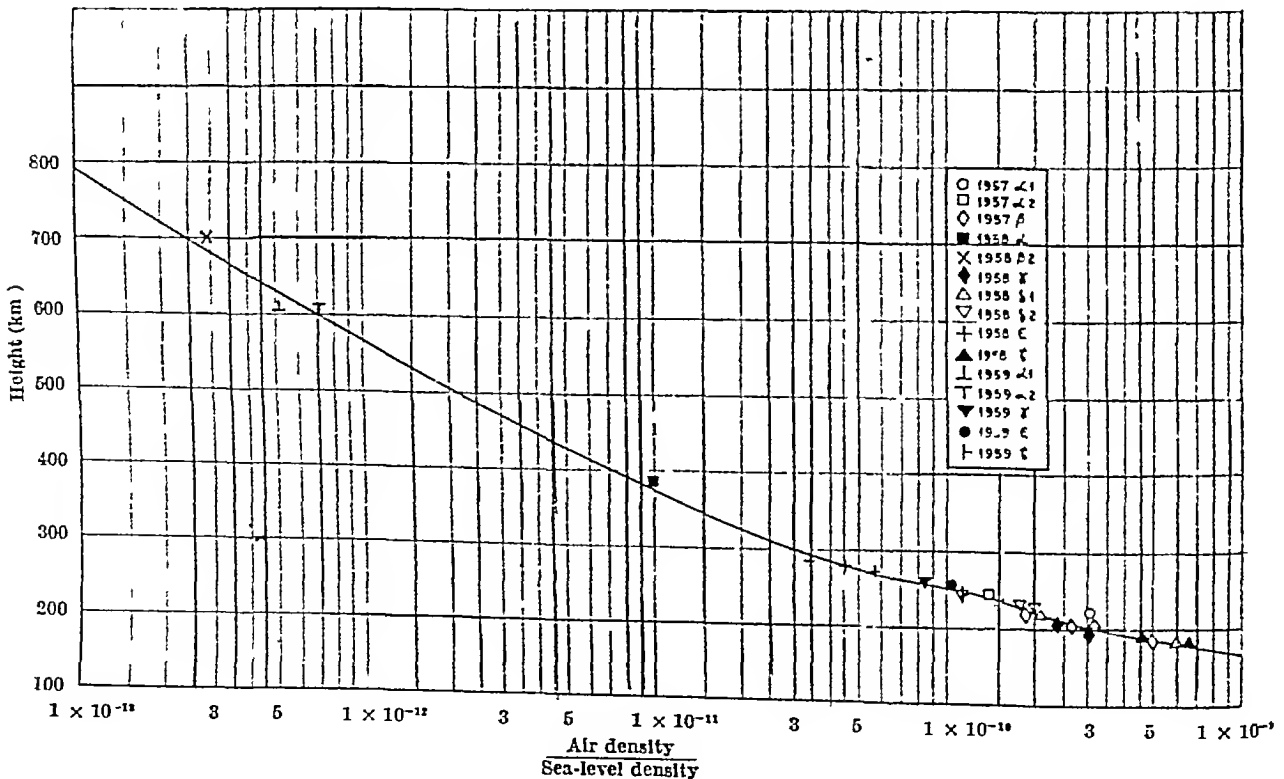


Fig. 1 Air density obtained from satellites 1957a to 1959c

determinations made in Britain³⁻⁵. For the US satellites, values have come from the orbital data issued by the Smithsonian Astrophysical Observatory and by Project Space Track, Bedford, Mass. For satellites with long lifetimes, the values of dT/dt have been averaged over intervals of several months.

The resulting values of air density are shown in Fig. 1, and a curve has been drawn through the points to represent average density. It is worth noting that the individual points lie close to the curve, except for *Sputnik 1* rocket for which, however, the orbital information is rather meagre. None of the other twenty points in the cluster below 300 km differs from the curve by a factor of more than 1.25. Some scatter is to be expected, because of the errors in δ and because the density varies from week to week by up to 30 per cent at 200 km. height¹ and by 60 per cent or more at 700 km.⁶ Because of the latter variations, and because of the possible influence of charged drag^{11,12} the three points above 600 km. are less reliable than those below.

The value of 0.7×10^{-12} gm/cc. for air density at 440 km., deduced¹⁴ from the rate of expansion of a cloud of sodium vapour from the Russian Geophysical Rocket of February 1958, differs from the curve of Fig. 1 by a factor of less than 1.25, and fills a gap in a rather empty region.

Variation of Density with Latitude and Season

The points plotted in Fig. 1 refer to latitudes ranging between 70° N and 50° S, and to all seasons, but there is no sign of any systematic variation of density with latitude or season. In view of the small scatter, it seems probable that the density at a given height below 300 km. does not depart from its average value by a factor of more than about 1.5 as a result of variations with latitude (between 70° N and 50° S) and with season. This is in contrast with the direct measurements from rockets^{11,12}, which suggest a much wider variation, by a factor of 5 or even 10, so it is worth seeking further evidence.

Such evidence can be obtained from the orbit of *Sputnik 3* between May 1958 and June 1959. During this time, the perigee latitude moved slowly from 50° N to 65° S, and the perigee height changed by less than 20 km. The rate of change of period of *Sputnik 3* thus provides a continuous indication of the air density at heights between 200 and 250 km., and over the range of latitude from 50° N to 65° S. The air density ρ_p at the current perigee height was calculated from the equation¹⁷:

$$\rho_p = -\frac{1}{38} \frac{dT}{dt} \sqrt{\frac{2e}{raH}} \left\{ 1 - 2e - \frac{H}{8ac} \right\} \quad (0)$$

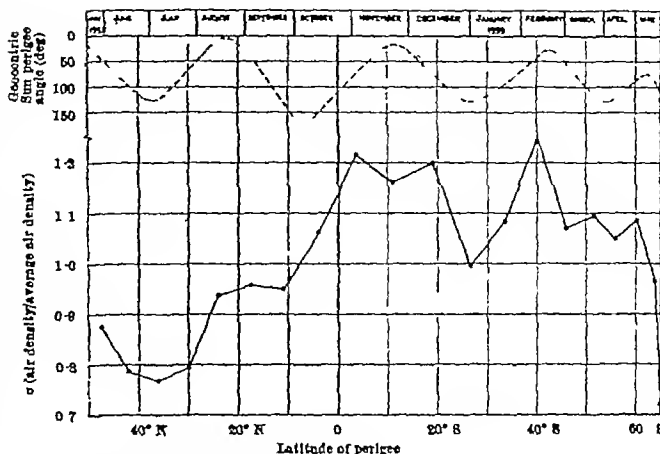


Fig. 2. Air density at the initial perigee height of *Sputnik 3* 226 km. variation with latitude and time

with $H = 30$ nautical miles (56 km.). The values of dT/dt were obtained from the records of orbital period kept by the Royal Aircraft Establishment (May–October 1958) and the Radio Research Station, Slough (October 1958–June 1959). The density at the initial perigee height y_{p0} (226 km.) was then found by multiplying ρ_p by $\exp\{-(y_{p0} - y_p)/H\}$, where y_p is the current height of perigee over an oblate Earth. This process gives the air density at the initial perigee height (226 km.) but at latitudes near the current perigee latitude. The resulting densities, calculated at 20-day intervals and expressed as a multiple σ of the average density, are plotted against perigee latitude in Fig. 2. A satellite encounters drag over a range of latitudes near perigee, and each point in Fig. 2 represents an average density over the 15–20° of latitude within which most of the drag effect occurs, rather than the density at the exact latitude where it is plotted. Consequently, there is no virtue in reducing the time-interval between the points in Fig. 2.

The chief errors in σ are likely to result from errors in dT/dt (estimated standard error 3 per cent), H and $y_{p0} - y_p$ (estimated bias errors 20 per cent each) and δ (maximum error¹ 5 per cent). The estimated standard errors in σ from these four sources are 3, 2½, 2½ and 2½ per cent, respectively, implying a standard error in σ of about 5 per cent.

The density at heights of 200–250 km. is known to vary with time, by a factor of up to 1.3, exhibiting a 28-day periodicity, which is attributed to solar disturbances¹⁻¹¹, and one of the reasons for choosing a 20-day interval in Fig. 2 was to avoid giving prominence to the 28-day oscillations. Fig. 2 represents the combined variation due to solar effects, latitude season etc. Since none of the values of σ differs from 1 by a factor of more than 1.4, and the standard error is about 5 per cent, Fig. 2 strongly suggests that the density does not depart from its average value as a result of seasonal and latitude effects, by a factor of more than 1.5, between latitudes 50° N and 65° S. A confirmation of this is given by the

Fig 1, it is very unlikely that strong seasonal and latitude variations do occur and happen to have cancelled out for *Sputnik 3*

It would probably be unwise to draw any positive conclusions about the variation of density with latitude and season from Fig 2, but the large drop at the right-hand end does encourage the speculation that the air density at heights of 200–250 km may be low at latitudes south of 60° S, at least in the winter

Day-to-night Variations in Density

The upper curve in Fig 2 shows the angle *SCP* subtended at the centre of the Earth (*C*) by the Sun (*S*) and the perigee (*P*) of *Sputnik 3*. If this angle exceeds 90°, the surface of the Earth below perigee is in darkness, if the angle exceeds about 105°, the perigee point itself is in darkness. Comparison of the two curves in Fig 2, though inevitably inconclusive because of the errors in σ , gives the impression that the air density is related to the angle between Sun and perigee, a possibility which has previously been suggested by Sedov¹⁸, Lidov¹⁹, Groves²⁰ and others. If so, the air density at heights of 200–250 km is rather higher on the sunlit half of the Earth than on the dark half, and this day-to-night variation, which had a period of about 90 days for *Sputnik 3*, and an amplitude of perhaps ± 10 per cent, would be superposed on the 28-day variation due to solar disturbances, which had an amplitude of about ± 20 per cent. A rather similar interpretation for a height of 700 km was recently proposed by Wyatt²¹, from analysis of the orbit of *Vanguard 1*, though at this greater height the angle between the Sun and perigee is, on Wyatt's interpretation, more important than solar disturbances. There is also some slight indication of a day-to-night variation for *Sputnik 2* and *Sputnik 3* rocket, though the 28-day variation is dominant^{7, 11}

Values of *H*

The slope of the density-versus-height curve of Fig 1 gives the value of the coefficient *H* in equation 3, and Table 2 lists values of density and of *H* derived from the curve. Other curves, of different slopes, could however be drawn in Fig 1, the individual values of *H* in Table 2 might, therefore, be in error by up to perhaps 20 per cent, though the mean value of *H* between 200 and 400 km height is almost certainly between 50 and 60 km.

The rather irregular values of *H* in Table 2 between 200 and 260 km result from the indentation in the curve of Fig 1. If, instead, a smooth curve were drawn, seven successive points, from six satellites of quite different shape, size and date of launch (*Explorer 4*, *Discoverers 2*, 5 and 6, and *Sputniks 1* and 3), would lie on the same side of the curve. The indentation, therefore, seems justifiable, though it might still be illusory, if several points happened to be in error in the same sense.

If the indentation is real, it indicates a rather large value of *H*—more than 50 km—at heights near 220 km., in accord with the values of *H* found from the decrease in the perigee distance of satellites^{1, 22}. The air temperature depends¹ on the product of *H* and *M*, the mean molecular weight of the air. So, unless *M* varies widely between 210 and 230 km,

Table 2 VALUES OF AIR DENSITY AND *H* GIVEN BY THE CURVE OF FIG 1

| Height (km) | Air density Sea-level density | Density (gm./c.c.) | <i>H</i> (km.) |
|-------------|----------------------------------|-----------------------|----------------|
| 180 | 0.4×10^{-10} | 7.8×10^{-13} | 27 |
| 200 | 3.2×10^{-10} | 3.9×10^{-13} | 35 |
| 220 | 2.0×10^{-10} | 2.5×10^{-13} | 52 |
| 240 | 1.4×10^{-10} | 1.7×10^{-13} | 46 |
| 260 | 7.7×10^{-11} | 0.4×10^{-13} | 32 |
| 280 | 4.5×10^{-11} | 5.5×10^{-14} | 47 |
| 300 | 3.0×10^{-11} | 3.7×10^{-14} | 57 |
| 320 | 2.1×10^{-11} | 2.6×10^{-14} | 62 |
| 340 | 1.6×10^{-11} | 2.0×10^{-14} | 68 |
| 360 | 1.2×10^{-11} | 1.5×10^{-14} | 75 |
| 380 | 0.3×10^{-11} | 1.1×10^{-14} | 77 |
| 400 | 7.2×10^{-12} | 8.8×10^{-15} | 79 |
| 500 | 2.1×10^{-12} | 2.6×10^{-15} | 80 |
| 600 | 7.1×10^{-13} | 8.7×10^{-16} | 90 |
| 700 | 2.5×10^{-13} | 3.1×10^{-16} | 99 |

the indentation corresponds to a peak in temperature near 220 km height, the maximum value being near 60 M°K. The value of *M* is not known exactly, but is probably near 20. Such a peak in temperature might imply the absorption of certain wave-lengths in the solar radiation at heights near 220 km, though this deduction must be regarded as speculative²³.

Conclusions

A consistent picture of the air density at heights between 180 and 700 km is obtained from the orbits of 15 satellites (see Fig 1 and Table 2). The picture is more complete and more reliable at heights below 500 km than above. All the results refer, however, to the years 1957–59, and it is probable that the density varies in the course of a sunspot cycle. There is some indication of a peak in temperature near 220 km height, but there is no sign that density varies with latitude or season by a factor of more than 1.5. Analysis of the motion of *Sputnik 3* confirms this latter conclusion, for a height of 220 km, and shows some evidence of day-to-night variation in density.

I wish to thank Mrs D M C Walker for preparing the diagrams and tables in this article.

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³ Staff of Royal Aircraft Establishment, Farnborough, *Nature*, 180, 879 (1957)

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⁸ Jacchia, L G, *Nature*, 183, 526 (1959)

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NEWS and VIEWS

Nobel Prize for Chemistry for 1959

Prof Jaroslav Heyrovsky

PROF JAROSLAV HEYROVSKY, director of the Polarographic Research Institute of the Czechoslovak Academy of Sciences in Prague, has been awarded the Nobel Prize for Chemistry for 1959, for his discovery and development of polarography. A native of Prague, he studied under Sir William Ramsay and F G Donnan in London before the First World War and then returned to Prague to continue his research work. It is of interest that the work on the determination of the electrode potential of aluminium which led eventually to the development of the polarographic method was suggested to him by Donnan. The first polarographic apparatus was made in 1925, but the method did not become widely recognized for a further decade, and Heyrovsky's major book, "Polarographie", did not appear until 1941. However the number of papers dealing with polarography now approaches the 10 000 mark, and the technique finds application in many fields of chemistry and biochemistry, it has had a profound influence on analytical chemistry, for some determinations which are difficult or impossible to carry out by other means yield readily to polarographic treatment. In addition, there have been made non-analytical applications. For example, the kinetics of electrode reactions and of chemical reactions associated with redox processes have been studied, redox potentials have been determined and the energetics of the reduction of organic compounds have been elucidated. Prof Heyrovsky has not enjoyed good health for some years, and is therefore prevented from accepting many of the invitations which he receives to lecture abroad. The present award is a timely recognition of his great services to analytical chemistry, particularly as he will celebrate his seventieth anniversary next year.

Glass Technology at Sheffield

Mr Michael Parkin

WITH the retirement of Mr Michael Parkin the Department of Glass Technology in the University of Sheffield lost its last member of that small team of pioneers recruited by Prof W E S Turner in the years immediately following the First World War to build up a department which has become world famous. Mr Parkin studied chemistry in the University of Sheffield; however, his studies were interrupted by war time services in an explosives factory and in the Royal Flying Corps. In 1920 he joined the Department of Glass Technology, and apart from a short period in industry (he was works chemist to Messrs Barr and Stroud Ltd, 1924-28) he has served the Department continuously. Until 1955 the Department performed dual functions carrying out the work of a University department and advisory work and investigations for the industry under the advice of the Glass Delegation, the members of which were roughly equally divided between the University and the glass industry. Mr Parkin made a major contribution to this work. This prevented his taking a direct personal responsibility for the research side of the work of the Department, but those whose responsibility it was to direct the research work would be the first to acknowledge the important part played by Mr

Parkin in assisting research workers. In 1955 the industrial work was taken over by the newly formed British Glass Industry Research Association, a step which Mr Parkin never pretended to approve but, as all who knew him would expect, he has during these past four years, spared no effort to help the University Department in its new regime to flourish. Perhaps the value which his present colleagues place on his services can best be emphasized by saying that he has been persuaded to continue as a part-time member of the staff for a short period while certain plans for future staffing of the Department mature.

British Association Representatives in the U.S.S.R.

THE British Association for the Advancement of Science has accepted an invitation from the U.S.S.R. - Great Britain Society conveyed through the Soviet Embassy in London, to send two representatives to the U.S.S.R. to visit schools, universities and scientific institutions to meet Russian scientists and to discuss future relationships and exchanges. The British Association's representatives are Dr W E Swinton who is an honorary general secretary of the Association, and Sir George Allen, who is its secretary.

European-American Nuclear Data Committee

A COMMITTEE for European-American Nuclear Data has been set up by the European Nuclear Energy Agency, in agreement with Euratom the United States of America and Canada, to assure collaboration among members and associate countries of the Organization for European Economic Co-operation in the measurement of nuclear properties. The Committee will be primarily concerned with measurements of nuclear cross-sections and other basic data essential for the technical development of nuclear energy. The Committee is to consist of thirteen experts from the United States, Canada, the United Kingdom, the Euratom and other O.E.E.C. countries. Its operations will be in accordance with existing bilateral agreements. The work of the Committee will include the critical review of existing knowledge of nuclear cross-sections and constants and of facilities, techniques and man power available for their determination. The Committee will also collect and correlate data from available sources, seek to establish a standard nomenclature and methods of presentation for such data, and recommend and sponsor, as necessary, technical meetings and symposia to further its objectives. Finally, the Committee will promote the pooling and exchange, where appropriate, of equipment and personnel. Further information can be obtained from the Organization for European Economic Co-operation, Château de la Muette, 2 rue André Pascal, Paris XVI^e.

New Forensic Science Society

A DECISION to form the Forensic Science Society was taken at a well-attended meeting held at the University of Nottingham on October 31. The object of the Society is to advance the study and application of forensic science in all its branches. With this aim in view, a series of symposia to be held alternately in London and in the provinces is being arranged.

Among the subjects suggested for discussion are blood, hypoglycaemia, street accidents and instrumentation. All persons professionally interested in forensic science are eligible for membership. The president of the Society is Dr J B Firth, and the secretary Dr E G C Clarke, of the Royal Veterinary College, London, NW 1, from whom further information can be obtained.

Preservation of the Malvern Hills

As a result of the confirmation, by the Minister of Housing and Local Government, Mr Henry Brooke, of an order made by the National Parks Commission under the National Parks and Access to the Countryside Act, 1949, about forty square miles of the countryside in the counties of Gloucester, Hereford and Worcester, including the whole of the Malvern Hills, are to be established as an 'area of outstanding natural beauty'. The designated area extends from Knightwick in the north to Bromsberrow in the south and from Suckley, Cradley, Coddington, Wellington Heath and Ledbury in the west to Welland and Great Malvern in the east. It includes such well-known features as the Worcestershire Beacon, North Hill and the National Trust's property at Midsummer Hill. The responsibility for preserving the landscape rests with the County Councils of Gloucestershire, Herefordshire and Worcestershire as the local planning authorities. Government grants can be made at the rate of 75 per cent towards the cost of treating derelict land, tree planting and preservation and removing disfigurements. Grants are also available towards expenditure incurred in making agreements or orders for public access to open country and in appointing wardens. Designation does not provide any right of access to land not already open to the public. Nor does it affect the existing use of land, such as the use of War Department land for military purposes.

Newly Available Endocrine Preparations

THE Endocrinology Study Section of the National Institutes of Health has the following highly purified pituitary hormones available for distribution free to qualified investigators: growth hormone, bovine, non-sterile for animal experiments only, follicle-stimulating hormone, ovine, sterile preparation, 25 mgm vials for experiment, 5 mgm vials for assay standard, luteinizing hormone, ovine, sterile preparation, 10 mgm vials, prolactin, ovine, sterile preparation, 25 mgm vials. Further information can be gained from Dr R T Hill, Executive Secretary, Endocrinology Study Section, Division of Research Grants, National Institutes of Health, Bethesda 14, Maryland.

National Science Foundation Grants for Private Foundations in 1957

GRANTS made by the National Science Foundation for scientific research and development by private philanthropic foundations and voluntary health agencies totalled 95 million dollars during 1957, of which about 59 million dollars was in support of basic research (No 15, Reviews of Data on Research and Development, National Science Foundation, Washington, D C). It is estimated that research expenditure for 1957 by private foundations and health agencies in the United States amounted to about 8 per cent of the estimated national basic research expenditure of 700-800 million dollars. Expenditures for research and development by these

institutions amounted to less than 1 per cent of the total expenditures for research and development by all organizations. Of 4,067 private foundations surveyed, 438 reported research and development programmes, and a total expenditure of 72 million dollars. Twelve foundations accounted for more than half this expenditure. 82 per cent was in the form of grants and related administrative expenses to outside organizations. The latter were predominantly educational institutions and their affiliated professional schools and hospitals. One in five foundations with research and development programmes reported expenditure for research in their own laboratories or facilities. The major part of support by foundations in 1957 covered the life sciences, accounting for 45 per cent of their total research and development expenditures. The social sciences were next in volume of support, and the physical sciences last, according to the report. Twenty-five of the thirty voluntary health agencies surveyed for 1957 reported expenditure for research and development, this amounted to 23 million dollars, of which almost one-half was for basic research. Four of the health agencies accounted for more than four-fifths of the total research expenditures, most of which were in the form of grants to outside organizations and individuals. Educational institutions and affiliated medical schools and hospitals were the major recipients. The voluntary health agencies concentrated almost exclusively on the support of biological and medical research.

Illuminating Engineering Society

At the meeting of the Illuminating Engineering Society held in London on October 13, Mr H G Campbell was installed as president of the Society for 1959-60. Educated at Oundle and Queens' College, Cambridge, Mr Campbell is managing director of Benjamin Electric, Ltd, and a director of Holophane, Ltd. The Leon Gaster memorial premium of the Illuminating Engineering Society for 1959 has been awarded to Dr R G Hopkinson and Mr J. Longmore (both of whom are with the Building Research Station of the Department of Scientific and Industrial Research) for their paper entitled "The Permanent Supplementary Artificial Lighting of Interiors".

U.S. Society of Protozoologists

THE following officers, for the academic year 1959-60, were elected or appointed at the annual meeting of the Society at Pennsylvania State University, during August-September. *President*, Dr Norman D Levine (University of Illinois), *Vice-President*, Dr. Reginald D Maxwell (Syracuse University), *Executive Committee (new members)*, Dr E R Noble (Santa Barbara College, California), Dr. Charles Ray, jun (Emory University).

Mond Nickel Fellowships

THE Mond Nickel Fellowships Committee announced recently the award of a Fellowship for 1959 to Mr D J O Mann (John Lysaght's Scunthorpe Works, Ltd), to study the practical applications of recent metallurgical research and techniques to the production of basic semi-finished steel, and Mr N J B Pocock (Copper Pass and Son, Ltd), to study developments in extractive metallurgy in the United Kingdom, Europe, the United States and Canada, and their dependence on the size and location of the organizations concerned.

University News

Hull

THE Department of Scientific and Industrial Research has made a grant of £6,000 to the Department of Chemistry towards the purchase of a mass spectrometer in support of research by Dr G C Bond.

The Nature Conservancy has made a grant of £4,900 to the Department of Geography for a three year investigation into the coastal geomorphology of Holderness and Spurn Head.

The following appointments to lectureships were made and took effect as from October 1: F J Bryant (physics) and I C Williams (zoology).

London

THE following titles are announced that of professor of physics in the University of London, conferred on Dr M Blackman, in respect of his post at the Imperial College of Science and Technology of professor of physical chemistry in the University of London, conferred on Dr F C Tompkins, in respect of his post at the Imperial College of Science and Technology, of reader in biochemistry in the University of London, conferred on Mr S P Datta in respect of his post at University College of reader in applied mathematics in the University of London conferred on Dr O W Kilmister, in respect of his post at King's College.

Oxford

RESEARCH grants are announced as follow by the Medical Research Council, a grant not exceeding £1,100, for one year as from October 1, for scientific assistance in a study by X ray analytical methods of insulin and related structures, to be carried out in the Laboratory of Chemical Crystallography under the direction of D M Hodgkin, reader in X ray crystallography, by the United Kingdom Atomic Energy Authority, a grant not exceeding £5,700 for three years as from October 1, 1959, for studies in inter ferometric spectroscopy, to be carried out in the Clarendon Laboratory under the direction of H G Kuhn, also a further grant not exceeding £1,250 during the period October 1 1959, to September 30, 1960, for work on the constitution of bismuth rich alloys, being carried out in the Department of Metal lurgy under the direction of Prof W Hume Rothery by the U.S Public Health Service, a sum of 14,160 dollars for one year from September 1, 1959, for the continuation of research on vision and light quanta being carried out in the Department of Physiology by M H Pirenne, under the direction of Prof E G T Liddell.

The Department of Scientific and Industrial Research has provided grants not exceeding £1,000 for one year as from October 1, 1959, for research on some natural products with biological activity, to be carried out in the Sir William Dunn School of Pathology under the direction of Dr E P Abraham, £1,500 for one year as from October 1, 1959, for research into perceptual limitations in high-speed performance in the Institute of Experimental Psychology by H Kay, under the direction of Prof R C Oldfield £22,860 for three years ending September 30, 1962 for an investigation of the geological ages of rock series by methods based on natural radioactivity, being carried out in the Department of Geology under the direction of Prof L R Wager, £1,220 for equipment for research on the biochemical mechanism of cell division, to be carried out in the Department of Biochemistry under the direction of Sir Hans Krebs,

and £25,725 for the period October 1 1959, to July 31 1962, for an investigation of materials, using magnetic resonance and double resonance techniques, to be carried out in the Clarendon Laboratory under the direction of Prof B Bleaney.

The Admiralty has supplied, for the year ending March 31 1960, a grant not exceeding £9,534 10s 0d, for the continuation of research on centimetre waves and fundamental problems being carried out in the Clarendon Laboratory under the direction of Prof B Bleaney and the Ministry of Supply a grant not exceeding £1,175 for a year from September 1, 1959 for the continuation of an investigation of fluoro carbohydrates being carried out in the Department of Biochemistry under the direction of Dr P W Kent.

Announcements

MR F O BRABY, chairman and managing director of Frodks Braby and Co, Ltd, has been elected chairman of the Council of the British Non Ferrous Metals Research Association in succession to Dr Maurice Cook, who retires from that office on December 31.

The Infra Red Development Co Ltd., Welwyn Garden City, has amalgamated with Hilger and Watts Ltd., 98 St Pancras Way, Camden Road, London, N W 1. The Infra Red Development Co was founded in 1946 and specializes in the analysis of gases by non-dispersive infra red techniques, primarily for industrial purposes, it has been under the technical control and management of Mr W B Bartley, who will remain managing director. It will continue to operate at its works and offices in Welwyn Garden City.

THE well known instrument makers, Griffin and George, Ltd., Ealing Road, Alperton, Wembley Middlesex, are opening a new branch at 626 Welbeck Road, Walker, Newcastle upon Tyne. To celebrate this step, two exhibitions are being held, at the Heaton Assembly Rooms, Heaton Road, Newcastle upon Tyne during November 17-20 and at the Corporation Hotel, Corporation Road, Middlesbrough on Tees, during November 23-25. The exhibitions will show a representative range of equipment of the latest type for education, research and development and industry.

UNDER the provisions of the Fulbright Programme travel grants are available to citizens of the United Kingdom and dependent territories, to go to the United States for an academic or educational purpose, provided that they have adequate financial support in dollars for the visit and have been accepted by an American institution of higher learning. Grants cover the cost of direct travel between the candidate's home and the American university or institution. They are available during June 1, 1959-August 15, 1960, for which applications must be submitted by March 14, 1959, and August 16, 1960-April 1, 1961 for which applications must be submitted by June 1, 1960. Application forms and further information can be obtained from the United States Educational Commission in the United Kingdom 71 South Andley St., London, W 1.

We regret that in the article entitled "Scientists in the Public Service in Britain" in *Nature* of September 10, p 858, the statement issued officially relating to Dr J W G Lund is incorrect. Dr Lund is in charge of the algological research of the Fresh water Biological Association, of which Mr H C Gillson is director.

BOOTS' NEW BIOLOGICAL RESEARCH LABORATORIES

By DR. G. I. HOBDAV

Director of Research

DURING a night-time air-raid on Nottingham in May 1941, nearly all the research facilities of Boots Pure Drug Co., Ltd., were destroyed. Blast and fire reduced virtually all the chemical and biological laboratories to heaps of charred rubble. The timing of this disaster could not have been more unfortunate. Under the stimulus of the national emergency we were expanding our research operations to enable the company to manufacture many vital drugs of European origin, supplies of which had been cut off by the War, penicillin, in the development of which we were to collaborate, was about to emerge. It was urgently necessary, therefore, to re-house our chemists and biologists as soon as possible. Because new construction was out of the question existing premises had to be converted. Choice of these was not easy since the Research Department was by no means the only one to suffer damage and every foot of space in the company's buildings in and around Nottingham was at a premium.

After due consideration, it was decided to re-house chemistry and biochemistry in a nearby building on the Island Street site and to evacuate the biological facilities, including bacteriology and pharmacology research and standardization, to a heterogeneous group of company buildings in West Bridgford, a Nottingham suburb. These latter, on which over the years a considerable amount of money has been expended, have served us well. Of course, it was evident from the beginning that they would answer our needs for only a limited period. But, as with many war-time expedients, building restrictions in the post-war years and the subsequent need to share out the capital cake among an increasing number of growing members of the company left us in occupation of them for longer than was originally intended. However, after about eighteen months of active planning we started construction of a new biological research building in September 1956, and occupation of it has just been completed.

The new building, which was designed by Boots' architectural staff, is sited in Nottingham a short distance away from the chemical manufacturing plant, but near enough so that services such as steam, electricity and water are drawn from the central works supply. It is near the present chemical and biochemical research laboratories and immediately adjacent to the site on which these facilities will be re-housed within the next few years. In plan, the building is in the form of an irregular H, one wing of four floors houses administration offices, Medical Department, library, canteen, conference

room and a fully equipped lecture theatre seating 200, the linking block contains the main staircase and lifts together with lavatories and cloak-rooms, the other wing, longer than the first and on seven floors with a basement, is entirely laboratories. The total floor area is approximately 90,000 sq ft. Externally, the building is of striking appearance, one wing is of brick and the other is faced with ceramic tiles in a checker-board pattern of grey and yellow. In internal design the administration wing and linking block are fairly conventional, but features of special interest include the pre-stressed concrete main staircase and the undulant ceiling in the canteen. The lecture theatre, which is acoustically designed, is fitted with stackable chairs which can be removed, entirely liberating the floor space for exhibitions, etc. Also to be noted is the pleasant medical and biological library housing 15,000 volumes, the stack room of which is fitted with mechanically operated stacking for economy of floor space. The décor throughout is modern, but not aggressively so, using mainly monochromatic treatments and avoiding disturbing colour contrasts. In the entrance lobby is a large colourful mural, abstract in design but intelligibly depicting the scientific disciplines provided for in the building.

The laboratory wing is functionally planned to accommodate the biological procedures employed, the common links throughout being laboratory animals and micro-organismal techniques. Required floor area and available site area comparison clearly pointed to a multi-storey building, this was quite acceptable, indeed in many respects desirable, since it permitted a plan of isolation of different functions on separate floors while reducing circulation distances.

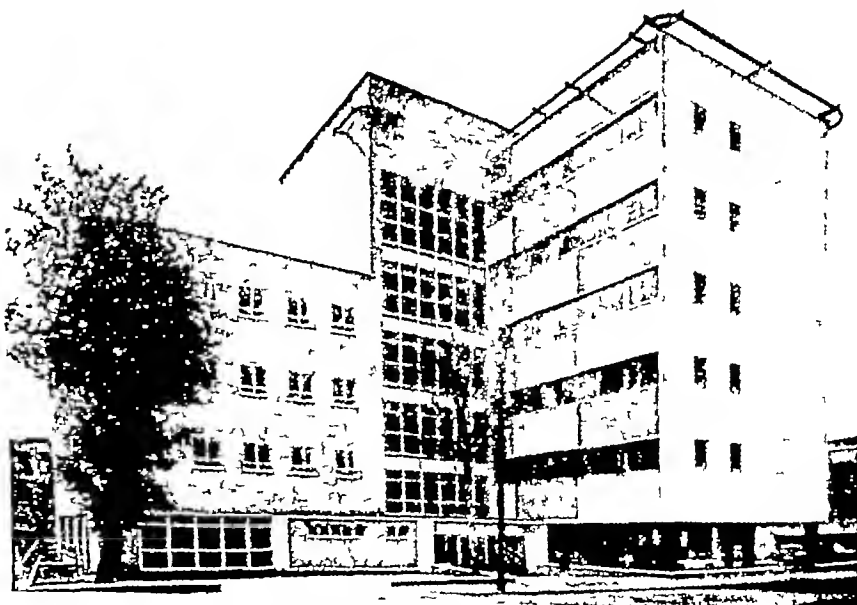


Fig. 1. Main entrance to Boots' Biological Research Laboratories. Administrative offices, library and lecture theatre are on the left, laboratories on the right.

and simplifying centralized servicing. The floors were planned on a 9 ft module in a block 200 ft long and 45 ft wide. This plan gave a spiral corridor arrangement which again helped in the separation of functions, since it was easy to form the areas at both ends into isolation units. A steel framed building was chosen with space-frame girders 3 ft 6 in. deep and 45 ft span. By this arrangement none of the internal walls is part of the structure, permitting alteration of the working areas as the need arises, it also provides a space between ceiling and floor above in which services are distributed. Vertical distribution of services is through a duct, 16 ft by 17 ft, which goes right through the building from top floor to basement. The whole of the laboratory wing is air-conditioned, inlet air being drawn in through an electrostatic precipitator and distributed through two separate systems, one serving the east side and the other the west side to give flexibility in taking care of solar gain through the large unopenable windows. A plenum system is used with pressure differences carefully arranged especially in laboratories where micro-organisms are used. All extracted air from areas of possible infection is filtered sterile before being vented to atmosphere. Where necessary, 'hospital' finishes on walls and ceiling are employed to facilitate cleaning and sterilizing, floor coverings are sheet polyvinylchloride in laboratories and hard asphalt in animal rooms and wash down areas. Stainless steel benches and steel under bench fittings are employed in all sterile areas and teak tops with wooden furniture elsewhere.

Equipment cleaning and sterilizing are centralized in the basement, where all refuse is incinerated. There are two systems of automatic hoists for handling separately dirty equipment to the basement and returning clean equipment to the requisite floors. All equipment and material passing from the isolation areas are heat-sterilized before proceeding down the 'dirty' hoist. Media-making is centralized and from a food store on the top floor animal diets are delivered to appropriate floors by chutes.

Facilities for work with radioactive labelled substances are provided in a self-contained suite. The

main units of this are a synthetic chemical laboratory, a biological laboratory with separately vented cage cabinets and a radioactivity measurement laboratory. The main radioactive store is in a shielded room in the basement.

The work in the laboratories lies in the fields of pharmacology, toxicology, bacteriology, mycology, virology and parasitology. Some routine testing and standardization work is done on chemical and pharmaceutical production material, such as sterility testing of injections and bio assay of insulin. Other wise the work is investigation, much of it comprising the biological component of research projects involving other research divisions. For example, in the field of parasitology trypanosomiasis is a major project, and chemical substances synthesized in the nearby chemical research laboratories, or new antibiotics isolated in the antibiotic research unit are screened in the new building by specialized laboratory tests. Those of potential value will undergo more specific tests for activity and, in another unit in the building, for toxicity. Any worthy of clinical or field trial will be passed over either to the Medical Department or to the veterinary research division at Thurgarton, about ten miles outside the city. Work of this kind has produced 'Ethidium' and 'Prothidium' for treatment and prophylaxis of bovine trypanosomiasis. In a similar way the parasitologists working on amebiasis have contributed to the development of 'Entamide' for the treatment of amebiasis. Likewise the bacteriologists have collaborated with the chemists and pharmacists in developing a new antibacterial substance 'Dybonal'.

Team operations of this kind provide much of the impetus for progress in the search for new substances for the treatment of human, veterinary and plant diseases. The new laboratories form a vital link in the chain of investigations between the first conception of a new drug and its final availability to the public. They serve the future in providing the type of working accommodation which the young research scientists of to day expect and need in order to make their most effective contributions in the fight against disease.

THE BRITISH FOOD MANUFACTURING INDUSTRIES RESEARCH ASSOCIATION

THE British Food Manufacturing Industries Research Association Laboratories at Leatherhead were open to members on September 16 and to invited guests on the following day. The wide range of the research programme of the Association was demonstrated the exhibits covering work in progress for the eight main groups into which the membership is divided, that is to say, cocoa and chocolate, sugar confectionery, meat and fish products, jams and jellies, pickles and sauces, oils and fats (including margarine and compound cooking fats), bakers' prepared materials and miscellaneous products ranging from table jellies to salted nuts and potato crisps. The work undertaken covers fundamental chemical, physical and bacteriological investigations alongside technological aspects of food manufacture.

For the chocolate industry an item of major importance is the study of the rheology of molten

chocolate. An experimental viscometer was on show which had been designed and built to the requirements of the Association to give measurements of viscosity over a wide range of rates of shear. A method of plotting the viscometric data has been developed which leads to the flow properties of chocolate being expressible in terms of two constants. The glyceride composition of cocoa butter is being studied by chromatographic techniques. Complete separation of the mono unsaturated triglycerides has been achieved by reverse phase paper chromatography using a non polar stationary phase and a suitably chosen mobile phase. An investigation into the volatile constituents responsible for the flavour of cocoa and chocolate by gas chromatography is in its initial stage.

The properties of high boiled sweets particularly their behaviour on exposure to the atmosphere is being investigated by means of an apparatus which

permits samples to be boiled under closely controlled conditions at low moisture content. The drying of certain types of confectionery deposited in starch moulds is being studied in two ways with the view of reducing the 'stoving time' necessary for their production. First, the effects of temperature and humidity on the rate of drying of gelatine and starch gums are being studied in a cabinet in which these factors can be closely controlled. Secondly, as corn-starch is used as a moulding medium, an investigation of its equilibrium relative humidity at elevated temperatures is of importance, and an apparatus for carrying this out has been devised and built by the staff of the Association. Other items of research connected with sugar confectionery manufacture are concerned with the properties of glucose used in confectionery (corn syrup), particularly the prevention of foaming on boiling and the tendency for the material to darken on storage.

The programme of research for the meat products group includes biochemical studies on residual tissue respiration and the measurement of oxidation-reduction potential. Colour changes and fading in cooked cured-meats are being studied with the aid of reflectance spectrophotometry. On the technological level, cooking properties of sausages and their colour stability during marketing are being investigated.

The Association's bacteriological laboratory is concerned on one hand with problems connected with bacterial spoilage of food, including the 'blowing' of canned goods, greening in cooked cured-meats and bacterial growth in vacuum-packaged bacon, and on the other hand, with bacterial aspects of the curing and processing of meat. Members are also advised on questions relating to general factory hygiene.

Problems connected with the canning of herrings are being studied by members of the Association's

staff at the Torry Research Station, Aberdeen. The work involves chemical studies of herring flesh and the correlation of changes in the constituents of the flesh with flavour changes and with changes in texture which occur during the canning process.

The Association maintains close contact with horticultural stations concerned with the breeding and development of new varieties of soft fruits and helps the industry to assess their suitability for jam manufacture. The tendency for raspberry seeds to go 'blind', that is to say, become less visible, in jam is another problem which has engaged the close attention of the Association.

Much of the work in connexion with pickles and sauces is concerned with microbiological spoilage, and spoilage organisms from a large number of spoiled packs have been isolated and identified. Problems connected with the production of low-acid pickles involve studies of the pasteurization procedures necessary for a product which will combine adequate shelf-life with desirable appearance and eating properties.

In conjunction with the National Institute for Research in Dairying, an instrument for comparing the 'spreadability' of margarines has been developed. This instrument, the 'Fira/Nird' extruder, has proved to have applications in connexion with other foods and, indeed, in other industries, where the rheological properties of semi-solid materials are important.

The Association maintains an extensive library of books and periodicals. Research reports and other publications are available only to members of the Association, who also receive monthly issues of abstracts from current scientific and technical literature. Some two thousand items are abstracted in a year.

B. R. KNAPP

THE STRUCTURE AND CHEMISTRY OF PROTEINS

SYMPOSIUM ON PROTEINS AT PARKVILLE, AUSTRALIA

THE intensification in recent years of research relating to the utilization of the primary products of Australia, wool, meat, wheat and milk, and in medical research, resulted in the organization during September 10-11 of a symposium on "The Structure and Chemistry of Proteins", at the Division of Protein Chemistry of the Commonwealth Scientific and Industrial Research Organization Wool Research Laboratories, Parkville, Victoria.

The meeting was well attended, with eighty-five delegates participating. Several overseas visitors were present, including some who had attended a symposium on "Haematin Enzymes" in Canberra, immediately preceding the symposium on proteins.

The topics of the twenty-two papers presented ranged over many of the fields currently being investigated in other parts of the world, a notable exception, however, being studies of amino-acid sequences. This reflects the pre-occupation of Australian workers with the isolation and characterization of protein components from natural products as a necessary first step to a more comprehensive understanding of their structure. Although the complex protein mixtures of these products are the focal

point of much of the Australian research, studies involving purified soluble proteins, such as insulin and lysozyme, plasma albumin and other proteins as well as synthetic peptides are, however, also in progress. The rapid advances which are being made in our knowledge of the amino-acid sequence, structure and behaviour of these classical proteins assist in the understanding and interpretation of the chemistry of the more complex biological systems.

The contributions that X-ray, infra-red and electron-microscope investigations have made in the study of the structural organization of keratin were illustrated by the work of R. D. B. Fraser, T. P. MacRae and G. E. Rogers. The application of X-ray crystallography to the study of the three-dimensional structure of a simpler compound, toluene-*p*-sulphonyl-L-prolyl-L-hydroxyproline monohydrate, was described by J. Fridrichsons and A. McL. Mathieson, and this contribution emphasized the stereo-chemical problem encountered with prolyl residues in a polypeptide chain. The properties of protein complexes of the insect cuticle were described by R. H. Hackman and interest was aroused in the nature of their strong bonding to chitin and quinones. The isolation

of nucleoproteins and labile plant viruses from leaves and their susceptibility to degradation by salt were discussed by J W Littleton.

The chemistry of thiols and disulphides is a prominent feature of protein chemistry and was exhaustively discussed S J Leach and J M Swan described the important analytical advances made in this field with the aid of the polarograph and the preparative applications of sulphite in the presence of an oxidizing agent such as cupric ions. The various methods of splitting disulphide bonds and their application in the extraction of soluble proteins from wool were discussed by J M Gillespie, I J O'Donnell and E O P Thompson, and H Lindley reported on the varying reactivity of the disulphide bonds of insulin. J M Creeth and D J Winzor were concerned with the specificity of the reaction of iodine with the sulphhydryl groups of ovalbumin, while the important role of thiols in disulphide interchange reactions was clearly apparent in the experiments of P J R Hird, R Frater and J R Yates on the nature of cohesive forces in dough. Disulphide interchange was also responsible for the inhibition of several —SH enzymes by 'sulphanilamide' disulphides in an investigation reported by E Boeri and L Brighenti.

The physico-chemical characterization of proteins isolated from naturally occurring mixtures was covered in a further series of papers. The aggregation and disaggregation of soluble proteins and the changes induced during denaturation figured prominently in the discussions of papers presented by J M Creeth and L W Nicol on ureases, by B S Hartup, I J O'Donnell and E F Woods on soluble wool proteins and by H A McKenzie on various enzymes and globular proteins. The various techniques used to follow conformation changes were critically examined and it became clear that the behaviour of a particular protein in any given system was not necessarily indicative of the behaviour of other proteins in the same system. The surface denaturation of proteins was discussed by F MacRitchie and the application of the spread monolayer techniques to a comparison of the surface chemical properties of various cereal proteins was described by N W Tschoegl. The preparative applications of electrophoresis were

illustrated by the work of J F O'Dea on the isolation of components of serum while P R Carnegie and R L M Synges described the electrophoretic behaviour of cupric complexes of oligopeptides and a possible method for selectively isolating dipeptides from mixtures of peptides.

Chromatography as an aid in the purification of proteins was introduced by A. G. M. Marr, who described the fractionation of serum proteins on 'DEAE cellulose'. D H Simmonds has applied this technique very successfully to the water soluble flour proteins and he also reported amino-acid analyses of the various fractions using ion-exchange chromatography with an automatic recording apparatus capable of handling eight ion-exchange columns eluted simultaneously. The continued interest of chemists in the quantitative analysis of protein constituents was evident in this paper and that of J H. Bradbury on an alternative method requiring paper chromatography of dimethylphenyl amino acids. This method was particularly applicable to the estimation of amide groups.

G Coleman and W H. Elliot described their work on the synthesis of an amylase by *Bacillus subtilis* and C J Shepherd discussed the effect of inhibitors of protein synthesis in *Aspergillus nidulans*.

A feature of the symposium was a lecture by Dr R L M. Synges on 'Naturally Occurring Peptides and Their Biological Significance'. Although the search for naturally occurring peptides has not been intensive it was apparent from the stimulating survey by Dr Synges that many unusual types of small peptide are already known. He went on to stress the necessity for quantitative data in the study of protein synthesis and expressed concern at the lack of experimental documentation for many of the generalizations by biochemists regarding the synthesis of proteins. A spirited discussion ensued and was continued in a subsequent session on protein synthesis.

Participants in the symposium were fortunate in having a range of papers presented covering most of the rapidly growing areas of investigation in the protein field and it may be hoped that similar conferences will be held in the future.

E O P THOMPSON

ELECTRONICS EXHIBITION

THE fourteenth Exhibition of Electronic Devices, organized by the Northern Division of the Institution of Electronics, was held at the Manchester College of Science and Technology during July 8-16. This annual exhibition is now well established and it provides an opportunity for new electronic apparatus to be demonstrated in rather less crowded conditions than obtain at the Physical Society Exhibition held in London during January.

A lecture programme was associated with the exhibition and, as is to be expected, a substantial part of this programme was devoted to transistor techniques. However topics of general scientific interest were by no means excluded, and lectures on the argon chromatograph, on photographic densitometry and on the use of X rays for micro-analysis were well attended.

The exhibition was divided into a manufacturers' section and a research section the research exhibits

forming much the smaller part of the whole. A relatively small number of research exhibits, especially from universities, has also been evident at the Physical Society Exhibition. Although research exhibits are of considerable general interest, and of special interest to those working in related fields, it is probable that for scientific workers as a whole the more important function of an exhibition of this type is to show instruments that are currently available. In the manufacturers' section this year's exhibition was notable for the extent of the exhibits of the various electronic agencies. These agencies handle the products of a number of manufacturers and they hold stocks of instruments and components. In the case of one agency the display occupied a whole room and included examples of the products of some sixty manufacturers.

Included in the new equipment on show were examples of 'second generation oscilloscopes'. Until

very recently, British manufacturers have been unable to offer high-performance oscilloscopes having trace brightness and amplifier band-width suitable for the display of single-pulses having fractional microsecond duration. This has meant that workers in such fields as nuclear physics and high-speed computing have either obtained equipment from North America or have constructed their own display systems. New types of oscilloscopes are now available from Messrs Cossors, EMI, Marconi Instruments and Solartron. The cathode-ray tubes are mostly of the post-deflexion acceleration type and run at voltages of 6–10 kV, amplifier band-widths are 10–20 Mc/s, and the deflexion sensitivity at full gain is about 100 mV per cm. This specification is adequate for all but the fastest applications, and for these, two manufacturers are offering oscilloscopes with distributed amplifiers having a band-width from

dc to 40 Mc/s. Messrs Cossor and Heathkit showed kits of parts that can be assembled to make items of test gear such as valve-voltmeters and simple oscilloscopes. The kits normally employ printed circuits, which simplify the wiring, and can be assembled with semi skilled labour. A wide variety of silicon devices are now available, and Messrs. Ferranti showed a range of silicon photo-voltaic cells, these have a response time in the microsecond region and have applications in equipments using modulated light. The new cells have a high conversion efficiency and in the larger sizes can be used as solar cells to provide electrical energy from sunlight.

This annual exhibition continues to be well attended and it provides an opportunity for scientific workers in the north-west of Britain to keep abreast of current electronic equipment and components.

V. H. ARTHUR

UNITED KINGDOM CIVIL SERVICE COMMISSION

THE ninety-third annual report of the Civil Service Commissioners, covering the year April 1, 1958–March 31, 1959, records an increase in the number of candidates successful in open competition from 13,057 to 14,616, but for the administrative class the number of successful candidates decreased from 39 to 37, though well above the 1956–57 figures, and some departments were short of recruits, although the number of unfilled vacancies is not large (Report of Her Majesty's Civil Service Commissioners for the period 1st April, 1958 to 31st March, 1959. Pp 36 (London: H.M. Stationery Office, 1959) 2s 6d net).

The Commissioners are continuing their efforts to attract a larger number of good candidates from the universities. Candidates in the limited competition for the administrative class further decreased in number. Recruitment to the senior branch of the foreign service was also disappointing, and the shortage of candidates for the statistician class persists. Less than 50 per cent of the declared vacancies as patent examiner have been filled and there was again a shortage of good candidates for scientific officer, engineering and draughtsmen posts, and many vacancies remain unfilled, particularly through a

dearth of physicists. Grave shortages remain in the telecommunications and other electronic fields, however, there was a small increase in the number of candidates in the senior scientific officer competition and most of the vacancies which had been notified were filled.

Applications in the assistant experimental officer/experimental officer competition remained remarkably steady and generally sufficient candidates were successful to meet departmental needs. The supply of biologists again exceeded the limited demand. The research fellowship competition continued to attract interest from workers in all fields of research, and thirteen candidates were offered the award. There is some evidence that it is becoming harder to attract good applicants for junior fellowships.

Results of interviews in Ottawa and Washington in April 1958 to select applications for research fellowships and scientific officer posts were less satisfactory than originally appeared likely, and in the event only one candidate joined the Service as Research Fellow and one as a senior scientific officer, although some well-qualified men appear to have been stimulated to return to Great Britain in the universities or in industry.

EUROPEAN NUCLEAR ENERGY RESEARCH

THE seventh annual report of the Netherlands–Norwegian Joint Establishment for Nuclear Energy Research*, describing the work of the Establishment during the period July 1, 1957–June 30, 1958, mentions that the research reactor, *Jeep*, was in almost continuous operation at 450 kW during the year, with a total release of heat of 105.6 MW days, but that the corrosive effects of the heavy water have grown worse and a minor leakage of heavy water occurred during April. The completion of the Halden boiling water reactor, which is an Institutt for Atomenergi project and which is situated inside a rock excavation near the paper pulp factory, Saug-

* Seventh Annual Report, July 1957–June 1958, of the Netherlands–Norwegian Joint Establishment for Nuclear Energy Research. Pp 32 (Kjeller near Lillestrøm, Netherlands–Norwegian Joint Establishment for Nuclear Energy Research, 1959).

brugsforeningen, will be delayed by about a year because of construction and design problems. The reactor tank was completed during the spring of 1958. The necessary amount of heavy water which was purchased from the United States of America is now stored at Halden, and part of the uranium ordered from Great Britain has been delivered. An agreement between Norway, Denmark, Sweden, Austria, Great Britain, Switzerland and Euratom, on the joint operation of the reactor, was signed by representatives on June 11, 1958.

Because of the higher demand for radioisotopes, and technical improvements in the production system, the number of isotope deliveries from Kjeller to customers outside the Establishment increased by 33 per cent over the previous year. The deliveries

were mainly to the Scandinavian countries. Detailed information about the type of isotopes produced and their distribution is given in the report. Separate sections deal with the activities of the Chemistry, Metallurgy, Reactor Engineering, Physics and Health Physics Divisions. The chemical analysis of uranium and D_2O is now carried out on a routine basis and the spectrographical methods used for impurity control of medical isotope products and the determination of plutonium have been improved. The main task of the metallurgical group has been the production of UO_2 pellets, and in addition to considerable computational work and experimental tests connected with the Halden boiling water reactor project, the Physics Division has obtained new neutron diffraction data on U_2O_5 and U_3O_8 . The Health Physics Division is responsible *inter alia* for the daily radiation monitoring in the laboratories, the radiochemical analysis of biological specimens and the general medical check up of personnel. Of the 191 persons controlled by the Division during the year, only one received a radiation dose exceeding 5 rems.

The Netherlands-Norwegian Reactor School was officially opened on April 12 and the first nine weeks standard course commenced on April 14 with twenty-eight students: fifteen from Holland, eleven from Norway and two from Switzerland. The construction of the new isotope building was started in January, and of an office building to house the ship propulsion group and the Engineering Division in April. As in former years the Establishment benefited from the exchange of scientists with similar institutions in other countries. Seven guest scientists worked at the Joint Establishment for Nuclear Energy Research for the whole or part of the period under review. The two sponsoring organizations of the Establishment, the Reactor Centrum Nederland and the Instituut for Atomenergi, took part in international co-operation in the field of atomic energy, in particular, in the European Atomic Energy Society, the Organization for European Economic Co-operation, and the International Atomic Energy Agency. Summaries of the main activities of the two organizations are given in the appendixes to the annual report.

THE FRANKLIN INSTITUTE

THE Board of Managers of the Franklin Institute in presenting their annual report for 1958 (*Journal of the Franklin Institute*, 267, 317, April 1959) express their gratification at the progress during the year in all the Institute's programmes of service to science, but point out that without increased funds the Institute cannot expand and may not be able to maintain its present activities. In addition to the Franklin Institute Laboratories and the Computing Center, both located in Philadelphia, the Institute owns and operates the Bartol Research Foundation in Swarthmore, Pennsylvania, and is trustee for the Biochemical Research Foundation in Newark, Delaware. The Institute conducts basic and applied research on a contract basis for government, industry and private concerns, and the Computing Center co-operates with the Laboratories which carry out projects under contract in the fields of engineering and the physical sciences. The Bartol Foundation is concerned with the study of fundamentals in physics: low-energy exploration and cosmic phenomena, and the Biochemical Foundation with cancer research.

It was to be expected that public interest in the activities of the International Geophysical Year, and in rockets, satellites and space travel, would largely colour the work of the Education and other divisions of the Institute during 1958. Of the twenty-one lectures presented at the Institute meetings during the year, eight were on subjects related to the space age: the exhibit, "Progress of Time", contributed to the Institute's Science Museum by the Hamilton Watch Co. included the Mars Space Clock, and other loan exhibits showed the successful launching of the Explorer rocket, the Vanguard satellite, and the Pioneer lunar probe. New presentations in the Planetarium were "The American Satellite" and "Astronomy in History", and the staff of the Planetarium were responsible for the operation of the Institute's Moonwatch Station, and the series of ten semi-technical lectures on astronautics sponsored by

the Astronomy Department were published in December as Monograph No. 6 entitled "Ten Steps into Space".

The Library of the Institute which began as a small collection in 1824 now comprises 102,054 volumes, of which 3,054 were acquired during 1958—980 by purchase, 544 by gift and 1,524 by binding. New acquisitions included eighteen Russian periodicals, four in translated English editions and a remarkable set of the owners' file copies of records and correspondence of the Penang Sugar Estates Co. (British Malaya), comprising twenty-three handwritten volumes of the work of the Company during 1870-97. A symposium on "Thermoelectric Effects" was held on September 8, primarily for research workers in this specialized field, and an all-day symposium on "Odeur" on October 21 during the "Cleaner Air Week" in Philadelphia. Three new titles were added to the series of monographs published under the auspices of the *Journal* "Particulate Emission", "The Airways Modernization Board—Its Mission and Methods" and "Ten Steps into Space" mentioned above.

Details are given in the illustrated report of the long range research programmes and new developments of the separate research organizations. These include air pollution research, thermoelectricity and semiconductor, electron microscope studies of dislocations in metals and zone refining of reactive metals, the physics of polymers, and flow loops in nuclear engineering. A novel etching technique has been developed for studying dislocation loops generated in metals under stress and their motion and growth in zinc have been filmed (*Journal of the Franklin Institute*, 267, 335, 1959). A simple sonic vibration method for the early detection of glaucoma has been demonstrated and an all-transistorized sensitive cane for use by the blind has been successfully tested. The report concludes with brief details of the finances of the Institute, the membership and staff.

ECONOMIC DEVELOPMENTS IN THE MIDDLE EAST

IN a report dealing with developments for the year 1957-58, published by the United Nations as a supplement to the world economic survey of 1958, there is included a useful survey of agricultural production and development, industry, petroleum production, and foreign trade in the several main countries included in this politically highly sensitive world region (Iran, Iraq, Israel, Jordan, Lebanon, Saudi Arabia, Sudan and Turkey). About one half of the text deals with factual summaries, and about one half gives statistical tables (Economic Developments in the Middle East, 1957-1958 (Supplement to World Economic Survey, 1958) Pp viii+104 (New York: United Nations, London: H.M. Stationery Office, 1959) 1 25 dollars, 9s, 5 Swiss francs).

The information given regarding the key product, oil, has special interest. The rapid recovery and expansion of this industry during 1957 (after the decline in production as a result of the Suez crisis) is remarkable. In 1957 there was an increase over 1956 of only 3.7 per cent, but this advanced by a further increase of 20.7 per cent in 1958. The total production of the Middle East as a share in world production rose to 23.6 per cent in 1958 as compared with 20 per cent in 1957. The main contributors to the large rise in oil production were Iran and Kuwait, but though producing relatively small quantities, other countries have been expanding their output at a high rate, and a new entrant was Syria where, in the north-east of the country, a field was discovered in 1958 estimated to have an output capacity of about 2 million tons. Agricultural production in the same year shows continued expansion at the rate

of about 3 per cent per annum, both in food production and in the output of industrial cash crops on which the several countries depend as a major source of foreign exchange. It is significant that the rate of growth in both exceeded the growth of population. A continued shift in the pattern of production towards industrial cash crops and greater use of fertilizers and agricultural machinery helped to maintain the rate of agricultural output, but the uncertainty of climatic conditions caused wide fluctuations.

Apart from the physical difficulties affecting production within the region, two comprehensive programmes of agrarian reform were started in the Syrian region and in Iraq late in 1958, and the social change and redistribution of income that these are likely to produce will very probably have a strong impact on the shape of future economic development. From these economic changes within, there emerges a picture of foreign trade and payments showing much variation, and with interesting evidence of change in operation leading to shifts in the geographical direction of trade, particularly of the cotton exporting countries, thus the United Arab Republic and Sudan moved away from Western Europe and the United States toward the U.S.S.R., Eastern Europe and the Far East. Iran, Jordan, Turkey and Israel, on the other hand, maintained their high share of trade with the United States and Western Europe, although an increasing proportion of the exports of Israel and Turkey went to eastern European countries in 1957 and 1958. Oil exports show a significant increase in their share to Asia and the Far East, though the dominant traditional markets in Western Europe are maintained. ALICE GARNETT

THE NATURE OF POLISHED METAL SURFACES

HOOKE, Newton and Herschel all held that the asperities in a roughly ground surface are cut away during polishing, leaving a series of fine grooves, the finer the polish the finer these grooves or 'scratches'. Rayleigh agreed that the asperities are worn down but thought that the material is removed in an almost molecular fashion. In 1921 Boilby advanced the radical view that, instead of the asperities being worn away, the depressions in the surface are filled in by material which is smeared across the surface, covering it with a layer which he thought was glass-like or amorphous in character. This has come to be known as the 'Boilby layer'. The idea of the layer being truly amorphous has been modified slightly in more recent times, but the basic concept of a layer which is physically distinct from the substrate and which has lost its obvious crystalline properties is still retained.

Boilby did not propose any specific smearing mechanism, although he inferred that surface tension forces were responsible. A most plausible mechanism was afterwards advanced by Bowden and Hughes which was based on observations that very high local temperatures can be attained when two solids rub

past one another. They suggested that asperities in the surface are melted when abrasive particles rub across them, the liquid so formed depositing in and filling adjoining depressions. It was further proposed that, due to very rapid chilling, this molten material solidifies in an amorphous-like condition.

A paper by L. E. Samuels reviews work carried out at the New South Wales Branch of Defence Standards Laboratories which strongly supports the earlier view that polishing is essentially a fine cutting process, and is believed to establish with reasonable certainty that the Boilby layer does not exist.

The new theory is that metallographic polishing occurs primarily by cutting, the individual abrasive particles acting in a similar manner to a planing tool. Material is removed and scratches are produced, the better the polish the finer the scratches. The surface is crystalline but deformed, the magnitude of the deformation decreasing with increasing fineness of polish to a surprisingly low level in the case of the finest polishes. Moreover, the deformation decreases rapidly with depth so that comparatively perfect material is exposed by a very light etch (*Austral J. Sci.*, 21, 6, 1959).

EEL MIGRATION

It seems probable that many of the difficulties that I have undermined Dr Tucker's belief¹ in the ability of European eels to return to the Sargasso Sea would have disappeared if he had compared the European eel with the Atlantic salmon, the return of which to spawn after a migration of comparable difficulty is more readily demonstrable.

Salmon, both Atlantic and Pacific, migrate to feed in the sea: here they may stay for one and a half to four or more years. This active feeding period is followed by a spawning migration during most of which the animal does not feed. Fasting begins as the salmon nears fresh water; the subsequent migrations upstream, often carried out under difficult physical conditions, are very fatiguing and call for a considerable expenditure of energy. Yet after a migratory fast lasting up to a year, millions of salmon survive to partake in most energetic spawning activities. In fact, about 5 per cent return to spawn again, and a small proportion may spawn three times.

Eels spend most of their lives feeding in fresh water. This feeding period of from six to twenty five years duration is as clearly preliminary to spawning migration as are the years spent by the salmon in the sea. I do not agree with Dr Tucker that European silver eels are starving and debilitated: the many thousands that I have handled have been vigorous, extremely energetic and in good condition. It is of interest that eel-dealers store living eels for long periods, yet these eels are in the end still fat enough to be sold as highly nutritious food.

On their 3,500 mile spawning journey, eels have to contend only with slow moving ocean currents, not to be compared with the fast-flowing streams encountered by salmon. If eels travel at a modest 40 miles a day the journey need take only thirteen weeks—not a long fast compared with that of many salmon.

Dr Tucker claims that American eels, because of their larger size and apparently juvenile sex condition, are better suited than European eels for their spawning migration. But size is not a criterion of condition: salmon, ranging from 3½ lb to more than 60 lb complete their spawning migration successfully, many reach the rivers of Britain in an advanced stage of sexual maturity, fast, and survive to spawn. Recent examinations of the state of the gonads in large samples of eels have convinced me that the European silver eel is not "already well advanced towards being a reproductive oceanic fish". The gonads of silver eels are not in an advanced stage of development. Many silver eels migrate when their gonads are scarcely more advanced than those of yellow eels. In fact, the gonads of the silver eels are in about the same developmental stage as those of female salmon smolts and unspawned male smolts.

One of the most strongly emphasized points in Dr Tucker's argument is that European silver eels are rarely caught at sea. But neither apparently are American eels. Nor is it surprising that eels at sea are elusive. They do not feed and so cannot be caught on long lines, nor are they likely to stay captive in any normal deep sea trawl. It is no cause for astonishment that eels are not caught in the Straits of Gibraltar, for no commercial fishing gear in use there can be expected to catch eels. Salmon are

rarely caught off shore, and salmon should be much more catchable, for they feed in the sea, they stay there much longer and they are not so shaped as to make escape from nets easy. Yet countless millions reach their spawning grounds yearly, though the number caught in the open sea is very small.

Finally Dr Tucker's hypothesis requires that a large proportion of the American eel population is 'lost' yearly as a reproductive potential, since American eels which spawn in the wrong place produce progeny which become European eels and never succeed in spawning. If this were a true account, there would be intense selection in favour of eels which found the 'right' spawning ground. It would be very surprising if natural selection on this large scale had failed to eliminate the European eel in a few generations.

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I must emphasize at the outset that Dr Jones's communication, even if it were acceptable in its entirety, contains nothing relevant to the fundamental problem of eel navigation and nothing which has any bearing upon my hypothesis that the two Atlantic *Anguilla* phenotypes may be environmentally differentiated and distributed without genetic intervention. For the rest, the difficulties which led to a heavily documented paper¹ are not likely to be dispelled by criticism which ignores not only literature already cited some of it on two occasions^{2,3}, but also that relevant to its own substation. Moreover, a recent independent review⁴ has made such a comparison as Dr Jones demands, and without detriment to the new theory of eel migration.

Both the salmon and the eel undergo migrations which raise problems of navigation, physical effort and osmo regulation. Thereafter the comparison breaks down to such an extent that knowledge of one casts little light on the ways of the other. The eel is catadromous, the salmon anadromous. The first migration of the eel is as a larva passively transported in the surface layers. Its second as a starving adult travelling in the deeper layers and probably by a different return route. Both of the migrations of the salmon are accomplished as an adult fish, travelling in substantially the same water masses along the same routes and actively feeding until the final return to fresh water. Eels are in peak condition shortly before the commencement of their final journey; salmon shortly before the end of it.

The European eel is, in Dr Jones's view, an oceanic traveller, accomplishing a long journey of at least 3,500 miles for the south west European stocks and at most 5,000–6,000 miles for the White and Black Sea stocks. The longest recorded journey for an Atlantic salmon is 1,730 miles in 328 days⁴ characteristically, its migrations are much shorter—a few hundred miles along the coast or to and from feeding grounds off the shelf—and fairly easily explained by internal changes in the osmo regulatory mechanism.

which prompt it to seek salt or fresh water and by a proved propensity to wander along the coast until it smells the outfall of its native stream. However arduous the last stage of the journey of the salmon up-river, it can and does alternate activity and rest and make use of slack water and pools for the latter purpose, for the eel in an opposing ocean current no such respite is possible without losing ground.

Segregation of breeding stocks of salmon provides excellent opportunities for adaptive variation and variation of inherited behaviour-patterns through genetic isolation, in the eel nothing of the kind is possible.

Given this summary of the habits of the two fishes, which further have very different patterns of locomotion and are widely unrelated, I see very little ground for generalization from one to the other, the analogy is rejected with good reason, but Dr Jones should not assume that it was ignored.

Salmon survival for subsequent spawnings is due in part to the fact that degenerative changes in the gut are confined to the mucosa, which is renewed in kelts that recover⁵, in the eel the changes are profound and lead ultimately to complete destruction of the gut^{2,6}. The personal findings of Dr Jones, like those of Prof. D'Ancona previously dealt with², do not affect the evidence that the gut of the European eel is self destroyed before the fish is more than a few hundred miles offshore.

Here a new point may be introduced. Experimental work on the eel has shown that in the sea it contrives to maintain effectively the internal environment of the freshwater fish. It does this by swallowing sea water, absorbing water and salts through the intestine, excreting an isotonic urine and discharging surplus chlorides through the secretory cells on the gills⁷. In European eels, once degeneration of the gut has proceeded merely far enough to impair the absorptive function, this mechanism can no longer operate, osmo-regulation must then depend wholly upon the relative impermeability of the body mucus and upon compensating liberation of water through breakdown of stored lipo-proteins. Failure of the whole apparatus would lead to rapid exsiccation and death. Experimentally induced failure, by preventing eels from swallowing sea water, does in fact produce an 11-14 per cent loss in weight and death within 3-4 days⁷. This situation, even more than the likely inadequacy of the food reserves to provide for locomotion, physiological work (for example, in chloride secretion) and gonad maturation, could account for the failure even of Mediterranean eels to reach apparently suitable breeding-grounds in that sea (*post*).

I am not subdued by Dr Jones's experience with thousands of eels. The great curse of the voluminous work upon eels, upon the Salmonidae and upon sundry other animals, has been that too much of it has been mechanical and repetitive, replete with experiments unintelligently planned and mountains of data inadequately pondered, parochial alike in the range of its geographical experience and in its isolation from relevant literature from alien countries and related disciplines.

The physiology of the eel is not "clearly preliminary to spawning migration", it could be, and I think is, atavistic and doomed to fruitless failure. We have no right to assume climax as normality in any incomplete behaviour-pattern or physiological process when climax has never been observed and no unequivocal circumstantial evidence of climax is available.

I agree that a 'stored' silver eel may well retain its condition like any other relatively quiescent animal, migrating eels, however, lose up to 20 per cent of their weight before they leave the Baltic⁸ (reservo fat amounts to about 25 per cent) and this over periods greatly in excess of that shown to be necessary for the initial osmotic adjustment⁷. Either the food reserves are being rapidly used up, or there is a loss of water showing that the osmo regulatory mechanism is already breaking down under the quite low salinities of the Baltic.

Dr Jones suggests a hypothetical "modest 40 miles a day" over thirteen weeks for the eel migration. Norwegian work⁹ summarized by Menzies¹⁰ has shown that, of 598 long-distance journeys by marked and recovered salmon, 569 were accomplished at 5-25 miles a day and only twenty-nine at higher speeds up to 62 miles a day. Speeds for Baltic eels marked on a comparable scale⁸ (the work was cited previously¹) are in general between 5 and 10 miles a day, the record is 32.5 miles a day sustained over a mere two days.

Comparative data for condition of American and European eels are hard to come by. Vladyskov¹¹ gives 411 gm for the mean weight of Quebec bronze eels of 61 cm, compared with Frost's 425 and 414 gm for 61 cm¹². Windermere yellow and silver eels, respectively. The superficial agreement does not allow for the fact that the American eels cited are at an earlier and probably much younger stage, nor deny that the average weight of migrating American females is four times greater than that of the European, that their maximum sizes and weights are greater and their potential journey much shorter. I do not think we can avoid the conclusion that the American eels are better prepared. Dr Jones's citation of the range of weights of salmon grilse is meaningless without an indication of the success-rates at different sizes and of the conditions overcome. Such data as are available for the migration speeds of the outward-bound salmon smolt¹³ show that these are much slower than those of the larger returning grilse. Further, maximum velocity in fishes is a function of length and frequency of tail-beat, though the latter does fall with increasing size, larger individuals are faster swimmers¹⁴.

My paper¹ mentioned merely "perceptible enlargement of the gonads", a statement in agreement with Dr Jones's findings. It then proceeded clearly to specify those characters of migration livery and bathypelagic adaptation in which, by comparison with the American eel, the European may be regarded as advanced.

A surprising variety of fishes, including other Apodes, have been taken in deep-sea trawls by scientific expeditions, I have before me 29 *Synphobranchius* from a single haul of an Agassiz trawl at 1,300 metres. There are at least 108 cases of records, with Scottish interest alone, of salmon taken at sea, 82 by trawls and various nets¹⁵. Salmon are surely less numerous than eels, being capable of a maximum velocity of 10 m.p.h. for short periods¹⁶, compared with the eel's peak 2.6 m.p.h.¹⁷, they should have greater chances of avoiding nets and not less. The infrequency of capture of eels in European seas remains significant. Non-capture of American eels is agreed, there is, however, no convergence of essential migration routes and intensive trawling comparable to that of north-west Europe. I did not write of "commercial fishing gear" in the Strait of Gibraltar but of an "intensive study", still more explicitly,

scientific investigations by Danish, French and Monagasque expeditions

Evolution by natural selection of a population which chose the 'right' spawning ground would be conceivable enough in the case of, say, salmon in polluted and unpolluted tributaries of the Welsh Dee. The case of the eel is not so simple. The Atlantic *Anguilla* forms are believed to be environmentally differentiated by differences in the temperature stratification¹ and are certainly differently distributed by the various movements of the surface layers of the Sargasso between lat 20° and 30° N. In the underlying deep waters in which the eels breed, the temperature and salinity conditions at a given depth are relatively uniform over a wide area, it is therefore unlikely that any sensory discrimination could pick a 'right' spawning ground directly related to a 'right' surfacing-area. Selection in relation to travel and ripening times could not have any genetic effect owing to the failure of the current-system to return the larvae precisely to the parental starting points along the American coast. While the new hypothesis may seem more spectacular, it is statistically no more remarkable than the normally high infantile mortality rate accepted in marine animals; the survival rate is still sufficient to maintain the population. Parallel cases of expatriated populations failing to breed are the British *Octopus vulgaris*², the Norwegian *Palnurus elephas*³ and the Lagos *Branchiostoma nigerense*⁴, all of which are maintained by immigrations of larvae bred elsewhere and so represent similar cases of wasted reproductive potential.

There is likewise no ground for belief in selection producing genetic restriction of the eco-phenotypic variability potential of the Atlantic *Anguilla*, that is, eliminating the phenotypes with 110-119 vertebrae as such, as opposed merely to those going to Europe.

Some further evidence in favour of the new hypothesis is very briefly noted.

Possible parallel cases. Bruun⁵ has commented on the hitherto unexplained coincidence that, of four pairs of Atlantic apodal 'species', having distributions roughly similar to those of the two types of *Anguilla* larvae and, moreover larvae which can be taken "at the same place and same depth within a certain area of the Sargasso Sea", the American 'species' of each pair has the lower number of vertebrae (Table 1). This situation may well be due to a common eco-phenotypy rather than to coincident genetic effects.

Table 1. NUMBERS OF VERTEBRAE OR MYOMERES IN SOME NORTH ATLANTIC EELS, MAINLY AFTER BRUUN (REV 21)

| | East Atlantic | West Atlantic |
|-----------------------------------|---------------|---------------|
| <i>Anguilla anguilla</i> | 110-119 | — |
| <i>Anguilla rostrata</i> | — | 103-111 |
| <i>Conger conger</i> | 104-103 | — |
| <i>Conger oceanicus</i> | — | 140-149 |
| <i>Synbranchistoma laevis</i> | 143-154 | — |
| <i>Synbranchistoma infernalis</i> | — | 131-140 |
| <i>Leptocephalus surmuletus</i> | 111-110 | — |
| <i>Leptocephalus similis</i> | — | 104-113 |

Likewise, Tams Lycho⁶, supporting the new hypothesis, has suggested that there is a similar pseudo-speciation in the Atlantic Paralepid fishes (order Inimoli).

Extended pelagic phases. 'European' eel larvae grow to a greater length and unmetamorphosed ago than the 'American' and are, on the new hypothesis regarded as an extended pelagic phase of one species.

Parallel cases of facultative prolongation of larval or juvenile life in marine animals under conditions unfavourable to metamorphosis occur in the surgeon fish *Acanthurus hepatus*⁷, the frogfishes *Antennarius* spp.⁸, the *Macrorhynchus* larvae of the benthic octopus *Scaligeria uncinatus*⁹, and in numerous Decapod Crustacea¹⁰.

Selection of breeding grounds by *Anguilla* and *Conger*. On the old hypothesis, *Anguilla anguilla* and *A. rostrata* were separate species with distinct breeding grounds in the Sargasso Sea. The American *A. rostrata* and *Conger oceanicus* shared a common breeding ground. The European *C. conger* shared the only breeding ground of *A. anguilla* but also used other breeding grounds between Gibraltar and the Azores and inside the Mediterranean¹¹.

I have already noted the fact that *A. anguilla* does not breed in apparently suitable areas much nearer Europe than the Sargasso¹. The paradox raised on hydrological considerations is now reinforced by *Conger conger* acting as a biological indicator. We may conclude that the 'European' eel is not breeding in the Sargasso any more than it is in the Mediterranean or Eastern Atlantic.

Location of the *Anguilla rostrata* breeding-ground. I previously suggested that the *A. rostrata* breeding ground had been placed too far west¹. In support of this contention, be it noted that, until 1920, catches of *A. rostrata* larvae from all sources totalled only 34 specimens¹². In 1920 the *Dana* took a further 1,000 specimens, because, however, her track out of Porto Rico towards New York¹³ followed the north-east boundary of the 15 mm *A. rostrata* contour, it follows that data for and within that contour remain thoroughly inadequate. The probable breeding ground between c lat 20-22° N, long 50-60° W has not been investigated at the proper season. Material of the other American Apodes cited above is likewise scanty by comparison with the European¹⁴.

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MECHANISM OF ANIMAL JOINTS

Sponge-hydrostatic and Weeping Bearings

ANIMAL joints are very efficient pivots. Charnley¹ gives 0.01–0.02 as the friction coefficient of a human ankle joint and shows that this low friction does not result from hydrodynamic lubrication. He points out that ordinary boundary (thin-film) lubrication would produce five or ten times the observed friction and suggests that Nature may have discovered, in its combination of cartilage and synovial fluid, a system which is very slippery even under conditions of boundary lubrication. The purpose of this communication is to propose an alternative system, which is, in fact, an example of a new and interesting class of bearings. The principle is illustrated by the experiments to be described.

A piece of closed-cell sponge rubber (cell size 0.7 mm and less) had one of its impervious cover sheets cut off to expose the cells. This surface, lubricated with soapy water, was placed against a glass plate with a loading of about 40 lb/in². The friction coefficient was then measured as a function of the time for which the load had been applied (Fig. 1, curve a). The friction coefficient is extremely low, but rises in the course of an hour or so. If the sponge is separated from the glass for a few moments and then replaced, the friction falls to its initial low value. This is consistent with the idea that most of the load is supported in a frictionless manner by the little volumes of liquid trapped in the pores of the sponge. It is, in fact, a 'hydrostatic' bearing. The sponge material itself, being surrounded by liquid, is pressed against the glass only by its own stiffness. This is small enough to produce very little friction but still large enough to seal the cells (hydrostatic lubrication is not new, but previous arrangements have depended upon mechanical design to contain the lubricant and upon external pumps to pressurize it). The liquid pressure was measured and found to be about that required to support the load. Observation, through the glass, of the working face of the sponge clearly showed the water-filled pores. The movements of a particular volume of water could be traced by using dye. Substantial outward seepage of the water had occurred in an hour, which seems to explain the observed increase in friction with time. For purposes of comparison a sample of sponge rubber with open cells, but otherwise of about the same texture, was used. This should allow much greater seepage of fluid. Note (Fig. 1, curve b) the tremendous increase in the rise of friction. Lastly, to check the technique of measuring friction, a piece of closed cell sponge was tested with its cover sheets intact (Fig. 1, curve c). This shows the high value expected for plain rubber once the wringing-out of lubricant established boundary lubrication conditions.

A difficulty arises if one attempts to explain animal joint lubrication by this principle. The animal joint appears to involve two similar surfaces rather than a hard, impermeable surface running against the equivalent of a sponge. Two sponges do not run very well against each other. Suppose, however, that the sponge has a smooth, porous surface layer. Because of the porosity, this layer is surrounded with liquid, and so is not pressed hard against its mating

surface. At the same time it is smooth enough not to become entangled with the similar layer on the other surface of the bearing. The effect of porosity was demonstrated with closed-cell sponge. One of the cover sheets, and the underlying cells, was perforated with a sewing needle. This porous surface was run against glass using soapy water lubrication and showed much less friction (Fig. 1, curve d) than the unperforated cover sheet (Fig. 1, curve c).

A true animal joint model with two similar surfaces was much more difficult to imitate. It was hard to find a porous material which did not have an enormous friction coefficient when rubbed against itself. I found the best material to be sausage casing made from sheep intestine, lubricated with soapy water. Imitation cartilage was made by stretching this over the cut-open face of closed-cell sponge. Running two 'cartilages' against each other gave the result shown in Fig. 2, curve a, where the friction coefficient starts low and rises as seepage occurs. To check that trapped water is necessary, open-cell sponge was substituted for closed-cell sponge in the previous arrangement (Fig. 2, curve b). Easy escape of the water quickly raises the friction. Finally, the sponges were replaced by impervious 'Neoprene' sheets. Fig. 2, curve c, suggests that hydrostatic lubrication is occurring. This is presumably because the sausage casing itself contains considerable free water.

It should be pointed out that although the reasoning in this communication arrives at the permeable-surface-sponge-backed bearing as a modification of the sponge-type hydrostatic bearing, it could equally well be thought of as a bearing with a thick film of lubricant, where 'weeping' through the porous wall supplies enough liquid to maintain the film.

Weeping bearings give friction coefficients as low as those in animal joints. They can be made by

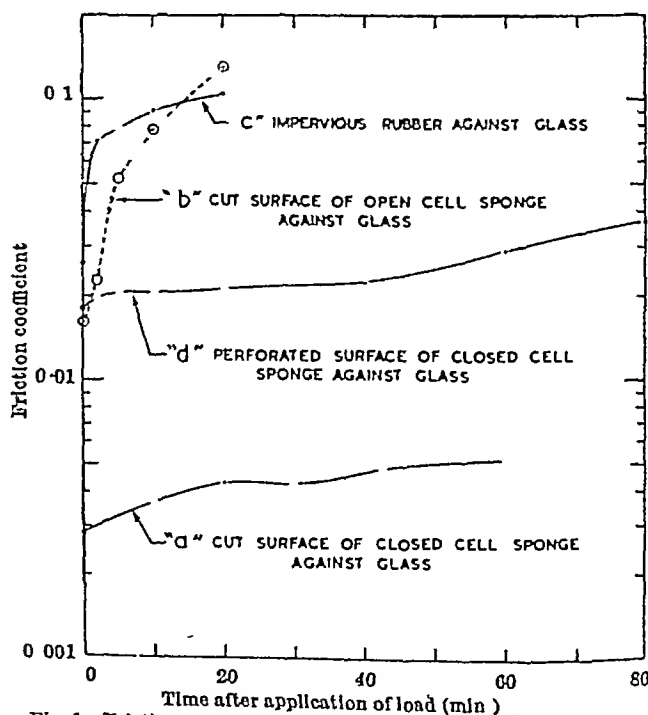


Fig. 1 Friction of various surfaces against glass when lubricated with soapy water

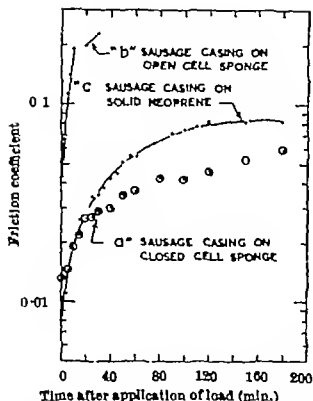


Fig. 2. Friction of various types of sausage casing against themselves when lubricated with soapy water

using surfaces and lubricants which do not give exceptionally low friction under boundary lubrication conditions (The animal-derived sausage casing used showed entirely ordinary friction coefficients once the excess lubricant had been wrung out.) Animals joints could operate in this way. In the following communication evidence is presented to suggest that they do

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¹Chamley J *The New Scientist* 6 No 138 61 (July 9 1959)

Experimental Evidence for Weeping Lubrication in Mammalian Joints

From existing reports¹ it is clear that the structure and mechanical properties of articular cartilage are just what are required for weeping lubrication to be possible. Its outer surface is formed by a narrow layer of flattened cartilage cells and below this is a relatively acellular zone extending for some hundreds of microns down to the calcified tissue. What cells there are in this zone are arranged in columns well separated by wide areas of intercellular matrix, which probably has a structure orientated normal to the surface layer. Articular cartilage is easily deformed by pressure but is very resilient, being almost perfectly elastic to intermittent pressures, and it has been suggested that this elasticity is due to oxidation and reabsorption of fluid.² Thus articular cartilage appears to resemble a rather stiff sponge, with an internal structure which would permit easy expression of fluid up to a smooth, presumably porous, outer surface.

Structural evidence alone is inadequate, so a few simple experiments have been made on articular surfaces from freshly opened joints of a number of mammals. Thin shavings were analysed for sodium and potassium with a flame photometer. The ratio of sodium to potassium found was of the order of 12-15 on a molar basis; so articular cartilage must contain a very high proportion of extracellular fluid, as suggested by histological preparations. Exudation of only a small fraction of this total extracellular fluid would provide an adequate lubricating film. That the superficial layer of flattened cartilage cells

is freely permeable to small molecules is easily shown by dropping aqueous solutions of dyes on to a freshly exposed surface. Dyes such as eosin, for example, rapidly penetrate to a depth of at least a hundred microns. Furthermore, if excess dye is washed off, some of that which has penetrated can be re-extracted by pressing filter paper firmly against the articular surface. The pore size in this superficial layer is probably quite small, since a graphite suspension with a particle size of rather less than 1μ did not appear to penetrate.

If an articular surface which has been well dried with filter paper is placed against a glass slide and the point of contact examined through the glass with a microscope, fluid can be seen to exude as pressure is applied. The amount of fluid exuded was estimated by placing a small piece of filter paper of known area on an articular surface and applying pressure for a brief period of time (less than a second). The sodium content of the filter paper was then measured with a flame photometer and the volume of exuded fluid calculated on the assumption that it had the same sodium content as extracellular fluid. Both dry and moist filter paper were used with substantially similar results. When the pressure applied was only sufficient to bring the filter paper into intimate contact with the cartilage, the amount of sodium collected was insignificant. As the pressure was raised, however, the amount collected increased and for pressures in the range to be expected in normal operation of the joint the volume of fluid exuded was calculated to be sufficient to form a layer 15-35 μ thick over the area of contact. Between two articulating surfaces twice as much fluid should be available which ought to be sufficient for adequate lubrication by the mechanism suggested in the previous communication.

Weeping lubrication could equally well occur where tendons change direction (for example the patella at the knee joint), for the cartilage surface concerned appears to have the same properties as that in the joint proper.

One possible disadvantage of weeping lubrication is the occurrence of a slow outward seepage of fluid from between the apposed surfaces, which might eventually come into contact. Joints seldom remain in a fixed position for very long when they are bearing a load. Animals which sleep standing up, for example horses, are said always to change their position at least every half an hour, and examples are quoted in the previous communication of model bearings which retain their low friction for at least this length of time. The rate of seepage would be markedly affected by the microstructure of the articular surface, but unfortunately little is known about this.

It has not proved possible to devise a crucial experiment which would prove conclusively whether or not 'weeping' lubrication is an important factor in reducing joint friction. Nevertheless the evidence put forward here strongly suggests that all the necessary conditions are present, so it would be strange indeed if this type of lubrication did not in fact occur.

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EXPERIMENTS ON THE DEVELOPMENT OF ISOLATED BLASTOMERES OF MOUSE EGGS

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EXPERIMENTAL research on the developmental potency of blastomeres of mammalian eggs has not, so far, advanced beyond the preliminary period. Nicholas and Hall¹ found that development of embryos starts to take place from both separated blastomeres of a 2 cell rat egg. These embryos, although completely normal in structure, did not, however, advance beyond the egg cylinder stage, and underwent resorption before the tenth day of development. Seidel² succeeded in obtaining two young rabbits which had developed from 2 cell eggs in which one of the blastomeres had been destroyed by piercing it with a glass needle, he did not carry out any checks of the development during pregnancy. Apart from a short note by Pincus³, there are no reports in the literature on the development of isolated blastomeres before implantation.

The investigations described below were carried out on mouse eggs, and were aimed at (1) tracing the entire embryonic development of 'half'-embryos, and, on this basis, (2) defining the regulation capacities of 'half'-blastomeres and of the factors on which they are dependent. Special attention was devoted to the structure of the blastocysts in order to ascertain to what extent the inner cell mass and trophoblast participate in their total mass. Experiments were also carried out on a smaller scale on the development of 4-cell eggs of which one or three blastomeres had been destroyed.

The blastomeres were destroyed under a dissecting microscope by piercing them through the zona pellucida with a glass needle fixed to a micro-manipulator similar to that described by Goldacre⁴. During this operation the eggs were drawn to and held against the mouth of a micro-pipette, with an outer diameter of about 40 μ , the suction power of which was regulated by means of the rubber bulb attached to it. All manipulations were carried out in mouse serum diluted 1:1 with normal saline. Directly, or a few minutes after piercing the blastomere, it disintegrated totally or partially. Using the technique previously described⁵, the eggs were then transferred to the oviducts of the recipients, which had been mated the previous night with vasectomized males. Animals with differing pigmentation were used as donors and recipients for the experiments, which were aimed at obtaining embryos from the second half of pregnancy or young.

Development before implantation. A total of about 100 'half'- and 'three-quarter'-cleaving eggs and blastocysts was obtained. The volume of most 'half'- and 'three-quarter'-blastocysts is similar or only slightly smaller than that of normal blastocysts (compare Fig 1 with Figs 2 and 4). Some 'half'-blastocysts were, however, encountered lying loosely within the zona pellucida (Fig 3). The volume of the inner cell mass of 'half'-blastocysts, treated as the

elliptical cap, is subject to wide variations, but in no case does it attain the smallest value found in normal blastocysts. Its average size, as a percentage of the size of inner cell mass of normal $3\frac{1}{2}$ day blastocysts, is 44.5. The volume of the inner cell mass of 'three-quarter'-blastocysts varies within the wide limits of variability observed for 'half'- and normal blastocysts.

After carrying out observations in the living state, the blastocysts were then fixed and mounted *in toto* in order to determine the number of cells composing the inner cell mass and trophoblast. The average total number of cells of 'half'- and 'three-quarter'-



(1) $3\frac{1}{2}$ -day normal blastocyst ($\times 300$) (2) 'Half' blastocyst. Size equal to normal, small inner cell mass ($\times 300$) (3) 'Half'-blastocyst lying loosely within zona pellucida ($\times 300$) (4) 'Half'-blastocyst without differentiated inner cell mass ($\times 300$) (5) 'Quarter'-blastocyst composed of about twenty cells. Most of them form trophoblast ($\times 300$) (6) 'Quarter'-blastocyst composed of only eight cells, six in inner cell mass and two in trophoblast. Stained with hematoxylin, mounted *in toto* ($\times 750$)

blastocysts was respectively 08.5 and 08.3, and number of cells of the inner cell mass is 33.0 and 58.4, again as a percentage of the number in normal 3½-day blastocysts.

The numerical ratio between the cells of the inner cell mass and trophoblast varies considerably in the various 'half' and 'three-quarter' blastocysts. Among the developing eggs there were several 'half' blastocysts without a differentiated inner cell mass (Fig. 4), and several morulas in which, despite the aggregation of a large number of cells, the differentiation of the trophoblast had not taken place.

It would seem that my results are connected in a logical manner with those of cytochemical investigations by Daley and his co-workers on the development of the eggs of rodents⁴⁻⁶. The following facts established by those authors are the most important for the interpretation of present observations: (1) the oocyte and fertilized undivided egg have a bilateral symmetry resulting from the disposition of the two cytoplasmic zones, which differ from each other cytochemically. The cytoplasm of the dorsal and ventral zones passes respectively to the cells of the inner cell mass and the trophoblast. (2) The plane of the first cleavage division has no established relation to the plane of symmetry of the egg.

The variations in the numerical ratio between cells of the inner cell mass and the trophoblast in 'half' blastocysts, and the variations in the volume of the inner cell mass itself, are presumably the result of variable distribution of the cytoplasm of these zones to each of the 'half' blastomeres. According to Jones-Seaon⁷, there is a tendency in the ova of rats to symmetrical or oblique placing of the plane of the first division. This would explain the fact that the majority of 'half' blastocysts consist of both the inner cell mass and trophoblast, and that forms having only one of these elements are relatively rarely encountered. As a result of the second cleavage division, the difference between the blastomeres as regards the character of the cytoplasm forming them, becomes even more emphasized⁸. The destruction of a blastomere chiefly composed of cytoplasm intended for the formation of either the inner cell mass or the trophoblast would result in wide variations in the structure of 'three-quarter' blastocysts.

A single 'quarter' blastomere is also capable at least in certain cases of forming a blastocyst composed of the inner cell mass and trophoblast (Figs 5 and 6). The degree of participation of these elements in the structure of these two 'quarter' blastocysts is, however, quite different.

Since the degree of formation of the inner cell mass and trophoblast in 'half' and 'quarter' blastocysts is not identical with that in normal blastocysts, the regulating capacities of 'half' and 'quarter' blastomeres cannot be considered complete. The fate of the cells which have arisen from a given blastomere must to a large extent be determined by the character of the cytoplasm forming that blastomere. The fundamental factor determining the developmental potency of 'half' blastomeres in each case would thus be the position of the first cleavage division in relation to the plane of symmetry. The first two 'sister' blastomeres can, but need not necessarily, be characterized by identical capacities for further development.

Development after implantation. Of 175 transplanted 'half' blastomeres, 54, or 30.8 per cent, were implanted, and 30, or 17.1 per cent, were developing normally at autopsy. In actual fact the capacity of

the 'half' blastocysts to become implanted and continue development is at least twice as great since only 50 per cent of the transplanted blastomeres are present in the genital tract of the recipients before implantation.

A series of 'half' embryos on successive days of pregnancy, from the fifth to the fifteenth was obtained. All the embryos were completely normal in structure. In the period from the fifth to the tenth day their size, calculated by adding up the areas of the sections, does not exceed half the size of the normal control embryos of corresponding age. The statement made by Nicholas and Hall¹ that the size of rat embryos developed from 'half' blastomeres comes within the limits of variation of the size of normal embryos is therefore somewhat surprising. In the first half of pregnancy, the rate of morphogenesis of 'half' mouse embryos is in certain cases completely normal, and in others slightly slowed down. Delay in reaching the successive stages never exceeds 24 hr and most often is considerably less.

Two periods of intensified resorption of 'half' embryos may be noted—one immediately following implantation, and the other at the beginning of the second half of pregnancy, about the eleventh day. On the eleventh day certain 'half'-embryos reach the stage and size characteristic of normal development; others correspond to tenth-day normal embryos. Dead embryos are also encountered. From the twelfth day on, the number of resorbed embryos increases markedly. On the other hand, all the surviving embryos are already at the same stage of development and of the same size as the normal ones. Rapid increase in the rate of development of 'half'-embryos, which takes place at this time, seems to be caused by two factors: (1) real increase in the rate of growth connected with the beginning of functioning of the chorio-allantoic placenta; (2) apparent hastening of development due to elimination of most retarded embryos by resorption.

Since all the embryos undergo normal development until the eleventh day, and complete regulation may be said to have taken place, resorption must be only the result of disturbance of the normal relations between mother and embryo, connected with considerable retardation in the rate of development.

In view of my observations it seems that resorption of all 'half' rat embryos during the first half of pregnancy, reported by Nicholas and Hall¹, had been caused to a large extent by improper experimental technique.

Three females gave birth to young which had developed from 'half' blastomeres (first female, 1 young one after 20 days, second female, 2 young ones after 10 days, third female, 3 young ones after 20 days). These young comprised four females and two males. All the animals were fertile, and each female gave birth to several litters. No abnormalities of the kind described by Seidel⁹ or elsewhere were found in the young or in the more advanced embryos.

A full account of this work will be published in *Acta Theriologica*.

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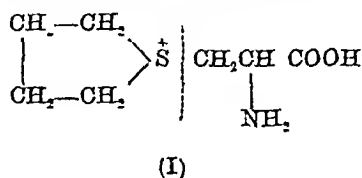
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METABOLIC AND CHEMICAL STUDIES OF 'MYLERAN': FORMATION OF 3-HYDROXYTETRAHYDROTHIOPHENE-1,1-DIOXIDE IN VIVO, AND REACTIONS WITH THIOLS IN VITRO

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IT has been reported recently¹ that the S-β-alanyl-tetrahydrothiophenium cation (I) is formed by the reaction of dimethanesulphonyloxybutano ('Myleran') with cysteine. This compound is labile under a variety of conditions, decomposing to tetrahydrothiophene, in which the sulphur atom has been derived from the cysteinyl moiety. Thus treatment with mild alkali (pH 8–9), electrolysis of its aqueous solution, or pyrolysis at 140°C lead to a nearly quantitative conversion into tetrahydrothiophene.

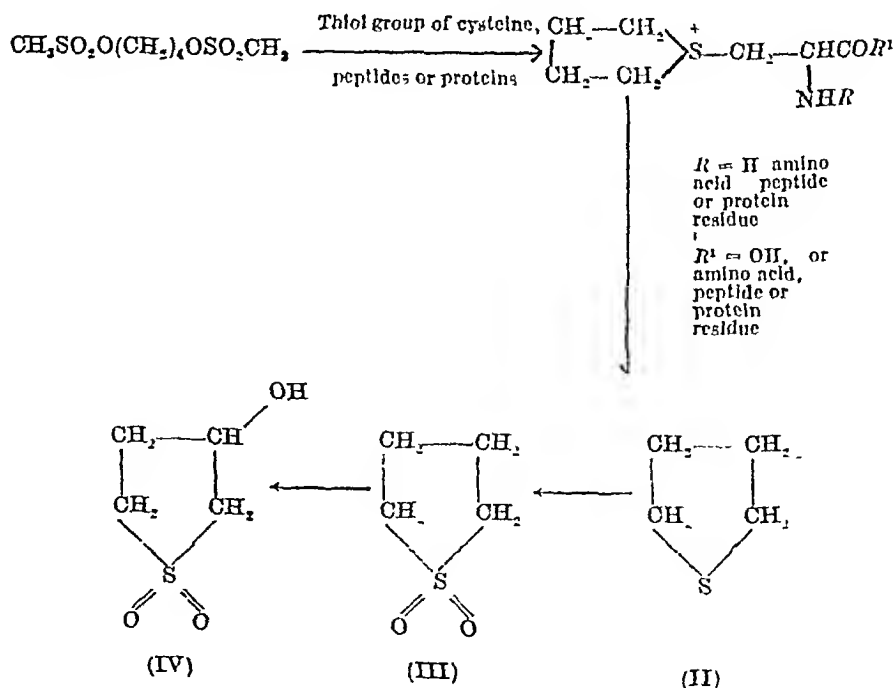


Since rats which had received injections of either 2,3-¹⁴C-'Myleran' (prepared by Dr P Brookos) or the corresponding labelled sulphonium compound (I) excreted the same major urinary metabolite, it seemed very likely that intermediate formation of a sulphonium compound of this type occurred also *in vivo* after injection of 'Myleran'. On the basis of the *in vitro* findings which demonstrated the lability of the sulphonium compound and the course of its decomposition, it was suggested that the major urinary metabolite was a derivative of tetrahydrothiophene. This has now been established, since injection into a rat of ³⁵S-tetrahydrothiophene (II) again led to the excretion of only one major metabolite, identical with that formed from 'Myleran' and the sulphonium compound as judged by its chemical properties, and its *R_F* value in several solvent systems. It was thus further evident that the metabolite contained a sulphur atom. The fact that it failed to give a positive test for sulphur on paper chromatograms suggested that one of the changes which had occurred involved oxidation of the sulphur atom. ³⁵S-Tetrahydrothiophene-1,1-dioxide (III), a likely product of oxidation *in vivo*, was therefore synthesized and shown to be converted in the rat into one major urinary metabolite which differed in *R_F* value from the parent dioxide, but which was again identical with that formed from 'Myleran', the sulphonium compound, and tetrahydrothiophene.

Possible pathways for the metabolism of tetrahydrothiophene-1,1-dioxide included reduction of the sulphone group, further oxidation, or ring substi-

tution. It seemed improbable that reduction was involved in view of the marked stability of the sulphone group to reduction *in vitro*. Further oxidation of the tetrahydrothiophene-1,1-dioxide could result in unsaturation of the ring, the formation of a ketone, or fission to a di-acid. It was concluded that these changes had not occurred as the metabolite was unaltered by treatment with bromine or warm neutral permanganate, was unreactive towards dinitrophenylhydrazine, and was neutral as shown by passage through columns of ion exchange resins. However, ring substitution by hydroxylation was considered possible, particularly in view of the enhancement of the reactivity of the ring carbon atoms towards nucleophilic reagents by the powerfully negative sulphone group. The presence in the metabolite of one or more hydroxyl groups was demonstrated by its reactivity towards acetyl chloride, or benzoyl chloride in pyridine, leading to the formation of new compounds from which the metabolite could be regenerated by hydrolysis with mineral acid.

Injection of necessarily small quantities of 'Myleran' into a rat had hitherto precluded isolation of the metabolite in a pure state and in quantities sufficient to isolate a derivative, but with the knowledge that tetrahydrothiophene-1,1-dioxide, a non-toxic compound, gave rise to the same major urinary metabolite, this difficulty was overcome. Moreover, it was demonstrated that the same metabolite was excreted by the rabbit after injection of ¹⁴C-'Myleran' or ³⁵S-tetrahydrothiophene-1,1-dioxide. Large doses of tetrahydrothiophene-1,1-dioxide with a radioactive carrier were injected into rabbits, and after extraction of the urinary metabolite into chloroform



the residual oil was treated with 3,5-dinitrobenzoyl chloride. The resulting ester was recrystallized to constant specific radioactivity from methanol, and formed almost colourless prisms, melting point 195–197°C

| | |
|----------|---|
| Analysis | $O_{11}H_{11}O_7N_3$ requires |
| Found | C = 40.0 H = 3.0 N = 8.3 S = 0.7 m.w. = 330 |
| | C = 40.5 H = 3.2 N = 8.3 S = 0.4 m.w. = 310 |

This same radioactive ester was prepared from the combined chloroform extracts of the urine obtained from two rabbits, one of which had received a small dose of ^{14}C 'Myleran' to act as carrier, and the other a relatively large quantity of tetrahydrothiophene 1,1-dioxide to enable separation of the derivative. It was also obtained from the chloroform extract of urine from rats injected with high doses of the β -alanine tetrahydrothiophenium salt (I) containing a radioactive tracer. Each derivative had melting point 195–197°C alone, and on admixture.

The foregoing experiments indicate that the urinary metabolite formed from 'Myleran' is monohydroxy tetrahydrothiophene 1,1-dioxide (IV). 2-Hydroxytetrahydrothiophene 1,1-dioxide, prepared via the 2-bromo compound* from radioactive tetrahydrothiophene-1,1-dioxide, was shown to possess a different R_F value from the metabolite. However, the 3,5-dinitrobenzoate of an authentic sample of 3-hydroxytetrahydrothiophene 1,1-dioxide (IV) (sulphenol), kindly supplied to us by Prof. E. Boyland, had melting point 195–197°C which was undepressed on admixture with the 3,5-dinitrobenzoate formed from the 'Myleran' metabolite.

The metabolism of 'Myleran' in the rat and the rabbit may be represented in the accompanying scheme.

In connexion with the possible mode of action of 'Myleran' it was of interest to determine whether the tetrahydrothiophene formed from the drug *in vivo* could have been derived by reaction with the

thiol group of peptides such as glutathione, or with larger molecules such as proteins. It has been shown that 'Myleran' reacts smoothly with the thiol group of glutathione in an alkaline medium forming tetrahydrothiophene, characterized as its mercurichloride. Similarly, thiol-containing proteins such as denatured egg albumin and reduced keratin have been shown to yield tetrahydrothiophene when treated with 'Myleran' in an alkaline medium, indicating that sulphonium ion formation is not restricted to compounds of low molecular weight.

This novel dethiolation reaction provides additional evidence to the *in vivo* findings in support of the view that reactions of this type may be responsible for some of the diverse pharmacological properties of the bifunctional alkylating agents. Sulphonium ion formation might lead to a modification of the function of certain proteins, but in addition dethiolation could conceivably have more far-reaching effects by actually altering the sequence of amino acids in a peptide or protein chain. It is hoped that work on these aspects may be continued.

Full details of this work will be published elsewhere. The work has been supported by grants to the Chester Beatty Research Institute (Institute of Cancer Research, Royal Cancer Hospital), from the British Empire Cancer Campaign, the Jane Coffin Childs Memorial Fund for Medical Research, the Anna Fuller Fund and the National Cancer Institute of the National Institutes of Health, U.S. Public Health Service.

We wish to thank Prof. A. Haddow and Dr. L. A. Elson for their interest in the work, and to record our appreciation for helpful discussion with many of our colleagues. We gratefully acknowledge technical assistance from Miss M. Morton.

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REGISTRATION OF THE SPERMICIDAL EFFECTS OF DIOCTYL SODIUM SULPHOSUCCINATE

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STUDIES of the kinetics of spermicidal effects are not possible without a method for the estimation of the proportion of living spermatozoa at a given time. This implies that the time required for this estimation has to be very short in relation to the period of time during which the process is to be studied. By working with dark field illumination, and using comparatively long photographic exposures, different pictures of the lucid spermatozoa, either immobile or in different kinds of movements, are obtained.

For the present investigation bull spermatozoa were chiefly used. Some experiments, however, were performed with human sperm cells, with identical results. A buffered egg yolk extract was used as an optically suitable diluent for the semen and the spermicidal substance¹. The optical equipment consists of a Zeiss microscope with dark field condenser, heating stage, plane-apochromatic objective ($\times 10$), compensating plane eyepiece ($\times 8$), and a Zeiss carbon arc lamp for microscope use. The microscope carries a Leica camera, somewhat modified in order to

facilitate a fast winding-on of the film. Using the Kodak film Tri X², 1/0 sec is found to be an appropriate time of exposure. Prints of the negatives are enlarged five times. The final linear enlargement is thus 400 times.

For each determination of the percentage of mobile spermatozoa two exposures are made with an interval of 1/0 sec. On the first picture the moving spermatozoa leave tracks according to their different ways of moving. A comparison between the first and the second picture in a pair reveals whether doubtful cases depend upon passive motions induced by other spermatozoa or upon active movements. It also renders possible classification of cells disappearing by swimming in the direction of the optical axes as moving.

When performed with all precautions two counts on the same sample generally do not differ by more than 1.5 per cent. All the operations described below are performed at 37°C with materials which have been preheated to this temperature. Of the semen diluted to give about 20 000 spermatozoa/ μ l. that is

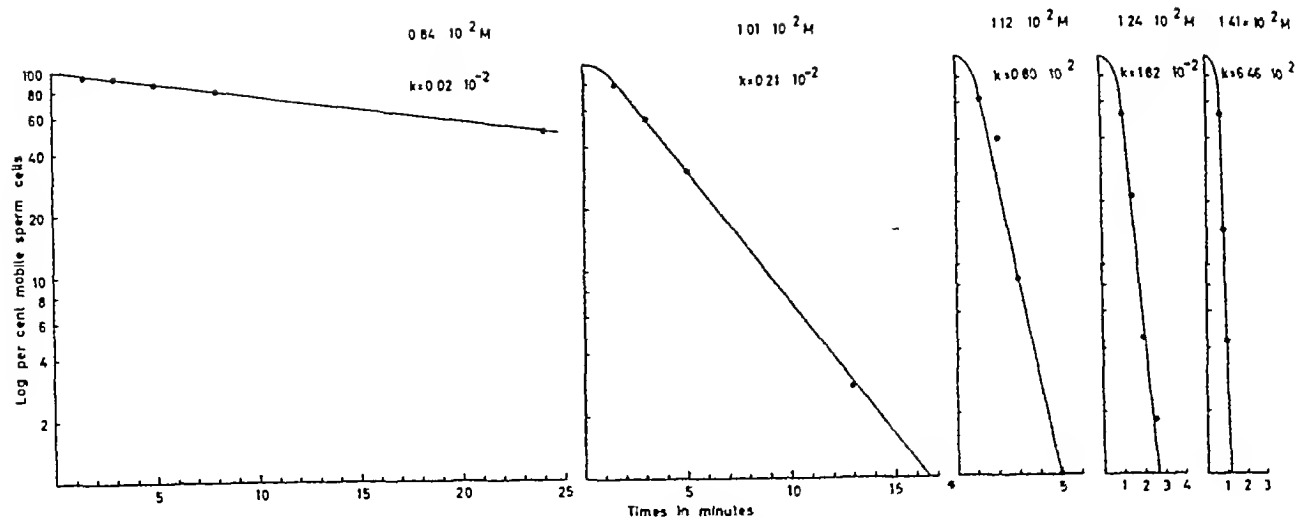


Fig 1 Semi-log plot of percentage of mobile sperm cells versus time in minutes at different concentrations of dioctyl sodium sulphosuccinate k , Apparent death rate constant

twice the final density wanted, 0.5 ml is brought into a thick-walled test-tube provided with a rod-shaped magnetic stirrer. The tube is placed in a rotating (180 r.p.m.) magnetic field and 0.5 ml of a solution of the spermicidal substance in diluent (twice the concentration to be studied) is added, all statements as to time being related to this moment as zero. About 10 μ l of this mixture are put on a slide, and a coverglass provided with a fine rim of 'Vaseline' along its edges is placed on the drop in such a way that no air bubbles are left between the two glasses. The preparation is thus protected from evaporation, aerobiosis being, however, permitted only for limited periods of time. The first exposures are made after 60 and 61 sec, and are followed by two exposures every fifteenth and thirtieth second.

A stock solution of dioctyl sodium sulphosuccinate in acetone (0.45 M, 20 per cent) is prepared and added to the diluent. The highest final concentration of acetone in our experiments was about 5 per cent. In control experiments this concentration had no effect on the percentage of mobile spermatozoa for periods of up to 2 hr.

Concentrations of dioctyl sodium sulphosuccinate ranging from $0.84 \times 10^{-2} M$ to $1.41 \times 10^{-2} M$ (0.38 per cent to 0.63 per cent) give exponential death-rate curves that are more easily read in logarithmic form (Fig 1). As in corresponding experiments with bactericides² these straight curves permit the calculation of 'apparent death-rate constants'. The analytical plotting of the relation between concentration of dioctyl sodium sulphosuccinate and the apparent death-rate constants is seen in Fig 2. According to the theoretical analyses given by Johnson, Eyring and Polissar³, these curves may give considerable information about the mechanism involved. Tentatively we have transformed their expression

$$\pi = 1 - p^m = 1 - (1 - e^{-kt})^m$$

into

$$\log(1 - \pi) = m \log(1 - e^{-kt})$$

and plotted $\log(1 - \pi)$ against $\log(1 - e^{-kt})$ choosing such a value of k as to give a straight line (Fig 3). This implies identical values of m and n . With decreasing concentrations of dioctyl sodium sulphosuccinate both k and n decrease. $\log n$ plotted against \log concentration gives a linear relationship. As the concentration of the spermicide is large it remains in excess, and may thus be considered

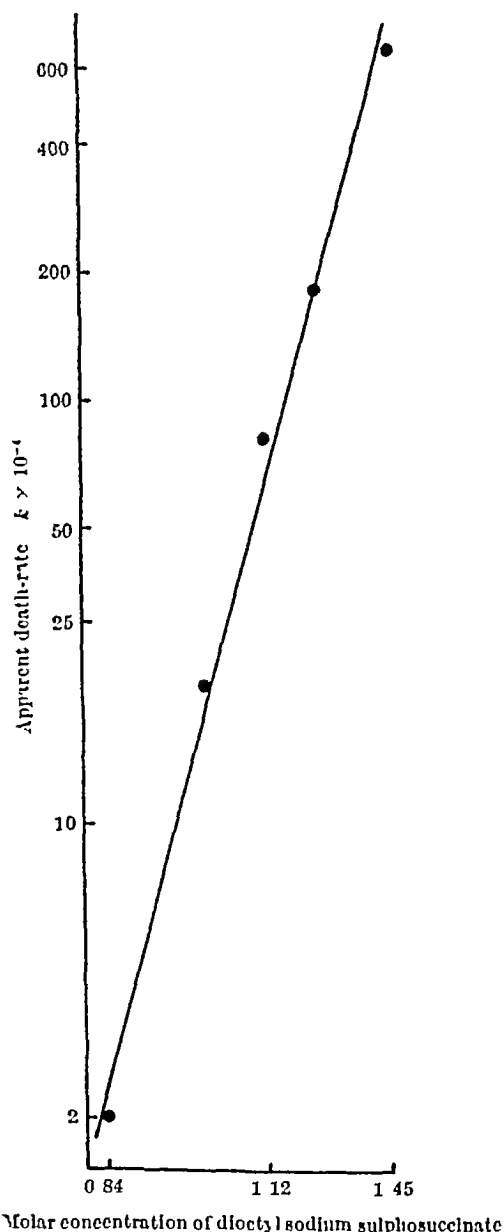


Fig 2 Log-log plot of the apparent death-rate constant versus different concentrations of dioctyl sodium sulphosuccinate

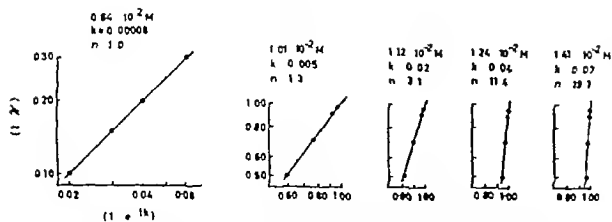


Fig. 8 Log-log plot of $(1 - \gamma)$ versus $(1 - \gamma_H)$ at different concentrations of diethyl sodium sulphosuccinate

relating log surviving sperm cells to time obtained with low concentrations ($0.84 \times 10^{-2} M$) of diethyl sodium sulphosuccinate show a sharp break, the death rate suddenly decreasing. This observation will be further analysed. The effects on the relationships described of anaerobiosis, temperature and ageing of the cells are being studied.

Corresponding results have been obtained with chloramin T and hydrogen peroxide.

constant*. According to Johnson, Eyring and Polissar n may thus represent the number of molecules of diethyl sodium sulphosuccinate combining with each molecule of protein in the cells. Occasionally curves

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GLUCOSE-6-PHOSPHATE DEHYDROGENASE AND HUMAN ERYTHROCYTES

Characteristics of Glucose-6-Phosphate Dehydrogenase from Normal and Primaquine-sensitive Erythrocytes

RECENT developments have emphasized the fact that genes may express themselves in terms of qualitative alterations of such macromolecules as human hemoglobins¹ and blood group substances². Whether or not such qualitative differences at the level of the enzyme usually account for the inherited enzyme deficiencies is not known, but some instances of qualitative alterations in enzymes have been reported. Immunochemical evidence³ exists for an inactive enzyme like molecule in mutants lacking tryptophan-synthetase. Qualitative differences in glutamate dehydrogenase have been found in mutants of *Neurospora*⁴. An opportunity exists to explore this possibility further in the case of primaquine sensitive hemolytic anemia⁵, an inherited defect in which the erythrocytes of affected hemizygous or homozygous persons have only 5-26 per cent of the normal activity of glucose-6-phosphate dehydrogenase.

In order to investigate possible qualitative or quantitative differences between the glucose-6-phosphate dehydrogenase in primaquine-sensitive and normal erythrocytes, a method of partially purifying the enzyme has been developed^{6,7} and preliminary comparative studies have been made. The partially purified preparation is hemoglobin free and represents a 66 to 86 fold purification of glucose-6-phosphate dehydrogenase in 20-66 per cent yield, with little or no contamination with 6-phosphogluconic dehydrogenase. This enzyme was assayed in final concentrations of 0.1 M Tris buffer, pH 8.0, 0.01 M magnesium chloride, 2×10^{-4} M triphosphopyridine nucleotide, and 6×10^{-4} M glucose-6-phosphate, by observing the increase in optical density at 346 mμ or by measuring the 450 mμ fluorescence in a photofluorometer, using 386 mμ exciting light. Within an accuracy of $\pm 5-20$ per cent, the preparation from both a primaquine sensitive male and a normal male control had Michaelis constants of 2.1×10^{-4} , 3.9×10^{-4} , and 6.9×10^{-4} M for triphosphopyridine nucleotide,

glucose-6-phosphate and 2-deoxyglucose-6-phosphate respectively. Both utilized the last substrate at 0 per cent of the maximum rate for glucose-6-phosphate. In a mixed buffer which was 0.05 M each in phosphate, Tris and glycine both preparations had the same pH-optimum curve from pH 6.0 to 10.0. Heat of activation ($20-40^\circ C$) was found to be 9.5×10^3 cal/mole for both preparations. Similar movement on anion-exchange column chromatography has been observed for the enzyme from both sources⁷. The percentage yield of activity for the enzyme from sensitive cells remained approximately the same as that for normal cells throughout the partial purification and all experiments. Similar labilities and the stabilizing effect of triphosphopyridine nucleotide have been reported⁸. The latter may be related to the inactivation of this enzyme by erythrocyte stroma which has been observed by others (ref. 8 and following communication).

Because of the many identical catalytic parameters, it seems unlikely at the present time that the greatly reduced activity of erythrocytic glucose-6-phosphate dehydrogenase in these persons is due to a qualitative difference at the catalytic site of the enzyme, if a qualitative difference exists at all. We are left, therefore, with the necessity of considering a gene which manifests itself through decreasing the rate of synthesis or increasing the rate of inactivation of this enzyme. The fact that the 80 fold purified preparation can be far more extensively purified indicates that the glucose-6-phosphate dehydrogenase constitutes only a very minute portion of the hemoglobin free proteins and emphasizes the necessity and opportunity for more definitive comparisons of relatively pure preparations of glucose-6-phosphate dehydrogenase. Some differences in labilities^{9,10} and pH optima³ between this enzyme in normal and primaquine-sensitive hemolytants have been reported. In view of the extensive contaminations with other proteins and the stabilizing effect of small amounts of various substances⁸, caution should be taken in drawing inferences as to molecular differences based on differences in lability of the glucose-6-phosphate dehydrogenase between normal and prim

aquino-sensitive haemolysates and crude preparations

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Mechanism of Inactivation of Glucose-6-phosphate Dehydrogenase in Human Erythrocytes

In the course of investigation of primaquine-sensitive haemolysis we found that glucose-6-phosphate dehydrogenase is inactivated by incubation with stromata in haemolysates of primaquine-sensitive and non-sensitive erythrocytes alike^{1,2}. Purified haemoglobin-free glucose-6-phosphate dehydrogenase from both kinds of erythrocytes appears qualitatively identical and is highly stabilized by triphosphopyridine nucleotide³.

We wish to report that in haemolysates of both types of cells 'Norit' inactivates glucose-6-phosphate dehydrogenase by adsorption of pyridine nucleotides⁴ as do stromata by pyridine nucleotidase activity. Inactivation of glucose-6-phosphate dehydrogenase by stromata is prevented by triphosphopyridine nucleotide, diphosphopyridine nucleotide and nicotinamide. Inactivation by 'Norit' in stroma-free haemolysates is prevented by tri- and di-phosphopyridine nucleotide but not by nicotinamide. Dialysed stroma-free haemolysates retain bound coenzyme and, in them, glucose-6-phosphate dehydrogenase is not inactivated by incubation unless stromata or 'Norit' is added. Glucose-6-phosphate dehydrogenase inactivation and removal of bound coenzyme occur concomitantly during incubation with stromata or 'Norit'.

Human erythrocytes washed with cold 0.145 M sodium chloride were haemolysed by rapid freezing and thawing. The haemolysate was diluted with four or five volumes of cold water, the stromata were removed by centrifuging for 60 min at 28,000g, 0°C either before or after incubation. After dialysis (usually overnight) in 0.067 M phosphate buffer, pH 7.4, the haemolysates were assayed for glucose-6-phosphate dehydrogenase and 6-phosphogluconic dehydrogenase activity by a modification of the coupled reactions with glutathione reductase previously described¹. In a final volume of 7.0 ml the complete reaction mixtures contained (1) *tris*-hydroxymethylaminomethane, 5×10^{-4} M, adjusted to pH 7.4 with hydrochloric acid, (2) ethylenediamine tetraacetic acid adjusted to pH 7.4 with sodium hydroxide, 5×10^{-5} M, (3) triphosphopyridine nucleotide (Sigma), 7×10^{-5} M, (4) oxid-

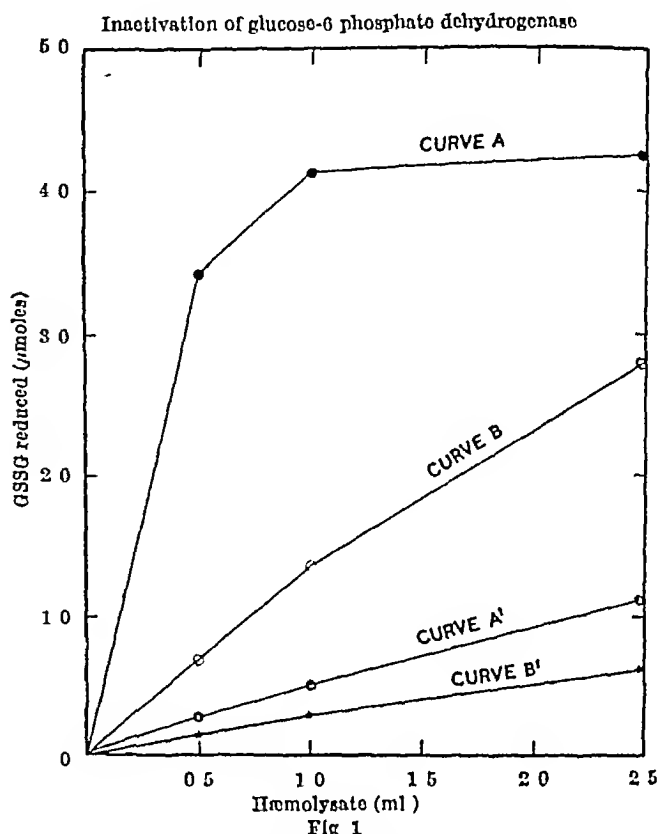


Fig 1

ized glutathione, GSSG (Schwarz), 5×10^{-5} M; (5) glucose-6-phosphate (Sigma), 4×10^{-5} M for glucose-6-phosphate dehydrogenase, or (6) 6-phosphogluconate (Sigma), 4×10^{-5} M for 6-phosphogluconic dehydrogenase, and (7) varying amounts of haemolysate as shown in Fig 1. Reactions were run for 15 min at 37°C, pH 7.4.

Fig 1 shows representative results from a male non-sensitive (A, A') and a male sensitive individual (B, B'). Curves A and B represent activity of glucose-6-phosphate dehydrogenase in dialysed haemolysates from which stromata had been removed immediately after haemolysis. Curves A' and B' show activity of glucose-6-phosphate dehydrogenase, after incubation of haemolysate from non-sensitive cells for 1 hr at 45°C and from sensitive cells for 1 hr at 37°C, prior to removal of stromata. Addition of tri- or di-phosphopyridine nucleotide (10^{-4} M) to those haemolysates before incubation provided 100 and 73 per cent protection, respectively, based on approximate integration of the curves obtained. Nicotinamide (5×10^{-5} M) provided protection ranging from 15 to 60 per cent in non-sensitive and 60 to 100 per cent in sensitive haemolysates.

Similar incubation of doubly centrifuged stroma-free haemolysates results in little or no inactivation either before or after dialysis. However, glucose-6-phosphate dehydrogenase is inactivated in stroma-free haemolysate by incubation with acid-washed 'Norit' (2.5–30 mgm per ml) or by incubation after removal of 'Norit'. Triphosphopyridine nucleotide completely protected glucose-6-phosphate dehydrogenase in stroma-free haemolysates incubated after removal of 'Norit'. Diphosphopyridine nucleotide protected it in non-sensitive haemolysates by 47 per cent and in sensitive haemolysates by 91 per cent. However, nicotinamide gave no protection, suggesting that its effect occurs by inhibition of stroma factor, whereas tri- and di-phosphopyridine nucleotide stabilize the enzyme itself.

Glutathione reductase and 6-phosphogluconic dehydrogenase in hemolysates, unlike glucose-6-phosphate dehydrogenase, remain active even after incubation with stromata or 'Norit'. This allows preliminary investigation of the binding of triphosphopyridine nucleotide to glucose-6-phosphate dehydrogenase because the former is also the coenzyme of 6-phosphogluconic dehydrogenase. Stromata free dialysed hemolysates retain sufficient triphosphopyridine nucleotide for the hemolysate to reduce GSSG in 1 hr at 37° C when 6-phosphogluconate but not triphosphopyridine nucleotide is added to the reaction mixture. However, under the same conditions, GSSG is not reduced after incubation with stromata or 'Norit' (Triphosphopyridine nucleotide is retained in hemolysate which has been dialysed for as long as 42 hr).

The inactivation of glucose-6-phosphate dehydrogenase and loss of triphosphopyridine nucleotide remaining in dialysed hemolysates occur together, suggesting that the non-dialysed fraction of triphosphopyridine nucleotide is bound to glucose-6-phosphate dehydrogenase and that this is active only when bound with its coenzyme. The 6-phosphogluconic dehydrogenase does not bind triphosphopyridine nucleotide or require it for stabilization.

Intact human erythrocytes have pyridine nucleotidase activity, both on the surface and within the cell. The surface activity is demonstrated by the inactivation of glucose-6-phosphate dehydrogenase in isotonic hemolysates during incubation with whole human erythrocytes; the intracellular effect is shown by a loss of glucose-6-phosphate dehydrogenase activity and bound triphosphopyridine nucleotide in erythrocytes incubated in isotonic saline for 2 hr at 45° C. Although no loss of glucose-6-phosphate dehydrogenase activity occurred during storage of non-sensitive blood, gradual loss of glucose-6-phosphate dehydrogenase activity in sensitive blood during four weeks of storage in acid-citrate-dextrose solution also suggests an intracellular action of pyridine nucleotidase.

These results show that triphosphopyridine nucleotide stabilizes glucose-6-phosphate dehydrogenase in hemolysates as well as in partially purified preparations and confirm the suggestion that this stabilization may be related to the inactivation of this enzyme by erythrocytic stroma (ref 5 and previous communication). Partial stabilization of glucose-6-phosphate dehydrogenase by nicotinamide is indirect by protection of the pyridine nucleotides from pyridine nucleotidase activity of stromata. Stabilization by diphosphopyridine nucleotide may also be indirect, by its enzymatic conversion to triphosphopyridine nucleotide, since diphosphopyridine nucleotide does not stabilize glucose-6-phosphate dehydrogenase of partially purified preparations. Nevertheless, protection of glucose-6-phosphate dehydrogenase of stroma-free hemolysates by di- as well as triphosphopyridine nucleotide indicates that the former can help to stabilize glucose-6-phosphate dehydrogenase in human erythrocytes, even though it is not a coenzyme for it. The key to the mechanism of primaquine hemolysis and possibly of cellular ageing may be related to these stabilizing processes.

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X-RAY DAMAGE AND RECOVERY IN MAMMALIAN CELLS IN CULTURE

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As measured by the ability to sustain unlimited proliferation, the X-ray sensitivity of microorganisms has been generally observed to be much greater than the sensitivity of important macromolecules. This, in itself, has been an important reason for associating the lethal effect of X-rays with the genetic apparatus of the cell. Puok and Marcus's¹ observation that mammalian cells in tissue culture were even more sensitive—10–100 times or more—than bacteria or yeasts further reinforced this view and led to their very reasonable proposal that the sensitive sites in mammalian cells are the chromosomes.

If the functional integrity of the genetic apparatus is required for viability, since the survival curves of most somatic cells are sigmoid (or multithit) it might be expected that survivors after X-irradiation would be more sensitive to subsequent exposure than the

parental population. This follows from the fact that multithitness implies a threshold type of response (which means damage must be accumulated before an effect is observed) and hence that surviving cells accumulated a sublethal amount of damage.

We have investigated the question of the presence of heritable damage in two cell lines of the Chinese hamster, *Cricetulus griseus*² (clone A ovarian tissue and strain V female lung tissue) propagated in tissue culture. We have found that essentially all the survivors after X-irradiation did not display heritable damage, as would be evidenced by their radiosensitivity, but rather that they repaired their accumulated damage before their first division after irradiation.

Our growth medium bears the designation HU 15. It consists of Eagles's amino acids and vitamins³ with glutamine at a concentration of 1 mM, 4 per

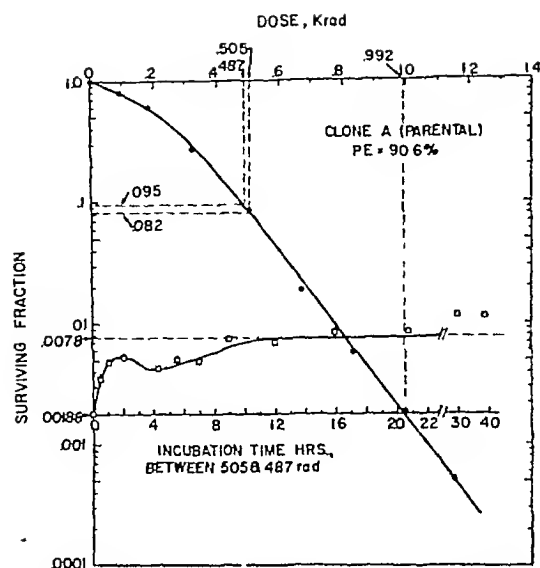


Fig. 1 Recovery of X-irradiated cells (between 505 rad and 487 rad doses) as a function of time of incubation at 37° C

cont Earle's *NCTC-109*⁴, Puck's⁵ saline *F* with the calcium content increased 6.5 times, and 15 per cent undialysed foetal calf serum (Colorado Serum Co., Denver). Both cell lines grow in this medium with a doubling time of about 12 hr.

Our X-ray source consisted of a Machlett OEG-60 tube powered by a full-wave rectified, 55 kV supply. The tube was operated at 12 mA with 0.175 mm aluminium filtration, absorbed dose rate 720 rads/min. After the attachment of cells in 9-cm. Petri dishes, the plate covers and growth medium were removed and the cells were irradiated at room temperature in a humidified atmosphere of 2 per cent carbon dioxide in air. Surviving clones were stained and counted after 12–18 days incubation at 37° C in a 2 per cent carbon dioxide incubator. Identification of abortive colonies was facilitated by the use of a projection technique, although our results are essentially the same whether or not abortive colonies are included. Plating efficiencies in most of our experiments were about 70 per cent, essentially the same results were obtained, however, in experiments having plating efficiencies from 10 to 90 per cent.

In discussing the observations, a multistage model will be assumed for simplicity although our conclusions apply equally as well to sigmoid or threshold type survival curves in general. For lag-phase cells, clone A was found to display hitness numbers of 4–5 and clone V 6–7.

X-ray dose fractionation was employed to test for repair of accumulated damage. Fig. 1 shows a survival curve for single clone A cells trypsinized and plated 2 hr before exposure (Standard errors are indicated where larger than the plotted points). In addition, the lower portion of the figure shows a recovery curve for cells which had received a first dose, 505 rads, followed by incubation at 37° C for various periods of time before receiving a second dose of 487 rads.

If there had been no recovery between the exposures, the two doses would have been completely additive, and the survival after a total of 992 rads would have been 0.0019. Alternatively, if there had been complete recovery between doses, the survival to the first and second doses would have been 0.082 and 0.095, respectively. The product of these latter values is 0.0078, which represents the survival corresponding to complete recovery between doses. The

points to be noted are: (1) as a function of time at 37° C, the cells recover in a manner which may involve repair of sites as well as fluctuations in sensitivity; (2) for clone A cells, recovery appears to be complete by about 10 hr and constant until about 25 hr, and (3) the survival rises above 0.0078 after about 25 hr, which probably represents the effect of cellular multiplicity on survival concomitant with the onset of post-irradiation division.

The likelihood of the last point was arrived at by two types of measurements. First, we showed that the 'principle of cellular multiplicity' holds for these cells. That is, the surviving fraction of colonies containing more than one cell is shifted upward by an amount governed by the average cellular multiplicity providing that each cell in the colony has the same average sensitivity and that it must be inactivated independently to suppress post-irradiation colony formation. Secondly, an estimate of division delay following a first dose of 505 rads was made by comparing the clonal growth of irradiated cells with unirradiated controls. The comparison was made after clones had reached a size, about 100 cells per clone, which permitted an unambiguous identification of such clones as survivors. In agreement with the recovery curve in Fig. 1, the latter measurement indicated a division delay of about 30 hr.

In addition to the preceding, we have also shown that recovery can take place at room temperature unaccompanied by division in the control population.

To verify that the plateau region in the recovery curve of Fig. 1 represents complete repair of the accumulated damage resulting from the first dose, the survival curve was repeated after 505 rads followed by 18.1 hr at 37° C. In Fig. 2, the non-fractionated survival curve was redrawn starting from the survival corresponding to a first dose of 505 rads. The figure displays an excellent fit of the re-drawn curve to the observed points and shows that, in the exponential regions of both curves, maximum recovery shifts the survival upward by a factor equal to the hitness number. It also follows from Fig. 2 that, at least in the region of full recovery, synergism between the first and second doses is probably absent and therefore the second dose measures the degree of repair of damage resulting from the first dose.

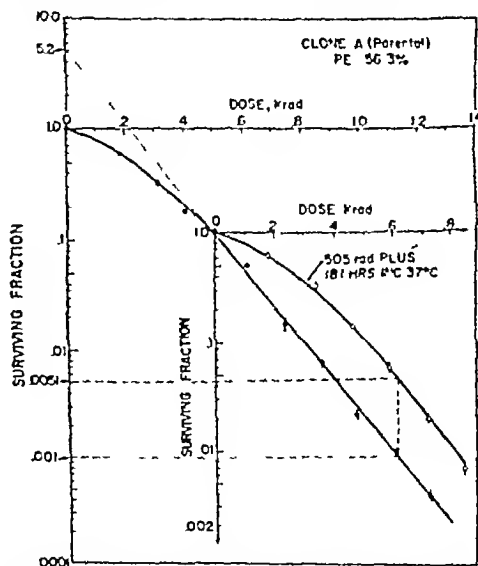


Fig. 2 Full recovery after a dose of 505 rads followed by 18.1 hr at 37° C as evidenced by the repetition of the non-fractionated survival curve

The preceding figures are part of a comprehensive study which will be reported in detail elsewhere. To the extent that these and the results to be reported are typical for somatic cells in general, it should be noted that (1) The vast majority of surviving cells completely repair their accumulated damage before their first division post irradiation. This means that if the hitness number is n in the exponential region survivors undo the effects of a maximum number of hits which is $n-1$. (2) The kinetics of recovery depend on the physiological state of the cells and/or can be caused to appear to undergo large oscillations depending on the recovery medium. These apparent oscillations may result from the combined effects of changes in sensitivity and repair of inactivated sites. (3) Although there are important quantitative differences, log phase cells respond similarly. (4) A cell can undergo repeated cycles of damage and repair with no apparent attenuation of the repair process(es).

There are several contexts in which these findings are of interest. If the chromosomes are the X-ray sensitive sites and chromosome breaks are the hits leading to lethality, then some new properties of restitution must be considered. First restitution goes to completion in surviving cells. Secondly, the cell's ability to reconstitute breaks remains unimpaired after repeated doses. In view of the preceding, Puck's⁴ report of a high yield of mutant characteristics in the progeny of cells surviving 5-7 mean lethal doses may be applicable to the material he was using. May be evidence of a radiation induced chromosomal lability which is expressed after recovery and during clonal growth may imply that mutation production and lethality are not, in general, closely connected or may indicate that the

chromosomes are not the primary sensitive sites related to viability.

Another area in which these results may apply is in connection with tumour therapy. Treatment protocols involving fractionation are common, permitting in general ample time between treatments for considerable if not complete recovery. Even for situations in which the hitness number may only be 2 a simple calculation reveals that if recovery is not duly accounted for the survival using fractionation can be higher than expected by several orders of magnitude. Of course tissue recovery in a general sense has been recognized by radiation therapists for a long time. These results, however, provide a cellular basis for this phenomenon and lend specific direction to the research that should be undertaken both to take advantage of as well as to control this effect.

Additional experiments are planned (or in progress) to examine the influence of dose-rate on survival, and the biochemical and cytogenetic aspects of recovery.

We are indebted to Dr. T. T. Puck for a sample of his clone A, ovarian tissue, which has been propagated in our laboratory without recolonization since August 1958 to Dr. Denys Ford for his P strain female lung tissue, which was recolonized in December 1958, and to Dr. George Yorganian, who supplied the Chinese hamsters for the original explants.

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TALLOWY DISCOLORATION IN CHEDDAR CHEESE

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Fat Oxidation and Trace Metals in Cheese

A SERIOUS fault in mature Cheddar cheese is the gradual appearance of bleached areas with a 'tallowy' flavour, aptly described as 'tallowy discoloration' or 'white streak'. The erratic incidence of this defect has for long hindered efforts to find the prime cause. In seeking the cause, most of the chemical features examined showed little, if any, difference between normal and tallowy portions, apart from the oxidized condition of the latter. The most striking differences were found in the disposition of trace metals. As compared with adjacent normal cheese the copper content of the centre of tallowy portions was always much lower, often as little as a third, but the iron content was always higher, usually by about a half. Experiments with threefold added copper did not affect the incidence of the tallowy defect, nor did added iron salts.

When normal cheese curd was treated with an excess of warm 5 per cent iron free brine, the portion that dissolved contained more iron than the undissolved cheese, which was shown to lose a corresponding quantity of iron. Moreover, treatment for a shorter period so that less cheese dissolved, resulted

in a higher iron content of the dissolved cheese. This indicated the presence of an iron compound more soluble than the cheese and also suggested a probable connexion between the salting process in cheese making and the appearance of tallowiness.

The degree of oxidation of iron in cheese was also studied. Practically no ferrous iron could be extracted from young cheese but the amount extractable increased with ageing at variable rates: some cheese yielding very little at maturity. Cheese tending to tallowiness had increased ferrous iron content while the actual tallowy seams had the highest ferrous content. This occurred in seams where oxidation was most advanced, as shown by high peroxide values and also by oxidation of the sulphhydryl groups of the protein. These results now indicate that an important part is played by an iron complex. The very low copper content at the centre of tallowy seams may be an effect of oxidation of a copper-sulphhydryl compound similar to that demonstrated by Strooks and Kolthoff¹.

Most of these investigations were carried out during a period of several years. In view of the recent finding by Rammoll (following communication) that hematin compounds can cause tallowy discoloration they support the view that these or similar iron complexes

have an important influence in causing tallowy discoloration

F BISHOP

¹ Stricks, W., and Kolthoff, I. M., *J. Amer. Chem. Soc.*, **73**, 1723 (1950)

Fat Oxidation and Hæmatin Systems in Cheese

MUCH work has been done in New Zealand on a defect of Cheddar cheese characterized by a coupled oxidation of the fat and carotene. The defect, commonly known as 'tallowy discoloration' or 'white streak', is seen in the interior of the cheese as bleached areas having a tallowy flavour. These bleached areas are invariably associated with cracks in the body of the cheese. The defect usually occurs only after at least 16–20 weeks storage at low temperatures (42–44° F). Previous attempts to find the major pre-disposing cause of this defect have not been completely successful.

As I believe the defect to be similar in several ways to oxidative changes described by Tappel¹, attempts were made to show the presence of a fat-oxidizing system in cheese, using methods similar to those of Blain and Todd². Such a system was found to be present in some cheese. As a result of these findings, cheese was made in which sterile, defibrinated cow's blood was added to the cheese milk. The experimental and control cheese were stored in a controlled curing room at about 55° F for 6 weeks. Sample plugs of the cheese were then stored in the presence of air, at 32–34° F for 4 weeks.

After this time, the cheese containing the highest amount of blood (0.02 per cent in the cheese milk) had developed typical tallowy discoloration. The control cheese containing no added blood had not developed the defect, it was of normal flavour and colour.

On obtaining these results, four of the original experimental and control cheeses were cut and examined. These cheeses had been at 55° F for 2 weeks followed by 9½ weeks at 42–44° F—a total of 11½ weeks. Tallowy discoloration was seen in the two experimental cheeses, being more extensive in the cheese containing the higher amount of blood. The two control cheeses showed no sign of the defect.

The possibility of abnormal amounts of blood in the milk being the prime cause of tallowy discoloration must now be considered. It has been shown that, during manufacture of experimental cheese, most of any red blood cells added to the milk become concentrated within the cheese curd. This concentration is further modified by the addition of salt to the curd, resulting in a partial hemolysis of the red blood cells. Higher concentrations of salt would then be expected to reduce tallowy discoloration. The effect of added salt provides a possible partial explanation of the results obtained by Bishop (preceding communication).

Full details of these and related experiments will be offered for publication elsewhere.

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NON-INVERTED VERSUS INVERTED PLOTS IN ENZYME KINETICS

IT was first shown, but not published, by Woolf (see ref. 1) that the Michaelis-Menten equation $v = V_m/(1 + K_M/S)$, relating the initial reaction-rate (v) of an enzymic reaction to the substrate concentration (S) can be written in three linear forms. The experimental (apparent) kinetic constants V_m (v , when $S \rightarrow \infty$) and K_M (S , when $v = V_m/2$) can be obtained from plots of the variables $1/v$ versus $1/S$, S/v versus S or v versus v/S . Since its first application by Lineweaver and Burk², the $1/v$ versus $1/S$ plot has been used most commonly.

However, it has been pointed out on several occasions (see ref. 3), that the v versus v/S plot, non-inverted with respect to v , has advantages over the two inverted plots, partly because it is less apt to obscure deviations from linearity. With respect to similar plots for determining the number of molecules of a small molecular compound bound to a protein, Scatchard⁴ states "this [inverted plot] has the disadvantage of concealing deviations from the ideal laws and of tempting straight lines where there should be curvature".

These considerations apply also to the determination of kinetic constants from enzymic reaction-rates at constant substrate concentration and varying concentrations of an inhibitor or activator (see ref. 5).

Despite the drawbacks it has remained customary, at least in enzyme kinetics, to use inverted plots in the evaluation of results. Even in a recent and authoritative text-book on enzymology⁶ that treats these graphical procedures extensively, the advan-

tages of the v versus v/S plot have not been fully recognized. For these reasons some further comment on this matter seems to be appropriate.

In an acid-base titration, or in the demonstration of the influence of the hydrogen ion concentration on the rate of an enzymic reaction, unwieldy graphs would be obtained if instead of pH the hydrogen ion concentration were used as one of the co-ordinates. This applies also to the influence of the substrate concentration on the rate of an enzymic reaction, and accordingly plots of v versus pS have been used in enzyme kinetics. The inflexion point of the theoretical sigmoid curve corresponds to pK_M .

Like other titrations, the enzyme-substrate 'titration' should be carried out over a range that includes substrate concentrations above as well as below this inflexion ('halfway') point. An ideal range is that of about one pS unit below to one pS unit above this point, that is, from about 0.1 to 10 K_M ^{6,7}, representing roughly the range of 10–90 per cent 'saturation' of enzyme with substrate. However, such a (semi) logarithmic plot is still of little value for the estimation of the kinetic constants because it is not linear. On this basis, the advantage of the v versus v/S plot becomes immediately apparent. It can be seen in Fig. 1 that for almost 80 per cent of its course this plot nearly coincides with the v versus pS plot. It has the additional advantage over the latter of being linear, which allows V_m to be determined by extrapolation to $S \rightarrow \infty$ (intercept with the ordinate). The (negative) slope is equal to K_M .

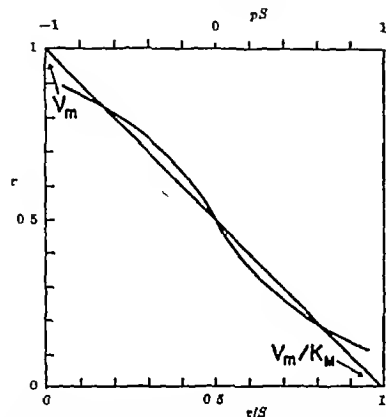


Fig. 1. Comparison of the v versus pS (sigmoid) and the v versus v/S plot (straight line). 1 has been taken as unity for the reaction rate (v) and K_M as unity for the substrate concentration (S).

If, in the ideal region, substrate concentrations are applied that correspond to about equal increments in pS , a procedure that has been found practicable in many cases (for examples see ref. 8), the reaction rates actually measured also change by about equal increments and are equally distributed over the v versus v/S plot. This is not the case with the other two plots when equal increments of $1/S$ or S are taken. In this connexion a few comments on statements made by Dixon and Webb (ref. 8, pp. 21-23) are in order. These statements are: "the experimenter is free to choose such substrate concentrations as will give the best distribution of points (one very rarely works at equal increments of v , indeed it is hardly practicable to do so)" and "it is a positive advantage to have most of the points concentrated near the left hand side in [the two inverted] methods, since it is this part of the graph which is most important for determining K_M ". When, in the inverted plots, the substrate concentrations are chosen so as to give equal distribution of points, one finds that the corresponding changes in rate decrease progressively at one end of the curve until they become too small to be measured accurately. On the other end of the curve, the increments in v become unnecessarily large. This is demonstrated by Figs. 2A and 2B for the case of the $1/v$ versus $1/S$ plot. Fig. 2 is based on a substrate concentration range of about 10 fold, but one frequently finds in the literature cases where the range is even smaller so that, for example, only the lower points of curve 2B are available. Although a more or less accurate V_m/K_M value (intercept with the abscissa in the non-inverted plot) may be obtained in this case, it is obvious that neither V_m nor K_M can be estimated with any accuracy from such data, even though the inverted plot might tempt one to do so. Similar difficulties obtain when only results at the higher substrate concentrations, close to saturation, are

available. From such data not even V_m can be estimated with certainty when substrate inhibition is involved.

Because only the v versus v/S plot shows the rates from $S \rightarrow 0$ to $S \rightarrow \infty$ on a finite graph, this plot generally demonstrates more clearly whether or not the results are sufficient for the estimation of the constants. When ample data are available, for example, over the recommended 100 fold range of substrate concentrations, the inverted plots are also the less convenient. As is seen in Fig. 2A all the activities below $V_m/2$ would be found on the first small part of the curve between $1/S = 0$ and $1/S = 1$ while those above this value correspond to the range of $1/S$ between 1 and infinity. Thus, the inverted plots over-emphasize the results on one side of the curve at the cost of those on the other side. This produces a lop-sided stretching of the curve and tends to obscure deviations from linearity (see ref. 3b).

No titration is complete, nor the estimation of the corresponding constants accurate, if it is not carried through on both sides of the half way point. Both these regions are of equal value in this respect. On the other hand, results obtained too far away from this point on either side are largely superfluous. From this it should be clear that the most important range of substrate concentrations for the determination of the constants are those of the order of K_M , around the value of which the curve should be symmetrical. This is the case only with the v versus v/S plot in which the half way point is equally spaced between the two limiting values

$$1/V_m \left(= \lim_{S \rightarrow \infty} v \right) \quad \text{and} \quad V_m/K_M \left(= \lim_{S \rightarrow 0} v/S \right)$$

Another largely unwarranted comment that has been made from time to time (see ref. 9) in favour of the $1/v$ versus $1/S$ plot is based on the fact that here the variables v and S are separated. With respect to estimation of the experimental error and the weighting of data, this does not constitute an argument against the v versus v/S plot when only the error in v needs to be considered, as is most often the case. In the v versus v/S plot an error in v simply displaces the experimental point along a line through the origin that

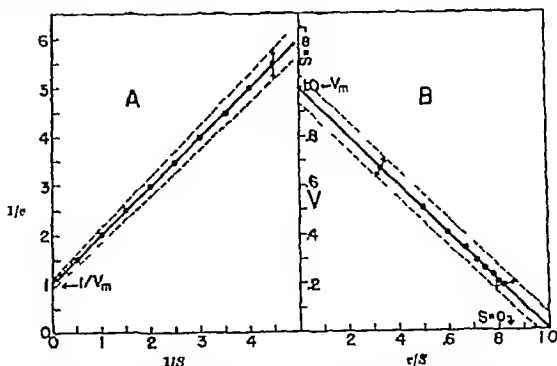


Fig. 2. Comparison of the same (hypothetical) data in a $1/v$ versus $1/S$ plot (A) and a v versus v/S plot (B) showing that (1) points that are equally distributed in the inverted plot correspond to an unfavourable distribution of rates actually measured, and (2) a limited set of results that do not allow extrapolation that is the points on the lower part of curve B are over-emphasized in the inverted plot (A). The arrows and the zones within the dotted lines correspond to an experimental maximum error in v of 5 percent.

represents a particular substrate concentration. The displacements are indicated by the arrows in Fig. 2A and 2B, where the dotted lines show the zone in which the experimental points are found when subject to a maximum error of ± 5 per cent. It may be noted that in the v versus v/S plot this zone runs parallel to the theoretical curve in contrast to the inverted plot.

In view of the reasons discussed above, it would seem then that there is no real basis for the continued use of the inverted plots.

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Palo Alto, California, U.S.A.

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THERE seems to be some confusion here between two things which are in reality quite distinct, namely, (a) the choice of the series of substrate concentrations which will give the best results, and (b) the best method of plotting the results obtained. These are largely independent. One is free to select the best series of concentrations without even knowing which method of plotting will be used, and when the results have been obtained one is free to plot them by either method.

With regard to the choice of substrate concentrations we have in fact made no recommendation that the series should give equally spaced points on the reciprocal plot (namely, "equal increments of $1/S$ "), as Dr. Hofstee seems to imply, nor do we recall any such recommendation by others. On the contrary, our statement that it is advantageous to have a concentration of points near the left-hand

side of this plot implies approval of some such series as "equal increments of pS ".

With regard to the method of plotting, both methods are of course perfectly valid, and it is our belief, based on experience of plotting results in both ways, that there is not a great deal to choose between them. This is where we differ from Dr. Hofstee, who believes that plot B (Fig. 2) is so greatly superior to plot A that there is no reason for the continued use of the latter.

The purpose of plotting is twofold: (a) to determine K_M and V_{max} , and (b) to check that the system obeys the Michaelis equation (linearity, that is, of the graphs). By actual use, we find that the two methods are about equally good in both respects; the accuracy of determination of the constants from a given set of results is about the same, and it seems to us that deviations from linearity are revealed almost equally well by the two methods. We venture to think that if the reader will plot a few cases in both ways he will come to the same conclusion.

A main argument for plot B seems to be that a series of concentrations of the kind commonly preferred will give a more uniform distribution of points along the straight line than in the case of plot A. It does not follow, however, that such a uniform distribution of points will give the most accurate results, for we would point out that the position of a straight line is determined much more precisely by points near its ends than by points near its centre.

Our main reason for preferring plot A is that one can readily identify the different points with particular substrate concentrations, and so see what is taking place. This is not the case with plot B, which has no scale of substrate concentrations; the quantity which is plotted depends both on the arbitrarily fixed concentration and the resulting observed velocity so that it is necessary to perform a division sum to discover what substrate concentration corresponds to a given point. Any error in v affects both co-ordinates, displacing the point obliquely. Also rather more calculation is involved in the actual plotting by this method. We think that many workers will continue to use plot A, the inverted, or as we would prefer to call it, the reciprocal plot.

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TWO-DIMENSIONAL HIGH-VOLTAGE PAPER ELECTROPHORESIS OF AMINO- AND OTHER ORGANIC ACIDS

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Amino-Acids

IT had been demonstrated before¹ that the application of high potential gradients to the electrophoresis of amino-acids leads to sharp separations after comparatively short running times. It was felt, however, that a higher degree of resolution and greater certainty of identification of the separated com-

pounds could be attained by the adoption of a two-dimensional technique, that is, subjecting the sample to electrophoresis on the same sheet under two different pH conditions with consequently differing migration patterns.

A two dimensional technique for the separation of amino-acids has been described by D. L. Durrum², who obtained encouraging results with mixtures of

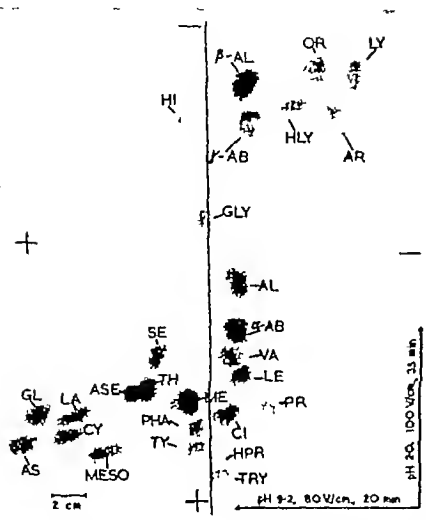


Fig. 1 Two-dimensional high voltage electrogram of amino-acids
Conditions first direction (bottom to top) Whatman No 3 $3 M$,
 12 in. \times 22½ in. 0.75 M formic acid, pH 2.0, 100 V/cm, 0.6
 maamp./cm, cooling water temperature 16°C, pressure 1.5 lb./in.²,
 35 min. acidified ninhydrin reagent (0.5 per cent w/v) in acetone
 10 μ m of each amino-acid second direction (right to left)
 0.05 M sodium borate solution pH 9.2 80 V/cm, 0.5 maamp./cm,
 20 min.
Amino-acids α -AB, α -amino-butyric acid β -AB β -amino-
 butyric acid γ -AB γ -amino-butyric acid AL α -alanine
 β -AL β -alanine AR arginine AS aspartic acid, ASE
 asparagine CI citrulline GL glutamic acid GLY glycine HI histidine, HLY hydroxylysine HPR
 hydroxy proline LA leucine LE leucine, LY lysine
 ME methionine MESO methionine sulphone OR ornithine
 PHA phenyl alanine PR proline SE serine, TH threonine
 TRI tryptophan TY tyrosine VA valine

up to 13 amino-acids, a potential gradient of 30 V/cm and a running time of 5 hr. Several authors² have since reported modifications to this technique employing relatively low voltages, but without an apparent significant increase in resolving power, expediency or speed of operation. A recently constructed apparatus of sufficient width and improved cooling efficiency made the application of high potential gradients (100 V/cm. and greater) to two dimensional separations of amino acids possible³, and the technique has since been improved and usefully employed in several investigations.

The procedure found most practical is as follows: a sheet of filter paper Whatman No 3 $3 M$, 12 in. \times 22½ in., is soaked in a 0.75 M formic acid solution of pH 2.0 and blotted to remove excess moisture. The sample is applied as a streak of ½ in. width, the sheet placed in the electrophoretic apparatus (sandwich type top and bottom cooling plates, 13 in. \times 20 in., strictly controlled pressure) and connected through a "Cellophane" membrane⁴ at each end with the thick paper pads dipping into the electrolyte vessels. It is run for up to 40 min., dried for 10 min. at 00°C and 1 hr. in a stream of cold air to remove most of the formic acid residue, trimmed to a length of 12 in., according to a developed guide strip showing the effective length of separation, and sprayed lightly (approx. 135 per cent moisture) from an atomizer with a 0.05 M sodium borate solution of pH 9.2. It is then

turned through 90°, placed carefully in the apparatus connected by two 12 in. \times 6 in. paper strips to the thick paper pads and thus to the electrode vessels, the joins being made by filling in the small gaps between sheet and strips with a slurry of cellulose powder (Whatman, standard grade) in borate solution. Simple overlapping interferes with efficient cooling and steadiness of moisture-level in the sheet. After completion of the second run, at 100 V/cm for 20 min., the sheet is detached from the connecting strips, dried for about 15 min. at 70°C and sprayed with a 0.5 per cent (w/v) ninhydrin solution in acetone, acidified by the addition of 3 per cent (v/v) of glacial acetic acid. It is advisable to place the sheet for spraying with borate solution on a frame provided with a grid of nylon thread and to handle moist electrograms with rubber gloves throughout, to avoid interfering finger marks.

Fig. 1 shows the pattern of 27 amino acids and amides separated by this technique.

The position of glutamine coincides with that of methionine and, if the presence of both is suspected, it was found practicable to treat the applied sample with two drops of 30 per cent hydrogen peroxide before the first run to convert the methionine to methionine sulphone⁵ which is well separated from glutamine. The treatment only works in an acid medium. Taurine and cysteine acid can easily be separated from all the other amino-acids at pH 2.0 and their identification requires no confirmation by a run at a different pH. In this case, they would be below tryptophan, separated by a wide gap from it and from one another. The position of tryptophan at pH 2.0 was always found as shown and not, as J. K. Whitehead reported⁶, near glycine.

Fig. 2 demonstrates the application of the technique to a commercial sample of acid hydrolysed casein

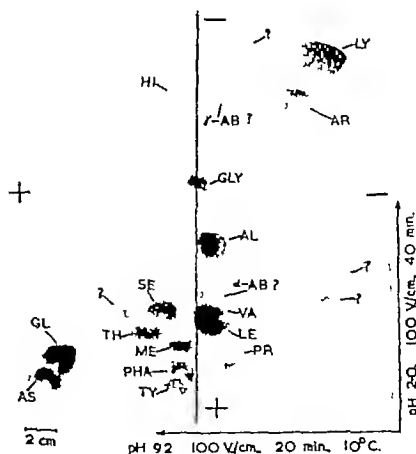


Fig. 2 Two-dimensional high voltage electrogram of a casein hydrolysate
Conditions first direction (bottom to top) Whatman No 3 $3 M$,
 12 in. \times 22½ in. 0.75 M formic acid, pH 2.0, 100 V/cm,
 0.5 maamp./cm, cooling water temperature 10°C, pressure
 1.5 lb./in.², 40 min. ninhydrin reagent as in Fig. 1, 0.05 M sodium
 borate solution second direction (right to left) 0.05 M sodium
 borate solution pH 9.2 100 V/cm, 0.5 maamp./cm, 20 min.
Amino-acids as in Fig. 1

Most of the common amino-acids can be identified by their positions, the appearance of some spots in unusual positions may be due to the presence of peptides or other ninhydrin-reactive compounds. No attempt has been made to identify the compounds against which question marks are placed. The partial overlapping of valine and leucine (or the leucines) is due to their relatively high concentrations. The slight difference in migration distances in the second direction is due to a lower temperature and moisture content of the sheet. Under standardized conditions the degree of reproducibility of the spot patterns is usually high. The time for the separation of less complex mixtures can be reduced in many cases to about one half.

Other Organic Acids

As a result of a systematic study of the migration-rates of non-volatile organic acids under varying conditions of pH, ionic strength and composition of background electrolyte⁷, it was found possible to improve greatly the resolution of complex mixtures by choosing three well tested buffer or electrolyte solutions of pH 2.0, 4.0 and 8.9 with advantageous differences in rate and sequence of migration.

With the availability of an improved electrophoretic apparatus of sufficiently large dimensions⁴, the feasibility of a two dimensional technique became apparent and was successfully tried. The two-dimensional technique, as in paper chromatography, allows the best use of the resolving power inherent in the electrolyte systems chosen, particularly in conjunction with the application of a high-voltage technique ensuring clean separations with a minimum of diffusion and liquid flow effects. This high degree of resolution is particularly desirable when dealing with a multitude of organic acids as potentially present in complex biological and plant extracts. The previously described⁶ 0.75 M formic acid solution, found most suitable for the separation of strong and moderately strong acids from weak acids, has the disadvantage of largely suppressing the ionization of the weak acids, with attendant loss of mobility.

At higher pH values the degree of ionization increases appreciably and with it the mobilities of the weak acids, which makes separation and identification of the individual acids based on their varying migration-rates feasible. Two electrolyte solutions, namely, a 0.5 M acetic acid solution adjusted with pyridine to pH 4.0, and an approximately 0.1 M ammonium carbonate solution of pH 8.9, were found to offer suitable variations in migration-rates without the formation of multiple spots resulting from partial dissociation. Ammonium carbonate solution had proved its usefulness in the electrophoresis of inorganic acids, volatile fatty acids⁹ and some non-volatile organic acids¹⁰.

The procedure adopted followed closely that developed for the two-dimensional separation of amino-acids. The first run was at pH 8.9 and the second run at pH 4.0 or 2.0. The sheet was soaked in the electrolyte and blotted before streaking the sample over a width of 2.5 cm, run and dried for 15 min at 90°C. Before the second run, the electrolyte was lightly sprayed from an atomizer on both sides of the paper sheet to a sufficient degree of moistness (about 135 per cent on dry paper) to ensure

electrical conductance without displacing the partially separated acids.

Runs of 25-min duration in each direction were found appropriate under the electrical conditions chosen, though with less complex mixtures the time can be reduced to 15 min for each run. The sheet was dried after the second run for 10 min at 85°C and kept for 1 hr in a stream of cold air to remove the residual acetic acid (formic acid required at least 3 hr) before being sprayed with a suitable reagent. The choice of a useful reagent for organic acids is restricted to indicator solutions of relatively high sensitivity (provided the background has been cleared of residual traces of free acids or bases) and low stability of colours and chemical reagents producing a colour due to the presence and pH of the acid on the paper and subsequent heating. The strength of such a reaction varies with the type of acid present, and its sensitivity is usually lower than that of an indicator reagent, but the stability of the colours is much higher and the presence of traces of residual electrolyte is not so critical.

Of the many reagents tried, the aniline-glucose reagent with heating at 115°C was found to give satisfactory results for most acids, and the ferric chloride-potassium ferrieyanide reagent¹¹ without heating proved useful for syringic, lactic, glycolic and tartaric acid.

A 0.025 per cent solution of bromocresol purple in ethanol-water (75:25) provided a useful and sensitive indicator reagent which could also be applied prior to spraying with the aniline-glucose reagent, the latter providing a permanent record of brown spots on a near-white background. Picric acid, a coloured compound, was used as a marker to indicate the progress of migration.

An example of a separation of twenty organic acids is illustrated by the electrogram in Fig. 3.

Thanks are due to Mr R. W. Butters for valuable technical assistance, Mr D. G. Harrison for skilful

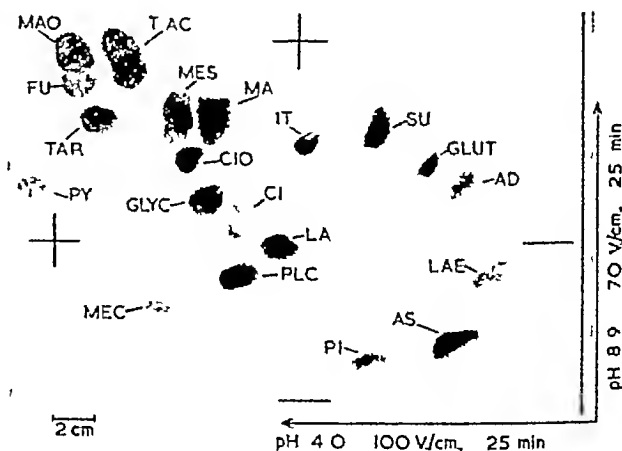


Fig. 3 Two dimensional separation of organic acids by high-voltage electrophoresis.

Conditions: first direction (bottom to top), Whatman No. 3 MM, 12 in. x 22 1/2 in., approx. 0.1 M ammonium carbonate solution (7.9 gm/l), pH 8.9, 70 V/cm, 8.2 m amp/cm, cooling water temperature 12°C, 1.5 lb./in.², 25 min.; second direction (right to left), 0.5 M acetic acid adjusted with pyridine to pH 4.0, 100 V/cm, 10 m amp/cm, 25 min., 60 µgm of each acid. Spraying reagent: glucose aniline (approx. 2 per cent of each) in ethanol-water (2:8).

Organic acids: AD, adipic; AS, ascorbic; CI, citric; CIO, citraconic; FU, fumaric; GLU, glutaric; GLYC, glycolic; IT, itaconic; LA, lactic; LAE, levulinic; MA, malic; MAO, malonic; MEC, meconic; MES, mesaconic; PI, picric; PLC, pyrrolidone-carboxylic; PY, pyruvic; SU, succinic; TAC, trans aconitic; TAR, tartaric.

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ACTION OF MANGANESE DIOXIDE ON SIMPLE CARBOHYDRATES

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UNDER mild conditions manganese dioxide (MnO_2) selectively oxidizes α unsaturated alcohols to the corresponding carbonyl compounds¹, N-alkyl and N,N-dialkylonitrides are also attacked, yielding amides². Elevation of the temperature (70–120°) results in a reduced selectivity of oxidizing action and a variety of reactions have been observed^{3,4}, some of which were carried out in aqueous media. We now report a preliminary qualitative survey of the action of manganese dioxide on simple carbohydrates.

Initially the activity of manganese dioxide preparations obtained by the following methods were compared: (1) alkali permanganate⁵, (2) acid permanganate⁶, (3) decomposition of manganese oxalate at 250°, (4) decomposition of manganese carbonate at 250°, (5) preparations (1)–(4) after nitric acid treatment⁷. The alkali permanganate product gave an aqueous extract pH c 10 even after multiple treatments with water, but the remainder gave neutral extracts. Three reaction conditions were employed in which a solution of the carbohydrate (50 mgm) in water (1.5 ml) was vigorously shaken with manganese dioxide (A) 50 mgm at 50° for 1 hr., (B) 50 mgm. at 05–100° for 1 hr., (C) 150 mgm. at 05–100° for 1 hr. These ratios of oxidant to substrate are considerably lower than those often used with other types of compound¹. The filtered solutions were examined by (1) paper chromatography (downward irrigation with the organic phase of a butanol/ethanol/water (4:1:5) solvent system), (2) paper ionophoresis (enclosed strip technique⁸) with a borate buffer⁹ pH 10 and an acetate buffer pH 5 and detection with anilino hydrogen phthalate¹⁰ and alkaline silver nitrate¹¹. Identification of products must be considered tentative although the application of chromatography and ionophoresis in conjunction permits a more certain identification¹². The chain length of each acid formed in the oxidations was determined by ionophoresis in acetate buffer, and mobilities expressed as M_{GA} values (GA = gluconic acid) give the sequence: gluconic acid 1.00, arabinonic acid 1.09, erythronic acid 1.27, glyceric acid 1.54 and glycolic acid 1.77.

Slight differences were observed in the effect of the various manganese dioxide preparations on glucose and fructose. The subsequent results were obtained with manganese dioxide prepared from the carbonate since it is the easiest and cheapest to prepare.

Aldoses and related compounds. From Table I it may be seen that the hexoses yielded pentoses

together with acidic products. The hexose \rightarrow pentose conversion is not a normal oxidation pathway of sugars, although it can be effected by glycol cleavage reagents¹³ and amino sugars may be degraded to pentoses by ninhydrin¹⁴. Both hexose and pentose were obtained *inter alia* from the heptose. The susceptibility of erythrose to oxidation was quite striking, it reacted completely under conditions B and C and hence did not appear as an oxidation product of the higher sugars other than of pentoses under condition A.

When galactose was treated under condition A with manganese dioxide obtained from the alkali permanganate reaction, in addition to the products shown in Table I traces of erythrose could also be detected and under condition B epimerization occurred yielding talose and tagatose. This observation is not surprising in view of the alkalinity of the reaction solution.

Table I. OXIDATION OF ALDOSES AND DERIVATIVES WITH MANGANESE DIOXIDE

| Aldose | Reaction condition | Products* |
|---|--------------------|---|
| Galactose† | A | Galactose trace lyxose |
| | B | Galactose lyxose traces of 50 and 40 acids |
| | C | Galactose lyxose 60 50 40 and 30 acids |
| D-Glucero-D-galacto-heptose | B/C | Heptose trace mannose |
| | | Heptose mannose traces of arabinose and 60 acid |
| Ribose‡ | A | Ribose trace erythrose 40 acid |
| | B/C | Ribose arabinose 50 40 and 30 acids |
| Erythrose | A | Erythrose, 30 acid |
| | B/C | 40 30 and traces of other acids (erythrose completely oxidized) |
| 2-Deoxy-D-galactose | A/B/C | Traces of unidentified products |
| 2-Acetamido-2-deoxy-D-glucose | | |
| 3-O-methyl glucose | | |
| | A | 3-O-methyl-glucose trace |
| | B/C | 2-O-methyl-arabinose 60 acid |
| | | 3-O-methyl-glucose 2-O-methyl-arabinose 60 acid |
| Rhamnose | A | Rhamnose 6-deoxy-arabinose 60 acid |
| | B/C | Rhamnose 6-deoxy-arabinose 60 40 30 acids |
| 2-Amino-2-deoxy-D-glucose hydrochloride | A/B/C | Complex mixture of products |

* Traces of unidentified compounds were detected in several cases and manganese ions were invariably present. This comment is also applicable to the results in Tables 2 and 3.

† Parallel results with glucose, mannose and other hexoses.

‡ Parallel results with xylose and arabinose.

Table 2 ACTION OF MANGANESE DIOXIDE ON SOME REDUCING DISACCHARIDES

| Disaccharide | Linkage | Reaction condition | Products* |
|--|--|--------------------|--|
| Sophorose Laminaribiose (<i>M_G</i> 0.66) | β 1 \rightarrow 2 β 1 \rightarrow 3 | A, B, C .1 | Insignificant reaction Laminaribiose, trace G-A (<i>M_G</i> 0.33), trace acid P (<i>M_G</i> 0.73) Laminaribiose, G-A, P, glucose, arab Inose |
| Maltose (<i>M_G</i> 0.30) | α 1 \rightarrow 4 | A B, C | Maltose, trace G-A (<i>M_G</i> 0.56), trace G-T (<i>M_G</i> 0.70) Maltose, G-A, G-T, glucose |
| Cellobiose (<i>M_G</i> 0.26) | β 1 \rightarrow 4 | A B, C | Cellobiose, trace G-A (<i>M_G</i> 0.57), trace G-T (<i>M_G</i> 0.77) Cellobiose, G-A, G-T, glucose, arabinose, Q (<i>M_G</i> 0.30) |
| Melibiose (<i>M_G</i> 0.74) | α 1 \rightarrow 6 | A B, C | Melibiose, trace Gal A (<i>M_G</i> 0.87), trace R (<i>M_G</i> 0.42) Gal A, R, trace acid S (<i>M_G</i> 0.94), trace galactose and lyxose |

* G-A indicates glucosyl-arabinose G-T indicates glucosyl tetrone acid Gal-A indicates galactosyl-arabinose *M_G* value is the ionophoretic mobility in borate buffer with respect to that of glucose (ref. 11), *R_G* value is the paper chromatographic mobility with respect to that of glucose

Enhanced resistance to oxidation is conferred by the absence of a C₂-hydroxyl group (2-deoxy-D-‘galactose’) and substitution at C₂ (2-acetamido-2-deoxy-D-glucose). The results with 3-O-methyl-D-glucose and rhamnose indicate that manganese dioxide oxidations might have some value for the synthesis of, for example, O-methyl- and deoxy-pentoses. Although a chromatographic separation of the product would be necessary, application of this technique is also frequently essential in the more classical synthetic methods.

Reducing disaccharides In examining the behaviour of disaccharides with manganese dioxide the analytical methods noted above were supplemented as follows. The acidic products were separated from the neutral components by absorption¹⁴ on ‘Deacidite FF 530’ (CO₃²⁻ form) followed by elution with ammonium carbonate. The neutral and acidic products were then hydrolysed separately with 2*N*-hydrochloric acid at 95–100° for 3 hr, and after neutralization with methyl di-*n*-octylamine¹⁵, the hydrolysates were examined by chromatography and ionophoresis.

From Table 2 it is seen that the disaccharides yielded less complex mixtures on oxidation than did the aldoses. The 1 \rightarrow 2 linked disaccharide (sophorose) was largely unaffected by manganese dioxide, whereas the 1 \rightarrow 3, 1 \rightarrow 4 and 1 \rightarrow 6 linked disaccharides were each degraded to give mainly a glucosyl-pentose together with a small amount of apparently a glycosyl-glyconic acid. Small amounts of hexose and pentose were also formed, but no 6-carbon or smaller acids. As might be expected from the aldose oxidations, glucosyl-tetroses did not accumulate on oxidation of the 1 \rightarrow 4 and 1 \rightarrow 6 linked disaccharides. The use of a large excess of oxidant did not completely convert maltose into its oxidation products. These results suggest that manganese dioxide oxidation might provide a convenient method for converting suitable hexosyl hexoses into hexosyl-pentoses (Glycol cleavage reagents might also be used for this purpose¹²). Although a column chromatographic separation would be necessary to isolate the required

product, it should be noted that, with the 1 \rightarrow 3 and 1 \rightarrow 4 linked glucosyl-glucose oxidation mixtures, the markedly different *M_G* values of the glucosyl-glucose and the glucosyl-pentose create an ideal situation for the application of borate-charcoal-‘Colte’ chromatography¹⁶. Further, the sensitivity of the 1 \rightarrow 3 linked disaccharide (laminaribiose) towards lime-water permits¹⁷ complete destruction of unoxidized disaccharide, leaving the 1 \rightarrow 2 linked glucosyl-pentose unaffected.

Ketoses and miscellaneous compounds From Table 3 it is seen that fructose variously yielded tetrose or underwent epimerization in addition to the formation of acids. Inosose, sodium gluconate and glucuronic were readily oxidized, but most of the products of these reactions have not been identified and they are being actively investigated. The conversion of hexitols to hexoses and pentoses is of interest. The symmetrical hexitols (galactitol and mannitol) gave a single hexose and pentose, whereas glucitol gave two hexoses and two pentoses, indicating attack at both ends of the carbon chain.

It is clear that a wide range of carbohydrates is attacked by manganese dioxide and that a variety of oxidation pathways is operative. Some of the reactions may be of potential value for the preparation of otherwise inaccessible carbohydrates.

A number of commercially available oxides were also examined for action on galactose and fructose under condition A.

Zinc oxide (ZnO), cadmium oxide (CdO), nickel oxide (Ni₂O₃) and black and grey cobalt oxide (Co₂O₃—Co₃O₄) caused slight epimerization.

Zirconium dioxide (ZrO₂) and lead oxides (PbO, PbO and Pb₂O₄) showed weak manganese dioxide-type properties (namely, galactose \rightarrow lyxose), but PbO and Pb₂O₄ effected slight epimerization. There was negligible effect on fructose. Under condition B almost complete destructive oxidation of the substrates occurred with the lead oxides.

The following oxides displayed no oxidative action: HgO (red and yellow), Hg₂O, UO₃, Cu₂O, CuO, Bi₂O₃, SnO, SnO₂, MoO₃, Nb₂O₅, Y₂O₃, Sb₂O₃, Fe₂O₃, Fe₃O₄, GeO₂, V₂O₅, Cr₂O₃, ThO₂.

Table 3 OXIDATION OF CARBOXYL-CONTAINING AND OTHER CARBOHYDRATES

| Compound | Oxidation condition | Products |
|------------------------------------|---------------------|--|
| Fructose* | A B, C | Fructose, tetrose, 6C acid Fructose, glucose, mannose, 6C, 5C, 4C and 3C acids |
| Inosose | A, B, C | Inosose, mixture of acids and reducing acids |
| Sodium glucuronate† | A B, C | No significant effect Glucuronic acid, trace of 4C, 3C acids, dicarboxylic acid and other unidentified components |
| Sodium gluconate‡ | A B, C | Gluconic acid, reducing acid, trace arabinose Gluconic acid, reducing acid, arabinose, unidentified com- ponents |
| Potassium gluconate | A, B, C | Gluconic acid, traces of re- ducing and acidic products |
| Galactitol§ | A B, C | Galactitol, trace galactose Galactitol, galactose, lyxose |
| Glucitol | A B, C | Glucitol, trace glucose and gulonic Glucitol, glucose, gulonic, xylose and arabinose |
| Methyl α -D-glucopyranoside | A, B, C | Traces of unidentified products |
| Sucrose | A B, C | Sucrose, trace of reducing com- ponent S (<i>M_G</i> 0.41) Sucrose, S, glucose, fructose and acid T (<i>M_G</i> 0.73) |

Parallel results with (*) sorbose, (†) glucuronic, (‡) gluconic δ -lactone (§) mannitol

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CROSS-LINKING OF CELLULOSE ACETATE BY IONIZING RADIATION

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RECENT studies on the polymerization induced by radiation of allyl esters have revealed that the conversion rate is markedly increased in the presence of polyvinyl chloride, while at the same time the polyvinyl chloride acquires a high density of cross linking¹. Polyvinyl chloride belongs to the class of polymers which undergo cross linking by radiation², so that the presence of the allyl ester serves to enhance the action of the radiation but no alteration of mode is involved. It is known that such alterations can occur, for example, in the presence of oxygen, many polymers which are normally cross linked by radiation may become degraded³. An artificial means of rendering a change in the reverse direction constitutes a worthwhile objective, as the benefits of cross linking could then be extended to a large class of polymers such as polyisobutylene and cellulose derivatives, but such means have not hitherto been described.

The enhancement of the density of cross linking in polyvinyl chloride by the presence of the allyl ester was of such magnitude that it seemed feasible to cross link by radiation, in this way, those polymers the normal response of which to radiation is degradation. Experiments with polyisobutylene and polymethyl methacrylate have given ostensible evidence of cross linking while with secondary cellulose acetate the results leave no shadow of doubt that heavy cross linking can be achieved. This polymer, like polyvinyl chloride, is normally plasticized to facilitate processing and advantage could thus be taken of the plasticizing action of the allyl ester.

The most obvious effect of replacement of normal plasticizers in cellulose acetate by a convertible plasticizer such as triallyl citrate was that irradiation caused a pronounced increase in tensile strength. This is shown in Fig. 1, where the tensile strength at room temperature of a composition initially containing 32 per cent triallyl citrate is given as a function of the radiation dose, using 2 MeV electrons from the scanned beam of a Van de Graaff accelerator. As shown in the accompanying curve normally plasticized cellulose acetate exhibited no change in tensile strength over the dose-range studied, despite the radiation damage which was betrayed by darkening, bubbling and reduction in ultimate elongation.

Elevation of the tensile strength at room temperature provided evidence for the polymerization of the triallyl citrate but not, in itself, of cross linking of the cellulose acetate. The accepted criteria for cross

linking are non fusibility, non solubility and reversible high elasticity. Measurements of fusibility were inappropriate in the present instance because of the high melting point of secondary cellulose acetate (c. 300°) (ref. 4). Measurements of rubber like behaviour were similarly thwarted by the inherent stiffness of cellulose acetate chains, and only solubility and swelling criteria can be employed. As is well known, secondary cellulose acetate can be dissolved rapidly in acetone. By contrast, irradiated solid solutions of secondary cellulose acetate in triallyl citrate were highly resistant to acetone. This is shown in Fig. 2, where for a composition containing 32 per cent triallyl citrate, the gel fraction (24 hr Soxhlet extraction with acetone) and the swelling index (24 hr in acetone at room temperature) are given as a function of dose. Even a dose as low as 10 Mrads has sufficed to confer a considerable degree of solvent resistance, matching that of similarly cross linked polyvinyl chloride⁵.

For the purpose of exploring the mechanism whereby cellulose acetate has been rendered insoluble it was desirable to measure the rate of polymerization induced by radiation of the triallyl citrate. Such measurements in the solid state pose a number of problems. Physical methods are generally superior, and density, spectroscopic and relaxation methods have been used⁶. In the present instance, the rate of conversion of the ester has been followed using a Beckman DK2 spectrophotometer. Solutions of triallyl citrate in acetone were used to construct a calibration curve relating the absorbance of the 1.025 μ allylic absorption band with the allyl concentration and this curve led, with appropriate corrections, to values for residual allyl concentration

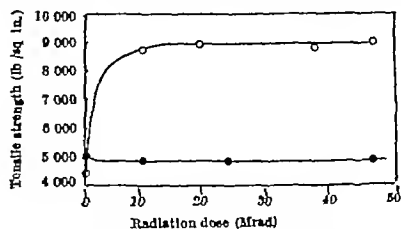


Fig. 1. Tensile strength of (irradiated cellulose acetate ●; Normally allyl plasticized ○ plasticized with 32 per cent triallyl citrate)

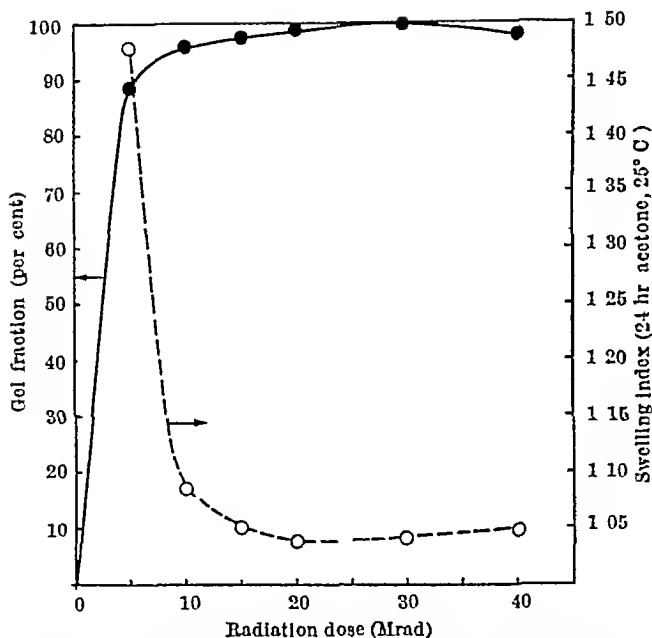


Fig 2 Solubility and swelling of irradiated cellulose acetate
●, Gel fraction (24 hr Soxhlet, acetone), ○, swelling index
(24 hr acetone, 25°C)

in irradiated solid solutions of cellulose acetate in triallyl citrate. The results are shown in Fig 3, whence, allowing for initial scatter, it is apparent that the disappearance of allyl is essentially proportional to dose up to at least 50 per cent conversion and that the slope is essentially independent of concentration.

The average initial allyl disappearance-rate was 0.202 micromole per gram per megarad, corresponding to $G(-allyl) = 200$. Corresponding figures for the electron-induced homopolymerization-rate are not available, but in view of the relatively small intensity dependence of allyl polymerization, comparison may be made with the rate of homopolymerization induced by γ -rays, which at an intensity of 11,700 rads/min gives $G(-allyl) = 103$ (Wycherley, V, unpublished work). It follows that while some enhancement of conversion-rate in the presence of cellulose acetate has occurred, the effect is small.

As an initial hypothesis, it may be considered that the components of the solid solution of cellulose ac-

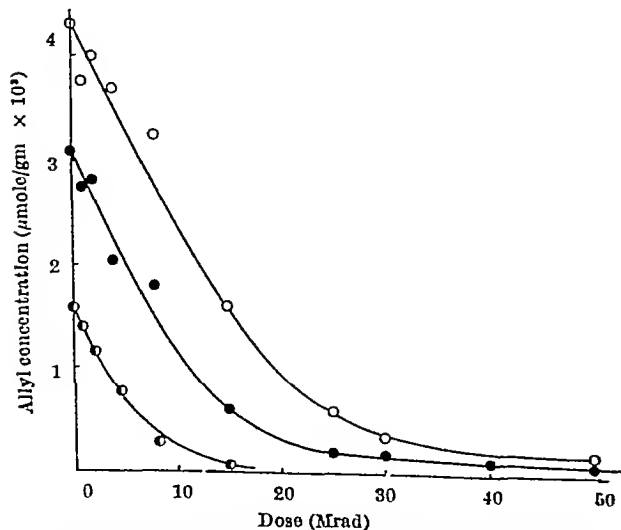


Fig 3 Variation of allyl concentration in cellulose acetate gels
Composition containing ○, 45 per cent triallyl citrate, ●, 32
per cent triallyl citrate, ◐, 16.4 per cent triallyl citrate

tate in triallyl citrate respond independently to radiation in their characteristic fashion. The hexafunctional monomer when irradiated alone has yielded gel at approximately 10 per cent conversion (Wycherley, V, unpublished work). The rate of radiolysis of cellulose acetate has not been reported, the closest approximation being the fracture-rate for irradiated cellulose, which has been given as $G(\text{fracture}) = 11$ (ref 6). If these processes are superimposed, it follows that the cellulose acetate component will be progressively rendered insoluble by irradiation of the mixture if it becomes attached to the allyl network at a rate exceeding that of radiolysis. The mode of attachment is simply that of initiation of an allyl chain, and it remains to consider semi-quantitatively the probable rate of initiation by polymeric cellulose acetate radicals relative to that of scission.

The ratio of frequency of chain transfer to frequency of propagation during normal polymerization of allyl esters lies in the range 10–20 (ref 7). Taking the mean for triallyl citrate leads to $G(\text{chain initiation}) \approx 13$. Since the condition for cross-linking is that the probability of forming cross-linking units should be at least half the probability of dislinking, that is, $p_0/q_0 < 2$, the minimum G -value for junction point formation on the cellulose acetate in order for gel to accumulate is 5.5. While it is entirely reasonable that the G value for radical formation produced by radiation in cellulose acetate might equal 5.5, such a rate of initiation could only lead to very slow aggregation of the gel. In point of fact, gel aggregation is rapid (see Fig 2), which is more consistent with a value of q_0 exceeding p_0 . While G values for initiation by cellulose acetate as high as 10–15 cannot be ruled out, on present limited data, such primary initiation rates seem abnormally high and it is more likely that a supplementary contribution is made by a process of effective chain-transfer, whereby a growing allyl chain abstracts a hydrogen atom from the cellulose acetate molecule rather than from an allyl monomer molecule, leaving the resultant macro-radical to re-initiate a further allyl chain and serve as a junction point with the network. In view of the similarity in the triallyl citrate conversion-rate in the presence or absence of cellulose acetate, there is no need, however, to postulate reactivation of resonance stabilized allylic radicals, as was found necessary in the case of polyvinyl chloride¹.

If this picture is correct, it may be concluded that cross linked cellulose acetate arises as a consequence of irradiation in the presence of a network-forming monomer, which has a short propagation chain-length and serves as an efficient trap for polymeric radicals whether produced directly by radiation or indirectly by hydrogen abstraction.

This work has been carried out in collaboration with BX Plastics, Ltd, and we wish to thank Dr R. R. Smith and Dr M. Pettit for discussion, and the Chairman of BX Plastics, Ltd, and the Chairman of Tube Investments, Ltd, for permission to publish this work.

¹ Pinner, S. H., *Nature*, 183, 1108 (1959).

² Chaplro, A., *Indust. des Plastiques Modernes*, 8 No 1, 41 (1957), *J. Chim. Phys.*, 53, 895 (1956).

³ Alexander, P., and Charlesby, A., *J. Polymer Sci.*, 23, 355 (1957).

⁴ Malm, C. J., et al., *Indust. Eng. Chem.*, 43, 684 (1951).

⁵ Pinner, S. H., and Wycherley, V., paper submitted to Wiesbaden Conference on High Polymers.

⁶ Charlesby, A., *J. Polymer Sci.*, 15, 203 (1955).

⁷ Bartlett, P. D., and Aitshul, R., *J. Amer. Chem. Soc.*, 67, 810 (1945).

FORTHCOMING EVENTS

(Meetings marked with an asterisk * are open to the public)

Monday November 30

ROYAL SOCIETY (at Burlington House Piccadilly London W1) at 2.30 p.m.—Anniversary Meeting

INSTITUTE OF METAL FINISHERS (in the Canterbury Room of the Charing Cross Hotel London W.C.2) at 2.45 p.m.—Mr A. A. B. Harvey "The Role of the Scientific Society" (Presidential Address)

UNIVERSITY COLLEGE (in the Physiology Theatre Gower Street, London, W.C.1) at 5 p.m.—Prof. B. P. Kennedy (University of Chicago) "The Biosynthesis of Complex Lipids" (First of two lectures in Biochemistry Further lecture on December 7)

ROYAL INSTITUTION LIBRARY CIRCLE (at 21 Albemarle Street London W.1) at 5.30 p.m.—Dr L. Pearce Williams "Faraday Through His Manuscripts"

ROYAL GEOGRAPHICAL SOCIETY (at 1 Kensington Gore, London, S.W.7) at 8.30 p.m.—Prof G. von F. Haimendorf "Sherpas of Eastern Nepal"

Tuesday December 1

UNIVERSITY OF LONDON (in the Anatomy Theatre University College Gower Street London, W.C.1) at 1.15 p.m.—Prof H. E. D. Bishop "Vibration Problems in Engineering"

INSTITUTE OF ELECTRICAL ENGINEERS MEASUREMENT AND ELECTRONICS SECTIONS (at Savoy Place London W.C.2) at 5.30 p.m.—Dr L. Eason Mr J. V. L. Parry and Mr J. McA. Steele "Frequency Variations of Quartz Oscillators and the Earth's Rotation in Terms of the N.P.L. Cesium Standard"

UNIVERSITY OF LONDON (at Imperial College of Science and Technology London S.W.7) at 5.30 p.m.—Prof H. K. Porter "Physiology has No Frontiers" (Inaugural Lecture)

UNIVERSITY OF LONDON (at the London School of Hygiene and Tropical Medicine Keppel Street Gower Street London W.C.1) at 5.30 p.m.—Dr J. L. Gowans "The Lymphocyte" (Twelfth of a series of lectures on "The Scientific Basis of Medicine" organized by the British Postgraduate Medical Federation Further lectures on December 3 & 10)

PLASTICS INSTITUTE (at the Wellcome Building, 183-193 Euston Road London, N.W.1) at 6.30 p.m.—Mr B. E. Ashenden "Plastics and the Law"

ROYAL AERONAUTICAL SOCIETY (at 4 Hamilton Place London W.1) at 7 p.m.—Dr I. M. Hall "Transonic Flow Over Swept Wings"

Wednesday, December 2

ROYAL STATISTICAL SOCIETY (at the London School of Hygiene and Tropical Medicine Keppel Street Gower Street London W.C.1) at 5 p.m.—Mr E. M. L. Beale "Confidence Regions in Non Linear Estimation"

INSTITUTE OF PETROLEUM (at 61 New Cavendish Street London W.1) at 5.30 p.m.—Mr J. Marchalend Mr P. de Radzinski "Potentialities of Urea in Dewaxing Middle and Heavy Distillates"

INSTITUTE OF INFORMATION SCIENTISTS (at the Bernal Hotel 10 Bernal Street, London W.1) at 6 p.m.—Discussion on "Languages in Information Work—To What Extent is Competence in a Foreign Language an Essential Qualification for an Information Scientist?"

Wednesday December 2—Thursday December 3

IRON AND STEEL INSTITUTE (in the Great Hall, Caxton Hall Caxton Street London, S.W.1) and the House Memorial Hall Church House Great Smith Street London S.W.1) at 9.30 a.m. daily—Autumn General Meeting.

Thursday December 3

UNIVERSITY OF LONDON (in the Anatomy Theatre University College Gower Street London W.C.1) at 1.15 p.m.—Mr P. R. Bell "The Origin of Indian Corn"

ROYAL SOCIETY (at Burlington House Piccadilly London, W.1) at 4.30 p.m.—Mr F. H. G. Edgcombe and Prof R. O. W. Norrish F.R.S. A Study of the Mechanism of Photochemical Electron Transfer Processes in Solution Mr I. M. Dawson and Mr E. A. G. Follitt "An Electron Microscope Study of Synthetic Graphtite"

INSTITUTE OF MARINE ENGINEERS (joint meeting with the INSTITUTE OF NAVAL ARCHITECTS, in the Well Hall 10 Upper Belgrave Street London, S.W.1) at 4.45 p.m.—Prof G. Aertsen "New Sea Trials on the Landing of Jets"

UNIVERSITY OF LONDON (at the London School of Economics and Political Science, Houghton Street London W.C.2) at 5 p.m.—Dr P. R. Leach "Rethinking Anthropology" (Malinowski Memorial Lecture)

ROYAL SOCIETY OF ARTS, COMMONWEALTH SECTION (at John Adam Street, Adelphi London W.C.2) at 5.15 p.m.—Mrs. Mildred Valley Thornton "Indians of British Columbia"

INSTITUTE OF ELECTRICAL ENGINEERS (at Savoy Place London W.C.2) at 5.30 p.m.—Dr C. B. B. Wood and Mr I. J. Shelley "The Transmission of News Film over the Trans Atlantic Cable"

SOCIETY OF CHEMICAL INDUSTRY MICROBIOLOGY GROUP (joint meeting with the SOCIETY FOR APPLIED BACTERIOLOGY at the Royal Society of Medicine 1 Wimpole Street London W.1) at 6.15 p.m.—

Dr P. Brown "Infective Ribonucleic Acid from the Virus of Foot and Mouth Disease"

ROYAL PHOTOGRAPHIC SOCIETY MEDICAL GROUP (at 16 Prince's Gate, London, S.W.7) at 7 p.m.—Sir Stanford Gage, K.B.E. G.B. F.R.C.S. "What I Want from a Medical Photographer"

Friday December 4

INSTITUTE OF ELECTRICAL ENGINEERS MEDICAL ELECTRONICS DISCUSSION GROUP (at Savoy Place, London W.C.2) at 6 p.m.—Discussion on "Nuclear Magnetic Resonance" opened by Dr V. Sheppard and Dr R. E. Richards

SOCIETY OF DYERS AND COLOURISTS (at the Royal Society Burlington House, Piccadilly London W.1) at 6 p.m.—Mr R. C. Oakley "Dyeing of Ribbons" Mr R. Woods "Dyeing of Carpet Yarns"

ROYAL INSTITUTION (at 21 Albemarle Street London W.1) at 9 p.m.—Dr H. A. Thomas "Electronic 'Brains'"

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned

ASSISTANT LECTURER IN PHYSICS—The Registrar The University Manchester 13 (November 30)

CHAIR OF CHEMICAL ENGINEERING—The Registrar University College Singleton Park Swansea (November 30)

ASSISTANT LECTURER IN PHYSIOLOGY—The Registrar The University Sheffield (December 6)

LECTURER IN PHYSIOLOGICAL PSYCHOLOGY—The Registrar (Room 22, O.R.B.) The University Reading (December 9)

LECTURER IN SOCIAL ANTHROPOLOGY and a LECTURER IN RURAL SOCIOLOGY IN THE FACULTY OF ECONOMIC AND SOCIAL SCIENCES—The Registrar The University Manchester 13 (December 12)

ORGANIC CHEMIST Scientific Officer or Senior Scientific Officer grade in the DEPARTMENT OF HOP RESEARCH for research problems related to the hop plant—The Registrar Wye College near Ashford Kent (December 12)

LECTURER or LECTURER IN APPLIED MATHEMATICS—The Registrar The University Sheffield (December 19)

ASSISTANT LECTURER or LECTURER IN THE DEPARTMENT OF ZOOLOGY—The Registrar The University Liverpool (December 19)

LECTURER/SENIOR LECTURER (with an interest in and qualified for teaching and research in any of the main branches of psychology) in PSYCHOLOGY at the University of Sydney Australia—The Secretary, Association of Universities of the British Commonwealth, 35 Gordon Square London W.C.1 (Australia December 19)

LECTURER IN FOREST PATHOLOGY at the Walke Agricultural Research Institute—The Registrar University of Adelaide Adelaide South Australia (December 21)

SENIOR LECTURER IN APPLIED ANATOMY at the University of Adelaide, Australia—The Secretary Association of Universities of the British Commonwealth 35 Gordon Square London W.C.1 (Australia, December 21)

SENIOR LECTURER or LECTURER IN PSYCHOLOGY at the University of Khartoum—The Registrar University of Khartoum c/o Inter University Council for Higher Education Overseas 29 Woburn Square London W.C.1 (December 22)

SENIOR PRINCIPAL SCIENTIFIC OFFICER (honorary graduate in science with appropriate research experience) with the Hill Farming Research Organization to act as Deputy to the Director of the organization and in particular, to be responsible to him for the development and co-ordination of the programme of research carried out by the Organization in scientific departments—The Secretary, Hill Farming Research Organization 48 Palmerston Place Edinburgh 12 (December 31)

ASSISTANT LECTURER or LECTURER IN PHYSICS—The Registrar University College of South Wales and Monmouthshire Cathays Park Cardiff (January 2)

READER IN MEDICAL MICROBIOLOGY at the University of Western Australia—The Secretary Association of Universities of the British Commonwealth 35 Gordon Square London W.C.1 (January 16)

LECTURER or ASSISTANT LECTURER IN PSYCHOLOGY—The Registrar University College of South Wales and Monmouthshire Cathays Park Cardiff (January 16)

SENIOR LECTURER and a LECTURER IN MATHEMATICS at the University of Khartoum—The Secretary Association of Universities of the British Commonwealth 35 Gordon Square London W.C.1 (January 29)

ADMINISTRATIVE ASSISTANT (male science graduate (preferably physicist) not more than 35 years old and interested in space research) with the Secretariat of the British National Committee on Space Research—The Assistant Secretary Royal Society Burlington House Piccadilly London W.1

AREA CHEMIST (with high academic and/or professional qualifications good general experience of modern analytical methods and particularly well versed in the technique of determining oils and greases)—The Director of Research (British Railway), British Transport Commission 222 Marylebone Road London N.W.1

BIOLOGIST (with a good honours degree in zoology and/or botany preferably a knowledge of both subjects and some postgraduate experience) with the Fauna Research Unit Kenya to carry out research in Kenya to provide data for the building up of life tables, details of feeding habits, enemies predators and diseases—The Director of Recruitment Colonial Office London S.W.1 quoting Ref No BOD 63/090/01

BOTANIST (PLANT PATHOLOGIST) (with a good honours degree in botany and/or zoology and at least 3 years postgraduate experience in plant pathology) in the Department of Agriculture, Uganda, to diagnose the cause of crop diseases and recommend control measures and to assist with the breeding of disease resistant crops—The Director of Recruitment Colonial Office London W.1 quoting Ref No BOD 63/090/01

ENTOMOLOGIST, Scientific or Senior Scientific Officer (with a good honours degree in zoology with postgraduate training or experience in entomology) at the West African Cocoa Research Institute, Ghana, for research on insect pests of cocoa—The Director of Recruitment, Colonial Office, London, S W 1, quoting Ref No BCD 107/200/92/C1.

GROSS ANATOMIST (with research interests preferably, but not exclusively, either in electron microscopy or optical (especially interference) microscopy)—The Chairman Department of Anatomy, Emory University, Atlanta 22, Georgia, U.S.A.

IRRIGATION RESEARCH OFFICER (with a university degree in agriculture or a science degree with agricultural experience, and training or experience in soil physics or irrigation) in Swaziland, to carry out irrigation experiments on sugar cane, citrus and other crops, and to take charge of a new experimental station—The Director of Recruitment, Colonial Office, London, S W 1, quoting BCD 63/70/014/T.

LABORATORY TECHNICIAN (able to work with the minimum of supervision, a sound knowledge of chemistry, and some experience of biological techniques)—The Administrator, Department of Biochemistry, The University South Parks Road, Oxford.

LECTURER (well qualified physicist, and preferably with experience of the application of physics in industry) in PHYSICS—The Registrar, Bradford Institute of Technology, Bradford 7.

MASTER to teach Chemistry, principally in the Sixth Form, up to scholarship standard with some Middle School work—The Headmaster, University College School, Frognal, Hampstead, London, N W 3.

PLASTICS CHEMIST or PLASTICS TECHNOLOGIST IN THE DEPARTMENT OF MATERIALS, to assist in the organization and supervision of the teaching laboratories and to participate in the research activities of the plastics group—The Registrar, The College of Aeronautics, Cranfield, Bletchley, Bucks.

TECHNICIAN or SENIOR TECHNICIAN IN THE ZOOLOGY DEPARTMENT—The Secretary, Royal Holloway College (University of London), Englefield Green Surrey.

TECHNICIAN (preferably with previous experience in bacteriological work), to work in the Virus Research Laboratory at Lodge Moor Hospital—Prof C H Stuart-Harris, The Royal Hospital, Sheffield 1.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

The Hannah Dalry Research Institute Report for the Three Years ended 31st March 1959 Pp 52+12 plates (Kirkhill, Ayr Hannah Dalry Research Institute 1959) [1419]

The Needs of Youth in Stevenage a Report to the Calouste Gulbenkian Foundation Pp 47 (London Calouste Gulbenkian Foundation, United Kingdom and British Commonwealth Branch, 1959) 3s [1410]

Department of Scientific and Industrial Research Road Research Laboratory Road Research Technical Paper No 45 Investigation of the Performance of Pneumatic-tyred Rollers in the Compaction of Soil By W A Lewis Pp iv+44+4 plates (London H M Stationery Office 1959) 3s 6d net [1410]

The Scottish Society of the History of Medicine Report of Proceedings, Session 1958-1959 Pp 27+1 plate (Edinburgh Scottish Society of the History of Medicine 1959) [1410]

Report of the Hydrographer of the Navy for the year 1958 Pp 26+4 plates (H D 514) (London Admiralty, 1959) [1410]

British Cast Iron Research Association Thirty-eighth Annual Report for the year ending June 30th, 1959 Pp 21+5 plates (Alce church, Birmingham British Cast Iron Research Association 1959) [1410]

Archives of Oral Biology, Vol 1, No 1 (August, 1959) Pp 1+88 Subscriptions (including postage) (A) For Libraries, Government Establishments and Research Institutions £6 (17 dollars). (B) For individuals who write directly to the Publisher and certify that the journal is for their personal use £3 10s (10 dollars) per annum (London and New York Pergamon Press, 1959) [1410]

Philosophical Transactions of the Royal Society of London Section A Mathematical and Physical Sciences No 1002 Vol 251 (8 October 1959) The Electronic Absorption Spectra of NH₃ and ND₃ By K Dressler and D A Ramsay Pp 553-604+plates 3-5 (London Royal Society, 1959) 21s [1410]

Council for the Preservation of Rural Wales Caernarvonshire Branch Fifteenth Annual Report, 1958-1959 Pp 22+4 plates (Pias Hebog, Beddgelert W Twiston Davies, Acting Hon Secretary, 1959) [2210]

University of Bristol The Annual Report of the Agricultural and Horticultural Research Station (The National Fruit and Cider Institute) Long Ashton, Bristol, 1958 Pp 183+18 plates (Long Ashton, Bristol Agricultural and Horticultural Research Station, 1959) 15s [2210]

Report of the Committee of Enquiry into the Financial Structure of the Colonial Development Corporation Pp iii+25 (Cmd 786) (London H M Stationery Office, 1959) 1s 6d net [2210]

Imperial College of Science and Technology (University of London) Research Report of the Royal College of Science, 1950-1959 Pp v+77 (London Royal College of Science, 1959) [2210]

Building Research Station Digest No 125 (August 1959) Small Underground Drains and Sewers, 2 Pp 5 (London H M Stationery Office, 1959) 4d [2210]

Young Darwin and the Origin of Species By Dr C F A Pantin (Commemorative Oration delivered at the dinner given by the Master and Fellows of Christ's College Cambridge, in the College Hall on Tuesday, 29 September, 1959) Pp 17 (Cambridge Christ's College, 1959) [2210]

Department of Scientific and Industrial Research. Pest Infestation Research 1958 The Report of the Pest Infestation Research Board with the Report of the Director of Pest Infestation Research Pp iv+55+8 plates (London H M Stationery Office, 1959) 5s net [2210]

Other Countries

European Productivity Agency of the Organization for European Economic Co operation Application of Atomic Science in Agriculture and Food Vol 2 Present Position, Future Trends and Techniques—Report of the Working Conference held at OEEC Headquarters Paris, July 1958 Pp 247 (Project No 306) (Paris European Productivity Agency of the Organization for European Economic Co operation, 1959) 1,300 French francs, 21s, 4 dollars, 14 50 Swiss francs [810]

Annals of the New York Academy of Sciences Vol 79, Article 4 Modes and Natural Frequencies of Suspension-Bridge Oscillations. By D B Steinman Pp 100-142 2 50 dollars Vol 79, Article 5 On the Design of Structural Models to Study the Thermal Stress Phenomenon By L Albert Sclipio II Pp 143-156 2 dollars Vol 80, Article 3 Amine Oxidase Inhibitors By D Wayne Woolley and 97 other authors Pp 551-1045 5 dollars (New York New York Academy of Sciences, 1959) [810]

Zoology Publications from Victoria University of Wellington No 25 Some Additional New Zealand Cephalopods from Cook Strait By R K Dell Pp 12 (Wellington Victoria University of Wellington, 1959) [1410]

Medicina Experimentalis, Vol 1, No 1, 1959 (International Journal of Experimental Medicine) Pp 11+68 6 numbers per volume (2 volumes annually) Subscription price per volume 56 Swiss francs (Basel and New York S Karger, 1959) [1410]

South African Council for Scientific and Industrial Research Thirteenth Annual Report, 1957-1958 Pp xii+226+xix-lix. (Pretoria South African Council for Scientific and Industrial Research 1958) [1410]

South Africa Advisory Council on Scientific Policy First Annual Report, December, 1956 to 31 December 1957 Pp 5 (Reprint from Commerce and Industry) Second Annual Report, 1 January to 31 December 1958 Pp 7 (Reprint from Commerce and Industry) Human Problems in the Scientific Age By Prof H O Monag. Pp 8 (Pretoria Advisory Council on Scientific Policy, 1958 and 1959) [1410]

Annals of the New York Academy of Sciences Vol 82, Article 2 Current Trends in Research and Clinical Management of Diabetes By Peter H Forsham and 93 other Authors Pp 191-644 (New York New York Academy of Sciences, 1959) 4 50 dollars [1410]

New Zealand Department of Scientific and Industrial Research Geophysics Division Seismological Observatory Bulletin No E 135 January to December 1954, Wellington, other New Zealand Stations and Fiji Pp 27 (Wellington Government Printer, 1959) [1410]

Kungl Skogshögskolans Skrifter, Nr 32 Studier Över Klimatets Humiditet i Sverige By Olaf J S Tamm Pp 48+2 plates (Stockholm Skogshögskolans, 1959) [1410]

Bulletin of the American Museum of Natural History Vol 118, Article 5 A Historical Review of the Mollusks of Linnaeus Part 7 Certain Species of the Genus Turbo of the Class Gastropoda By Henry Dodge Pp 207-258 (New York American Museum of Natural History, 1959) 1 dollar [1410]

The Carlsberg Foundation's Oceanographical Expedition Round the World 1928-30 and previous "Dana" Expeditions Dana Report No 40 Morphologie und Funktion des Kiefer- und Kiemenapparates von Tiefseefischen der Gattungen Malacosteus und Photostomias (Teleostei) Isospondyli, Stomatolidae, Malacosteidae Von Klaus Günther und Kurt Deckert Pp 54 (Copenhagen Andr Fred Høst & Son, 1959) Danish kr 15 [1410]

The Scientific Film in Germany By Gottfried Wolf Pp 80 (178 black and white and 16 colour plates) (Wuppertal Elsefeld Sam Lucas, Ltd 1959) [2210]

Chicago Natural History Museum Fieldiana Zoology Vol 39 No 30 (May 22, 1959) Review of the Colubrid Snake Genus Spalerocephalus By Hymen Marx Pp 347-361 (Chicago Chicago Natural History Museum, 1959) 40 cents [2210]

Smithsonian Institution Freer Gallery of Art Occasional Papers, Vol 3 No 2 Calligraphers and Painters a Treatise by Qadi Ahmad, Son of Mir-Munshi (circa A D 1015/A D 1600) Translated from the Persian by V Minorsky With an Introduction by B N Zakharov Translated from the Russian by B Minorsky Pp x+223 (Publication 4330) (Washington, D C Smithsonian Institution, 1959) [2210]

Colony and Protectorate of Kenya Forest Department Annual Report, 1958 Pp ii+53 (Nairobi Government Printer, 1959) Sh 4 [2210]

Smithsonian Contributions to Astrophysics Vol 3, No 8 Meteor Trails By Robert F Hughes Pp ii+70-04 (Washington, D C Government Printing Office, 1959) 20 cents [2210]

State of Illinois Department of Registration and Education Natural History Survey Division Bulletin, Vol 27, Article 4 Food Habits of Migratory Ducks in Illinois By Harry G Anderson Pp iv+280-344 Biological Notes No 40 Night-Lighting—a Technique for Capturing Birds and Mammals By Ronald F Labisky Pp 11 (Urbana, Ill Department of Registration and Education—Natural History Survey Division, 1959) [2210]

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LETTERS TO THE EDITORS

ASTRO- AND RADIO-PHYSICS

Directional Observations of Radio Noise from the Outer Atmosphere

ALTHOUGH many observations have been made in the past of the spectra of the radio emissions of the Earth's outer atmosphere in the frequency band 2-40 Kc/s^{1,2}, it is only recently that a technique has been developed for continuously monitoring the occurrences of these phenomena³. This has revealed that radio noise bursts lasting some hours are normally associated with disturbances of the geomagnetic field and follow many high frequency radio outbursts from the sun. It seems likely that these very low frequency noise bursts are caused by the interaction between auroral streams of charged particles and the plasma of the outer atmosphere and proposed mechanisms include Cerenkov radiation^{4,5} and gyro or synchrotron radiation⁶. Studies of their spectra, however, have not provided any clear out tests of these theories and it appears that additional information is required.

Many bursts of very low frequency noise have a relatively narrow spectrum usually about 2 Kc/s wide and centred at about 5 Kc/s³. It is conceivable that these are caused by synchrotron radiation from particles at a distance of about 6 Earth radii where the geomagnetic gyro frequency is about 5 Kc/s. In this case the radiation would be guided down the lines of force of the Earth's magnetic field and would enter the ionosphere at geomagnetic latitudes greater than 66°.

Location of the geographical position of the entry point of very low frequency radiation into the ionosphere might therefore be expected to provide a test of the synchrotron hypothesis. This test would be possible if, after penetrating the ionosphere, the radiation spread horizontally in the ionosphere Earth wave guide. The entry point would then not act as a virtual source which could be located by normal direction finding techniques. However this picture may be incorrect since it is possible that the radiation spreads horizontally within the ionosphere and only reaches the ground as an evanescent wave which would not provide useful directional information. Indeed, attempts in the past to locate the entry point of whistling atmospherics with direction finders have been unsuccessful⁷.

Before attempting the problem of locating the position and size of the virtual sources of the very low frequency emissions it is therefore necessary to establish that it is possible to identify the direction of the noise. Here we report preliminary results obtained with a direction finder operated at Camden N S W at a wave frequency of 4.5 Kc/s. The equipment consists of a two 2-50 Kc/s amplifiers connected to two mutually perpendicular vertical loop antennas each of which is 100 sq. m. in area and has 4 turns. The outputs from the amplifiers are scanned by a rotating condenser goniometer. This system is equivalent electrically to a single loop rotating once every 4 min. The output of the goniometer is fed to a narrow band

amplifier (40-50 Kc/s) and after detection to a minimum reading pen recorder.

When the direction finder is receiving horizontally propagating plane wave radiation its output goes to zero every two minutes when the plane of the equivalent loop is perpendicular to the direction of propagation. If, on the other hand, the virtual source of the radiation is of large extent either in azimuth or elevation non zero minimums are recorded and it can be shown⁸ that the ratio of the minimum to maximum output per rotation is a measure of the source size for an assumed source brightness distribution.

Using this direction finder it has been found possible on many occasions to locate the direction and to estimate the size of the virtual sources of the very low frequency radiation at 4.5 Kc/s. The source size was calculated in each case by assuming a uniformly bright source distributed in azimuth only. Table 1 shows the results obtained since May, 1959. It can be seen that generally the sources were of large angular size, most being between 70° and 70°. Most directions lay either in the southern or the northern quadrant of the compass; the ambiguity resulting from the use of simple loop antenna without a sense necessary. However because of the relatively low geomagnetic latitude of Camden (42° S) it is considered likely that all virtual sources were to the south. The ambiguities of direction and source brightness distribution will be reduced to a considerable extent in future observations by the use of separate widely spaced direction finders.

Fig. 1a shows a sample record of a noise burst recorded at 3/4" per hr while Fig. 1b shows the corresponding direction finder record of this burst. The considerable modulation of the direction finding records resulting from the directional properties of the noise is easily visible. Fig. 1c shows a record made of another noise burst at a chart speed of 2 per hr in order to demonstrate the change in the modulation depth. During this burst the modulation depth increased with time and simultaneously the noise intensity decreased.

It appears from these observations that on many occasions it should be possible to map the positions and sizes of the regions from which very low frequency radio noise from the outer atmosphere emerges below the ionosphere.

Suitable techniques for such a study would include either a network of direction finders or perhaps radio link interferometers similar to those used in radio astronomy.

Table 1 LIST OF DIRECTIONS AND ANGULAR SIZES OF APPARENT SOURCES OF 4.5 Kc/s RADIATION

| Date (1959) | Local Time | Minimum Power Maximum Power | Direction Magnetic | Size in azimuth |
|-------------|------------|--------------------------------|-----------------------|--------------------|
| May 15 | 0400 | 0.10 | 190° | 77 |
| May 16 | 1830 | 0.02 | 19 | 32 |
| July 11 | 1800 | 0.0 | 205 | 44 |
| July 12 | 0010 | 0.40 | 280 | 120 |
| July 13 | 0400 | 0.12 | 275 | 64 |
| July 14 | 2100 | 0.10 | 120 | 62 |
| July 15 | 2000 | 0.25 | 225 | 96 |
| July 16 | 2020 | 0.30 | 160 | 114 |
| July 18 | 2020 | 0.14 | 140 | 75 |
| July 18 | 2200 | | | |

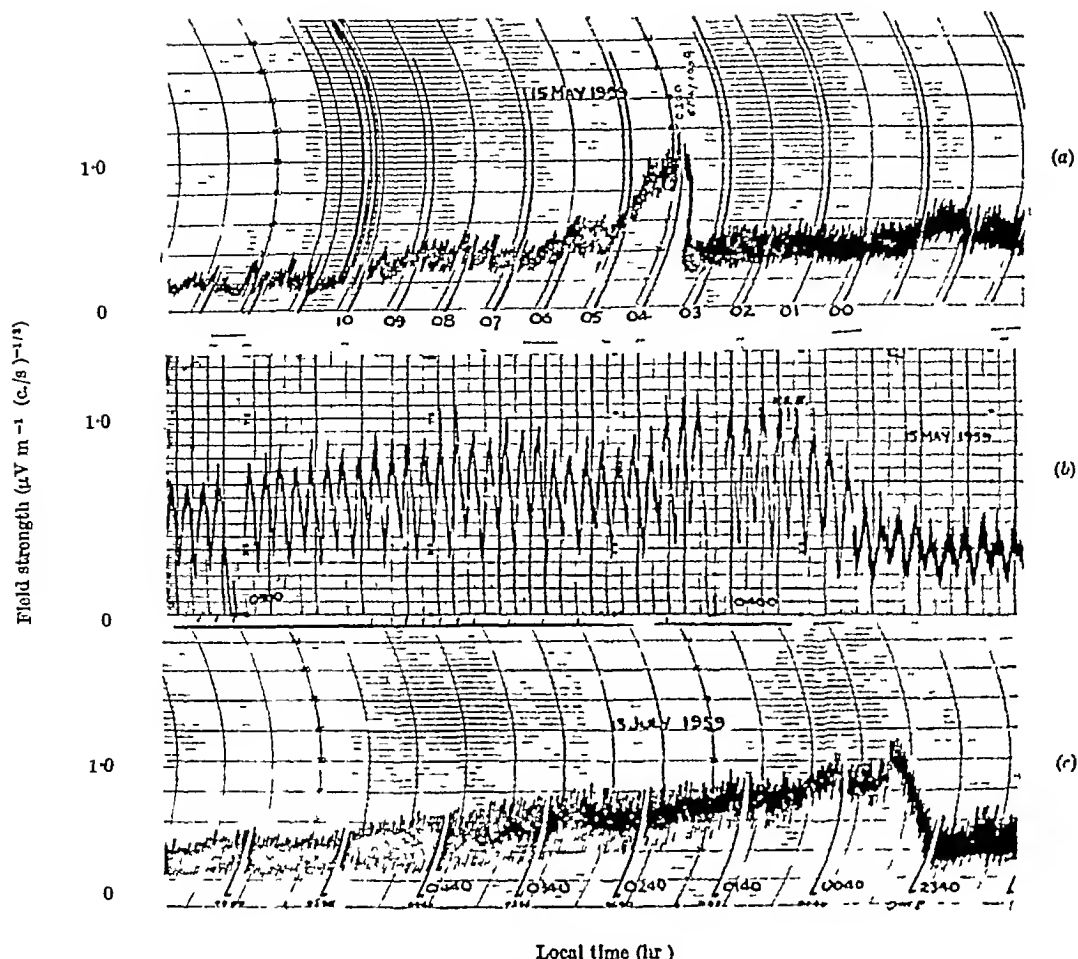


Fig. 1. a, 4.5 kc/s noise bursts recorded at Camden, New South Wales; b, direction finding record of noise burst at 4.5 kc/s showing change in direction finding modulation depth with time; c, direction finding record of portion of the noise burst of a.

Thanks are due to Mr D M Adams for assistance in the construction of the equipment.

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The Inner Solar Corona during June 1959

STUDY of the solar occultation of the Taurus A radio source has yielded new information concerning the structure of the solar corona at large distances¹, however, the interpretation of the observations is somewhat hampered by lack of knowledge of the electron densities prevailing in the corona at the time of the occultation. Although observations made with the K-coronameter² at Chmax, Colorado, do not extend out to the region of occultation, the measurements in Table 1 should give some indication of the conditions existing in the corona at the time of the recent passage.

In Figs 1-4 appear polar graphs of the product of polarization p times radiance B of the K-corona in

units of the radiance of the centre of the solar disk for the dates involved.

To analyse the more complete data of June 10 in detail, we plot as a function of height above the limb: (1) pB averaged at 10° intervals (heligraphic) all around the solar limb (Fig 5), (2) pB averaged at 10° intervals (heligraphic) over the south polar region A (Fig 5), (3) pB averaged at 10° intervals (heligraphic) over the latitude regions B and C (Fig 6), (4) pB at the centre of the active region D (Fig 6). In each case, except the axis of the active region, the variation of pB with height is well represented by the relation found by van de Hulst³.

Since the Taurus A source passes to the south of the Sun, the south polar region is of particular interest. On June 10 the polar region marked A was quite weak. Assuming for simplicity in integrating along the line of sight a model with spherical symmetry, we find that electron densities over this region would be about 0.3 times the values tabulated by van de Hulst for a corona at sunspot maximum. Region A was flanked by regions B and C in which the densities were nearly equal and considerably higher than in A. On the same assumption, B and C have densities about that given by the van de Hulst model. The central axis of the active region D

| TABLE 1 | | |
|---------|---|---|
| Date | Scan distances (min. of arc from limb) | Remarks |
| June 9 | 2.4 | low weight data (calibration several hours later) |
| June 10 | 1.0, 4.4, 6.4, 8.4, 11.4, 15.4 | standard weight data |
| June 11 | 2.4, 4.4, 6.4 | low weight data (calibration made in cirrus) |
| June 17 | 2.4 | standard weight data |

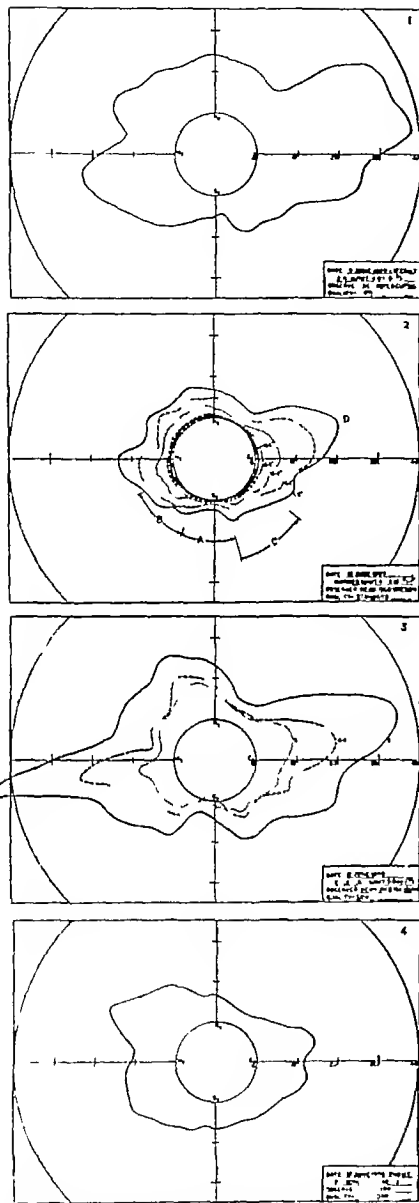


Fig. 1-4 Polar plots of the product pB where p is the polarization and B the radiance for the A-corona at the sun heights indicated. The unit is compared to the radiance of the centre of the solar disk and all position angles are heliographic. The scanning aperture is 2.4 min. of arc diameter.

is unusual in that the enhancement of electron density seems restricted to the lower 250,000 km

(6 min. of arc above the limb) of the corona. Whether or not this structure is related to the flare and subsequent large loop prominence of June 9 is not known.

Observations of June 9 and 11 are not of sufficient quality to allow more than the determination that the general shape of the corona did not change significantly during the period. By June 17, however, the dip near the south pole had disappeared and the electron densities across the south polar cap would have been those of the van de Hulst model if the single scan at 2.4 above the limb can be considered as indicative of the rest of the corona.

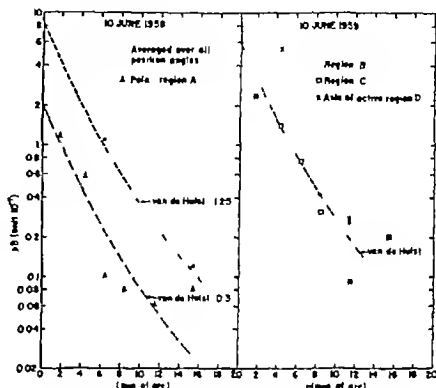


Fig. 5

Fig. 6

Fig. 5 Radial dependence of pB for June 10, 1959 for the average of all position angles and for the average over region A (see Fig. 2). At $r=16$ min. of arc the error in measurement is approximately 60 per cent, while at $r=2$ min. of arc the error is about 10 per cent.

Fig. 6 Radial dependence of pB for June 10, 1959 averaged over regions A and C and along the axis of the active region D (see Fig. 2).

The scanning aperture of 2.4 min. of arc diameter does not allow the detection of small scale structure such as polar brushes. The tracings do show a ray like structure in the south-east which has its base at a position angle of approximately 160° heliographic during the interval June 9-11. The feature seems to bend toward lower position angle (equator ward) at greater distances from the sun.

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GEOLOGY

The Geological Time-Scale

RECENT contributions¹⁻³ on post-Proterozoic geochronology are timely, for national organizations in the U.S.S.R. and in the United States are now preparing reports on this topic for submission to the International Geological Congress next year. In the recent discussions two questions have been raised (a) the validity of the extended time-scale proposed by investigators at the University of Oxford, and (b) the validity of age determinations made on the Upper Cambrian kolm of Sweden. On both these issues there is much more evidence than has been cited.

The time-scale proposed by Dr K. I. Mayne¹ and his colleagues puts back the date of the uppermost Cambrian strata from 450 to 650 million years. The structure of evidence forming the foundation for this conclusion has, deservedly, been demolished by Prof J. L. Kulp² and his associates, of Columbia University, but the latter go too far in asserting that the scale of the Oxford workers "is not supported by measurements other than their own". While for reasons given below I do not accept this scale, it is very relevant that it is upheld by recent determinations reported from the laboratories of the United States Geological Survey⁴. These record a uraninite from Triassic strata in New Jersey giving concordant lead/uranium and lead/lead determinations of 228, 228 and 230 m.y., and a uraninite from Lower Pennsylvanian strata in Pennsylvania giving various ages ranging from 296 to 337 m.y.

This greatly extended time scale is however ruled out, in my view, by an immense weight of other evidence. The Oxford team claims to have evaluated earlier researches, with rejection of all save eleven determinations, "because the stratigraphy of the samples or their measured age is not free from unwarranted assumptions", but of their 11 acceptances, which are mostly transgressive igneous rocks of debatable stratigraphy, no less than ten values are rejected by Prof Kulp. Lately, in preparing a geochronological table to be published elsewhere⁵, I have culled from world-wide literature more than two hundred age determinations on Mesozoic and Palaeozoic rocks, mostly executed during the past five years. Of these, more than half were adjudged unacceptable because of inadequacies of sampling, analysis or documentation, and the remainder comprises 91 values, all relating to stratigraphically well-defined samples, which cannot be so rejected. Of these values, 66 are derived from Russian literature. The great variety of techniques represented includes rubidium/strontium determinations on micas and glauconite, potassium/argon assays on micas, glauconite, sylvite, primary feldspar, and authigenic feldspar, potassium/argon assays on lavas, tuffs, minor intrusions, slates, horn-felses, and some granitic rocks, potassium/calcium analyses on sylvite, lead/alpha studies on zircon, and helium studies on magnetite. In ten instances two or more methods have been employed on the same sample, with good agreement.

To establish a geochronology from these data without incurring suspicion of subjective selection, an average age has been calculated for the rocks of each system. Where there are sufficient data this should approximate to the mid-point of the period in question. In Table 1 the values derived from recent experiments

Table 1 MID-POINTS OF THE GEOLOGICAL PERIODS (MILLIONS OF YEARS)
Holmes B Belousov Oxford Recent experiments (Number of records)

| | | | | | |
|---------------|-----|-----|-----|-----|------|
| Cretaceous | 92 | 90 | 100 | 100 | (27) |
| Jurassic | 140 | 130 | 160 | 153 | (9) |
| Triassic | 167 | 169 | 225 | 174 | (5) |
| Permian | 162 | 205 | 275 | 212 | (3) |
| Carboniferous | 239 | 250 | 350 | 234 | (5) |
| Devonian | 244 | 292 | 440 | 329 | (11) |
| Silurian | 332 | 323 | 510 | 303 | (6) |
| Ordovician | 390 | 363 | 600 | 410 | (8) |
| Cambrian | 470 | 423 | 700 | 517 | (15) |

are compared with the mid-points on the Holmes, Belousov and Oxford scales.

The records from which these averages were compiled include potassium/argon determinations on feldspars and whole rocks. If there has been loss of argon from feldspar, these ages will be less than the true values. But, notwithstanding Dr Mayne's conclusions to the contrary², the evidence strongly suggests that in unweathered and unmetamorphosed rocks such loss is exceptional. Where sets of analyses are available (in four instances), there is no significant difference between age determinations on biotites, on non-perthitic feldspars, and on whole rocks. It seems that potassium/argon ages on feldspar have quite unjustifiably received a bad name as a result of many demonstrations of loss of argon from pegmatitic microclines. Since Dr S. S. Sardarov⁶ has shown that this loss is directly proportional to the degree of development of perthite or microperthite (thus being dependent on the late thermal history of the rock), we have an acceptable explanation why ages based on pegmatitic feldspars tend to be low, while whole-rock ages on granodiorites, plagiogranites and unmetamorphosed eruptives devoid of perthitic structures agree well with determinations on the biotites which the same rocks contain.

A final word about kolm. Prof. Kulp rejects my contention that although the uranium and lead in the alum shales is syngenetic, these elements are largely epigenetic in the kolm concretions. It would be wise to bear in mind the practical researches of Dr E. V. Rozhkova and others⁷, who have shown that even hydrocarbons as highly anthracitized as the middle Proterozoic shungite of Karelia still retain a marked capacity for adsorbing uranium. Since the groundwaters of the alum shales are, and presumably always have been, highly uraniferous, and since there has been no demonstration that the adsorptive capacity of kolm is out of line with that of similar hydrocarbons, the hypothesis that uranium has been continually introduced into the kolm throughout the ages should not be dismissed so cavalierly. In brief, this material is no more suited to be a geochronological bench-mark than was the uraniferous phosphorite on which Strutt made his pioneer age determinations more than fifty years ago.

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PHYSICS

Sedimentation and Effective Viscosity

In the course of a more extensive calculation, a set of equations has been obtained which relates the sedimentation velocity u of particles falling through a liquid to the effective viscosity μ of a suspension of similar particles having the same density as the fluid. The volume concentration c is the same in both cases.

To a mixture with mean settling velocity u and concentration c , let us add a particle B the density of which is that of the fluid, that is it is in suspension. Its mean velocity averaged over all possible positions, is equal to the mean fluid velocity modified by the pressure gradient in the fluid due to the falling particles A .

$$v = v_f + v_p \quad (1)$$

Now assume that its density is increased to that of the other particles A , so that its mean velocity increases to v' . The increase is:

$$U = v' - v \quad (2)$$

is caused by the extra external force on it, the forces on the other particles being unchanged. Consequently, if the equations of motion of the fluid are linear, U is also the velocity of fall of B through a suspension of particles A with the same density μ , and, from Stokes's law

$$U\mu = V\mu_s \quad (3)$$

where V is the Stokes velocity of the particle in pure liquid of viscosity μ_s .

Finally if B is typical of the particles A , its mean velocity of fall is that of the suspension, namely

$$u' = u \quad (4)$$

Combining the last three equations

$$\mu u = V\mu_s + \mu v \quad (5)$$

It is now necessary to estimate the velocity v of B when suspended in the settling mixture. Provided $v \ll u$ it can be neglected and we obtain the approximation

$$\mu u = \mu_s V + \text{const} \quad (6)$$

This is certainly true in the limit $c \rightarrow 0$, when $\mu \rightarrow \mu_s$ and $u \rightarrow V$. It is also an admittedly crude but valid approximation to u for all concentrations.

An approximate value of v , which might apply at low concentrations, can be obtained by neglecting the effect of a pressure gradient and assuming that a suspended particle B moves with the fluid. In a closed vessel the fluid rises as particles fall through it with a mean velocity $-cu/(1-c)$ determined by the equation of continuity. Assuming that:

$$v + v_p = -cu/(1-c) \quad (7)$$

we obtain from equation (5):

$$\mu u = \mu_s V(1-c) \quad (8)$$

This approximation seems to agree with the experimental results up to concentrations of about 20 per cent (ref. 1). Above this the value of μu rises fairly rapidly. It is rather surprising that equation 8 holds over such a range of concentrations. In a suspension where the force on a particle is k times its volume, one expects a pressure gradient of the order k in a closed vessel in the direction of the force and this corresponds to $v_p \sim \frac{1}{2} cV$ for a spherical particle. This is of the same order of magnitude as v_f and in the opposite direction and quite large enough to alter considerably the correction factor in equation 8.

As the concentration rises and v_p increases the value of u should certainly increase and this agrees once more with experiment. If this analysis is correct, the increase can be used to estimate v_p . Finally, it

would be very useful if measurements were made of this drift velocity of a particle suspended in a fluid containing sediment, they should not be difficult.

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METALLURGY

A New Nitride Precipitate in Iron-Silicon Alloys

RECENT work has indicated the presence of a new nitride precipitate in iron-silicon alloys. Leak, Thomas and Leak¹ using internal friction methods investigated nitrided iron-silicon alloys and deduced the presence of an unknown precipitate thought to be an iron-silicon nitride. Turkdogan, Bills and Tippet², using X-ray diffraction methods, examined nitrided iron-silicon alloys and found precipitates with an unknown structure which varied with the composition and heat treatment of the specimen. After the precipitates had been isolated from the alloys by the Beeghly³ bulk-extraction method they were found to be $\alpha\text{-Si}_3\text{N}_4$ silicon nitride. It was suggested² that the precipitates formed in the metal specimens were a complex nitride that decomposed during isolation. With the advent of the extraction replica method in which included material can be isolated from metal specimens after very mild chemical treatments compared with bulk-extraction methods a further attempt has now been made to isolate the new precipitate.

A high purity iron-silicon alloy (B.I.S.R.A. Code No. 33AF2) of composition given in Table 1 was

| TABLE 1 | | | |
|--|-----------------|----------|-------------------|
| Silicon | 3.95 per cent | Carbon | 0.0026 per cent |
| Manganese | <0.005 per cent | Nitrogen | 0.0014 per cent |
| Sulphur | 0.0040 per cent | Oxygen | 0.0010 per cent |
| Aluminium | 0.001 per cent | Hydrogen | <0.00005 per cent |
| (Phosphorus, nickel, chromium and copper were not determined.) | | | |

nitrided for 18 hr at 640°C and furnace-cooled producing a nitrogen concentration gradient extending for about 0.22 in. inwards from the surface. Much of the nitrided zone had a mottled appearance when examined with the optical microscope. Extraction replicas obtained by the single-etch method⁴ after etching for 3 min with 10 per cent alcohol iodine solution were examined in the electron microscope and showed the structure to be due to numerous cubo-shaped particles up to about 0.2 μ in size (Fig. 1). Although the appearance of the particles suggested that they possessed a regular crystalline form only weak transmission electron diffraction patterns were obtained. The patterns did not appear to correspond to any of the known iron or silicon nitrides and were not identified.

After the above examination the specimen was further annealed for 6 hr at 820°C and furnace cooled. This caused a considerable change in the appearance of the specimen: the mottled structure being replaced by a coarser more definite structure. Examination of extraction replicas obtained in a similar manner showed that the structure was due to the presence of rod-like particles identified from electron diffraction patterns as silicon nitride ($\alpha\text{-Si}_3\text{N}_4$). The rods occurring in the regions of low nitrogen concentration were few and large (Fig. 2) whilst those at higher concentrations were smaller and more numerous.



Fig 1 Precipitates formed in an Fe-3 per cent Si alloy after nitriding and furnace cooling from 640°C. Extraction replica (Electron micrograph $\times 20,000$)



Fig 2 Precipitates formed in an Fe-3 per cent Si alloy after nitriding and furnace cooling from 640°C and then further annealing at 820°C. Extraction replica (Electron micrograph) $\times 2,000$

The results strongly suggest that the cubic-shaped particles are the new precipitate and demonstrate that it transforms within the metal specimen to $\alpha\text{-Si}_3\text{N}_4$ when the temperature is increased.

Thanks are due to Mr R. A. Hacking, director of research, for permission to publish this communication.

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Identification of the High-Temperature Constituent in Mild Steel Surface-Hardened by Carbo-Nitriding

DURING an investigation on the heat treatment of mild steel in raw town-gas and ammonia atmospheres¹ an unidentified constituent was observed in the surface layers which appeared as a dark-coloured phase visible in the etched condition. This phase is unstable at room temperature and can be eliminated by slow cooling or reheating. With the limited information available at the time the constituent was presumed to be an iron-carbon-nitrogen compound, positive identification has not been possible until now.

A method of removing thin oxide films from metal surfaces^{2,4} has been adapted for stripping thicker scales^{3,4}. A thin plastic film is applied to the surface and the specimen is immersed in an oxygen-free solution of iodine in alcohol, which penetrates discontinuities in the plastic and oxide films and dissolves metallic iron. When the surface deposits have been undermined sufficiently, the plastic film and the oxide particles adhering to it can be removed for X-ray examination. This technique has been applied to machined surfaces, and both sulphide inclusions and cementite lamellae have been extracted.

The method was used to extract the iron-carbon-nitrogen constituent from a mild steel rod that had been treated for 50 min at 800°C in an atmosphere containing 10 per cent ammonia. Before the iodine extraction the specimen was shot blasted to remove any adherent oxides, it was then coated with a plastic consisting of polyvinyl chloride/acetate resin ('Rhodopas AACM') in acetone³. After stripping the plastic film was dissolved in hot acetone and the residue collected by centrifuging. When the residue was completely free from plastic it was dried and a small portion was mixed with Canada balsam, coated on a hair and mounted in a 19 cm X-ray powder camera. The photograph obtained with Co K radiation (Fig 1) was measured and could be indexed (Table 1) as a hexagonal structure, having lattice parameters $a=2.636 \text{ \AA}$ and $c=4.316 \text{ \AA}$.

| TABLE 1 | | |
|---------|-------|-------|
| d | hkl | hkl |
| 2.231 | m | 100 |
| 2.158 | s | 002 |
| 2.017 | vs | 101 |
| 1.507 | m | 102 |
| 1.318 | m | 110 |
| 1.218 | m | 103 |
| 1.120 | m | 112 |
| 1.103 | m | 201 |

This structure is the same as the ϵ -iron nitride (Fe_3N) reported by Jack⁶. The parameters are somewhat lower than any observed by Jack but fit well on an extrapolation of his curves to 4.0–4.5 per cent nitrogen (by weight). Jack has also shown⁶ that nitrogen in the ϵ -phase can be partially replaced by carbon and that this reduces the lattice spacing, this indicates that the observed parameters can be accounted for with rather less extensive extrapolation by the presence of carbon. Iron nitrides are notoriously difficult to isolate by preferential solution of the matrix and the successful extraction of this constituent lends support to the inference that it has been stabilized by carbon, and can be identified as ϵ -iron carbonitride.

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CHEMISTRY

Effect of Hybridization Changes on the Bond Energies of Carbon-Carbon Single Bonds

It has previously been suggested¹ that the energy of a bond is related to the overlap integral of the two atomic orbitals which are thought to form the bond. To try to provide a quantitative expression of this idea we have assumed that the bond energy is directly proportional to the overlap integral of the bond orbitals. The proportionality constant can be evaluated by using the bond energy of the $C_{sp^3}-C_{sp^3}$ single bond obtained from experimental values of the heats of formation of saturated long chain hydrocarbons². The bond energies of the five other types of carbon-carbon single bonds may then be calculated by using tables of overlap integrals³ and the appropriate bond lengths⁴ (Table 1). Then by using the $C_{sp^3}-H$ bond energy, obtained from the same set of data as the tetrahedral carbon-carbon bond energy and the observed² heats of formation of ethylene, propylene, acetylene and propyne, the bond energies for the carbon-carbon double and triple bonds and the $C_{sp^2}-H$ and $C_{sp}-H$ bonds can be calculated (Table 1). This table of 'standard' bond energies can then be used to predict the heats of formation and heats of hydrogenation of any unsaturated hydrocarbon for which steric effects are small (Table 2). It is seen that the predicted values are quite close to the experimental ones even in cases where there is usually considered to be considerable resonance or hyperconjugative stabilization in fact most of the results show a small destabilization energy probably due to the simplifying assumption of neglecting polar effects and non bonding interactions. This conclusion that resonance and hyperconjugative effects are small in comparison with changes in hybridization for non aromatic compounds is in accordance with the recent views⁵ that compounds

may be classified into two types (1) those for which two or more classical structures of equal energy can be written, for example benzene, for which the resonance stabilization is considerable, (2) those for which only one low-energy classical structure may be written, for example, butadiene, cyclopentadiene.

Recent examination of the experimental observations originally put forward as evidence for the predominance of resonance or delocalization effects in governing bond lengths⁶, dipole moments⁷, force constants⁸, chemical reactions⁹ and electronic spectra¹⁰ support the view that in type (2) molecules, at least these effects are small compared with other factors previously ignored.

We should like to record our appreciation for many fruitful discussions with the late Dr A. Burawoy.

One of us (J. E. B.) wishes to acknowledge the award of an Imperial Chemical Industries Fellowship at the University of Manchester during the tenure of which this work was carried out.

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Table 1. CALCULATED BOND ENERGIES*

| Bond type | Bond distance (Å) | Overlap integral | Bond energy (kcal/mole) |
|---------------------|-------------------|------------------|-------------------------|
| $C_{sp^3}-C_{sp^3}$ | 1.543 | 0.617 | 85.48 |
| $C_{sp^2}-C_{sp^2}$ | 1.330 | 0.668 | 91.42 |
| $C_{sp^2}-C_{sp^3}$ | 1.460 | 0.716 | 94.48 |
| $C_{sp}-C_{sp^2}$ | 1.470 | 0.716 | 94.48 |
| $C_{sp}-C_{sp^3}$ | 1.490 | 0.754 | 103.60 |
| $C_{sp^2}-C_{sp}$ | 1.380 | 0.800 | (88.67) |
| $C_{sp^2}-H$ | | | 85.40 |
| $C_{sp}-H$ | | | 102.38 |
| $C\equiv C$ | | | 143.10 |
| $C\equiv N$ | | | 187.23 |

* Using $I_{C-C} = 171$ kcal, $D(H_2) = 104.18$ kcal

Table 2. HEATS OF HYDROGENATION (REF. 2) IN KJ/MOLE

| Substance | Observed ($-\Delta H$) | Calculated ($-\Delta H$) | Stabilization energy |
|----------------------------------|-----------------------------|-------------------------------|-------------------------|
| Ethylene | 32.82 | | |
| Propylene | 30.12 | | |
| Acetylene | 176.06 | | |
| Propyne | 69.70 | | |
| 2-Butene (trans) | 27.92 | 27.43 | -0.20 |
| 1,3-Butadiene (trans) | 57.07 | 56.50 | -1.57 |
| 1-Methyl-1,3-butadiene | 54.11 | 53.60 | -1.31 |
| Styrene (trans) | 28.20 | 26.72 | -1.48 |
| Styrene (trans)* | 20.10 | 20.82 | +0.72 |
| 1,4-Diene* 1,3-butadiene (trans) | | | |
| (trans)*† | 44.00 | 44.02 | +0.02 |
| 2-Butyne | 65.12 | 64.73 | -0.39 |
| Diphenylacetylene* | 63.34 | 60.65 | -2.69 |
| Diphenylacetylene* | 126.00 | 124.67 | -1.33 |
| Cyclooctatetraene | 98.00 | 95.84 | -2.16 |
| Cyclopentadiene | 26.02 | 27.38 | +1.36 |
| 1,3-Cyclopentadiene | 50.90 | 51.38 | +0.48 |
| Heptatriene | 82.63 | 86.00 | +3.37 |

* Refers to hydrogenation of all aliphatic multiple bonds only
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Quantitative Paper Chromatography based on the Sub-Micro Titration of Derivatives containing Nitro Groups

An extensive literature on the quantitative paper chromatography of a large variety of organic compounds already exists. Most of these methods are based on (a) measurement of the optical density of a coloured spot produced on the paper chromatogram by spraying with a suitable reagent or (b) measurement of the optical density (in ultra violet or visible light) of an extract of the component considered, after separation from other components by paper chromatography.

A very simple and rapid method has been developed by us for the quantitative determination of different carbonyl compounds in complex mixtures.

The carbonyl compounds are converted to their dimethylphenyl hydrazones. The mixture of these derivatives is separated on paper using a modification of the method of Matthes.¹ The bands are cut out, concentrated on a small surface if necessary and put into a small titration vessel containing oxygen free acetic acid. After addition of a suitable amount of sodium acetate excess 0.003 N titanous chloride solution is added (~0.5 ml) and the mixture stirred for 5-10 minutes (if necessary at about 50°C). After acidification with hydrochloric acid the excess is back titrated with 0.03 N ferric chloride delivered from a micrometer syringe, using rhodanide as an indicator.

The reduction rates of different dinitrophenylhydrazones proved to be different. The results obtained with a number of dinitrophenylhydrazones after development of a paper chromatogram are summarized in Table 1.

Table 1. RESULTS FOUND BY TITRATION OF DINITROPHENYLHYDRAZONES ON WHATMAN-1-PAPER WITH TITANOUS CHLORIDE recoveries from 20.0 µgm carbonyl compound

| 2,4-Dinitrophenylhydrazone of | Time and temperature of reduction | | |
|-------------------------------|-----------------------------------|----------------|---------------|
| | 5 min 20°C | 15 min 20°C | 5 min 50°C |
| Formaldehyde | ~10 | 17.0 | 20.6 |
| Acetaldehyde | | 17.0 | 19.2 |
| Propionaldehyde | ~15 | 19.3 | 19.4 |
| Acetone | ~19 | 19.9 | 20.0 |
| Butanone | ~16 | 20.0 | |
| Pentanone-2 | 16.4 | | 21.2 |
| Cyclohexanone | 16.4 | ~18 | 19.3 |
| Heptanone-2 | 20.6 | ~22.8 | 24.0* |

* Reproducibility excellent

From these results it is clear that a reaction period of 5 minutes at 50°C will, in general, suffice for the quantitative reduction of the nitro groups. We found that under these conditions the reproducibility is very satisfactory.

Difficulties due to the stability of the titanous chloride solution² were completely overcome by proper exclusion of air. In contrast with a statement in the literature² we found that light had no influence. A 0.003 N solution of titanous chloride in 0.6 N hydrochloric acid, stored in a colourless glass bottle did not show a decrease of titre for about one month.

The method described is not restricted to carbonyl compounds. Work is in progress to adapt the method to the analyses of alcohols (dinitro esters), phenols, amines, and amino-acids (dinitro aryl-derivatives). The quantitative reduction of many of these derivatives on paper is possible. The quantitative conversion of the parent compounds to the derivatives is being studied. In principle the method is applicable to all substances containing groups which are reduced by titanous chloride in a reproducible way.

A more detailed description of this work will be published elsewhere.

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BIOCHEMISTRY

Distribution of 5-Carboxymethylhydantoinase

THE enzyme 5-carboxymethylhydantoinase, which reversibly cyclized carbamylaspartate to 5-carboxymethylhydantoin, was demonstrated in *Zymobacterium oroticum* by Lieberman and Kornberg¹. No enzymatic activity was found in rat liver or in two corynebacterium strains². In recent studies on pyrimidine metabolism in man this enzyme was found to be absent in erythrocytes and normal or leukemic leukocytes^{3,4}. The absence of this enzyme in mammalian cells and its presence in bacteria suggested the possibility that chemotherapeutic agents might be developed as competitive inhibitors of 5-carboxymethylhydantoinase. Inhibition of the growth of *Lactobacillus casei* by thiohydantoin-5-acetic acid has been reported⁵. A survey of the distribution of the enzyme in micro-organisms was therefore undertaken.

dl-5-Carboxymethylhydantoin-¹⁴C was synthesized from orotate-¹⁴C as previously described¹ with specific activity of 1.9×10^4 c.p.m./µmole. Enzyme assay was based on the hydrolysis of 5-carboxymethylhydantoin-¹⁴C (3×10^{-4} moles) to carbamyl aspartate-¹⁴C during 1 hour incubation at 37°C, pH 8.2 (*tris*). Following the addition of 10 µmoles carbamylaspartate carrier and protein precipitation, carbamylaspartate was isolated by elution from a 'Dowex'-1-formate column (1 × 10 cm) with sodium formate buffer pH 3.2 (50 column volumes wash using 0.02 M, 20 column volumes using 0.05 M). Specific activity was determined in duplicate tubes³ and the rate of synthesis calculated by the standard carrier formula. *Zymobacterium oroticum* was grown using a modification of the method of Friedmann and Vennesland⁶. Other bacteria were grown in standard laboratory media, harvested by centrifugation, and disrupted by sonication for 10 min using a Raytheon 10 kc/s Oscillator. By analogous reactions as for 5-carboxymethylhydantoin synthesis, 1-5-carboxyethylhydantoin was synthesized from 1-carbamyl aspartic acid m.p. 164–165°C (dec). Calculated (per cent) C 41.86, H 4.68, N 16.28, found C 42.07, H 4.91, N 16.39, and 1-5-sulphonylmethylhydantoin from 1-carbamylcysteic acid potassium salt m.p. 270–274°C (dec). Calculated (per cent) C 20.70, H 2.59, N 12.08, S 13.80, found C 20.75, H 2.35, N 12.27, S 13.52.

The results can be summarized briefly. The presence of 5-carboxymethylhydantoinase in *Zymobacterium oroticum* was readily confirmed with rates of synthesis of carbamylaspartate of approximately 13 µmoles/mgm protein/hr. Tracer enzymatic activities, approximately 1–2 per cent of that in *Zymobacterium oroticum*, were found in *Pseudomonas fluorescens*, *Protococcus vulgaris*, and *Staphylococcus aureus*. No significant enzymatic activity could be detected in *Bacillus subtilis*, *Alcaligenes faecalis*, *Lactobacillus leichmannii*, *Escherichia coli* B, beta hemolytic streptococcus, *Salmonella st. pauli*, Brewer's yeast, or the Ehrlich ascites cell tumour. Neither of the structural analogues were an effective inhibitor of 5-carboxymethylhydantoinase from *Zymobacterium oroticum*. These results and those previously cited demonstrate that 5-carboxymethylhydantoinase has a very limited biological distribution. The metabolic significance of this spur reaction off the general pathway of pyrimidine synthesis has remained obscure, and its limited activity in pathogenic bacteria does not recommend it as a focus for chemotherapeutic attack.

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Enzymic Conversion of L-Rhamnulose to L-Fucose in *Escherichia coli*

In a previous paper¹ indirect adaptation to D arabinose induced by L-rhamnose in some D arabinose negative strains of *Escherichia coli* has been reported. These strains when grown on L-rhamnose, metabolize D-arabinose and utilize it for growth. This effect is not due to selection of mutants but to enzymic adaptation. Induction of D arabinose isomerase by L-rhamnose has been demonstrated.

This indirect induction can possibly occur through the enzymic conversion of rhamnulose (phosphate) to fucose (phosphate). Fucose is known in fact to be an inducer of the metabolic enzymes of D arabinose.² Rhamnulose and rhamnulose phosphate are normal products of rhamnose metabolism in *E. coli*.³

Huang and Miller in their studies on lactaldehyde metabolism⁴ also put forward the hypothesis that fucose was formed from rhamnulose.

We have identified fucose phosphate among the sugar phosphates obtained by incubating rhamnose with an homogenate of *E. coli* (strain 30) cells in the presence of adenosine triphosphate.

E. coli (strain 30) was grown on a synthetic medium containing 0.3 per cent rhamnose and the cells were collected during exponential growth. Homogenates obtained by grinding with alumina or by the Hughes press were diluted with 1:1 per cent potassium chloride.

For the preparation of the sugar phosphates, rhamnose was at first isomerized to rhamnulose under the following conditions: rhamnose 0.35 m mole homogenate (containing 15–17 mgm protein per ml), 8 ml, 0.2 M borate buffer 30 ml, cobaltous sulphate, 10^{-4} M (final concentration). The reaction was followed by the method of Dische and Borenfreund⁵ for the determination of rhamnulose until the equilibrium was reached. At this point 0.35 m mole of adenosine triphosphate (as the disodium salt), 5 ml of homogenate and magnesium chloride so as to give a final concentration of 10^{-4} M were added.

After 2 hr incubation the reaction was stopped with trichloroacetic acid. The precipitate was removed by filtration and the filtrate was brought to pH 8. Sugar phosphates were precipitated as the barium salts with ethanol and the precipitate was dissolved in 0.1 M acetic acid. Barium was precipitated as sulphate and the nucleotides adsorbed on charcoal until the absorption at 260 mμ disappeared.

Sugar phosphates were chromatographed on Whatman No. 1 paper with 80 per cent ethanol containing 0.8 per cent acetic acid. Two yellow and a green spot were obtained with the orcinol reagent⁶. The green spot was due to free rhamnulose; the others which were due to sugar phosphates also appeared with the ammonium molybdate reagent⁷.

The sugar phosphates corresponding to the yellow spots were eluted from paper and hydrolysed with acid phosphatase ('Polidase S', Schwarz). The free sugars were chromatographed on Whatman No. 4 paper with benzene-ethanol-water 169:47:15 v/v using authentic samples of rhamnulose and fucose as standards.

After hydrolysis, the slow moving yellow spot gave with the orcinol reagent a yellow and a green spot; the first one had the same *R_f* and colour as fucose, the second as rhamnulose. The fast-moving yellow spot gave one green spot moving as rhamnulose.

The sugar moving as fucose was eluted from the paper. By the cysteine carbazole reaction it gave a

red colour with an absorption maximum at 550 mμ. By the orcinol-ferric chloride reaction⁸ it showed absorption maxima at 425 and 520 mμ like all keto-methylpentoses. By the Dische and Shettles reaction⁹ it showed the 400 mμ maximum characteristic of methylpentoses.

This sugar was also treated with an homogenate of *E. coli* 30 cells containing D arabinose isomerase. After this treatment two sugars could be detected by paper chromatography with butanol-acetic acid-water 4:1:5 v/v as solvent, using the benzidine spray reagent; these sugars showed the same chromatographic behaviour as fucose and fucose respectively.

Fucose phosphate, which we have tentatively identified among the sugar phosphates obtained from rhamnose is probably formed by the inversion of carbon four of rhamnulose phosphate.

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Ionized Calcium in Biological Media

THE unsatisfactory status of the important problem of the determination of ionized calcium in biological media has recently been re-appraised by W. F. and M. S. Neuman¹. After critical examination of methods then existing and of available data on the medium most generally investigated, serum, they state that "the amount of ionized calcium in normal serum now seems to be pretty well established—approximately 1.3 mM/litre".

Using a direct general method quite recently developed, which is based on the absorbance of metal (or *pH*) indicators at two wave lengths², we have re-determined the concentration of ionized calcium in the serum of normal adults using murexide as indicator. The effect of light scattering by serum, and of its variation with the wave length, is eliminated in this two wave length method by the use of serum as a blank at each wave length. Anion dye binding has also been considered by investigating solutions of Armour serum albumin and apparently is not of significance in this method.

Samples were taken at random from healthy student nurses. Equal volumes of the serums were pooled as a means of obtaining the equivalent of an average normal serum and were analysed almost immediately after being collected. This simple approach was used in order to make a comparison of the results obtained by the new method with those adopted by authorities in the field.

In the following table the values for the formation constants *K_f* used for the calcium murexide complex correspond to ionic strength 0.15 and the measured *pH* value of each pooled serum (found to be within 0.2 *pH* of the normal).

Table 1

| Sample No | No of pooled serums | Ionized calcium found ($\mu M/l$) |
|-----------|---------------------|-------------------------------------|
| 1 | 6 | 1.32 |
| 2 | 2 | 1.27 |
| 3 | 6 | 1.29 |

In addition, serums were collected from hospital patients without obvious metabolic disorders and kept refrigerated for one week. These showed values probably due to alterations of serum on ageing.

There is good agreement between the foregoing results for normal subjects and the value adopted by the Neumans. As emphasized by them, an error of 2 or 3 per cent due to competing ions such as magnesium can be ignored for practical purposes in the frog-heart method. When using spectrophotometry, magnesium does not interfere as in the physiological assay since it remains practically unchelated by murexide in the physiological pH-range as previously stated by Raaflaub³. This has been verified by us, for we have found a difference of 0.01, at the most, in the absorbances of murexide regardless of the presence or absence of magnesium ions, corresponding to a maximum error of 2 per cent in the value of ionized calcium, which is well within the range admitted in spectrophotometric determinations.

The fact that there is such close agreement between the numerical values for the concentration of ionized calcium in normal serum obtained from methods so different in principle as the new direct method based on *pM* indicators, and indirect methods such as the frog-heart method of McLean and Hastings⁴ and the Yendt bioassay technique using the mineralization of cartilage from rachitic rats in human serum as quoted and discussed in the review by the Neumans¹, reinforces the conviction that it is actually the ionized calcium that is determined by all these methods.

Because the usual *e m f* determinations cannot be used with some of the most important metal ions and since the new membrane electrodes are unsuitable for media containing many different ions, the introduction of suitable new *pM* indicators for the study of metal ions in biological systems seems highly desirable due to the directness and simplicity of purely physico-chemical methods as compared to biological ones.

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Formation of Noradrenaline from Adrenaline by Rat Liver Mitochondria

By condensation with ethylenediamine, adrenaline gives noradrenaline as the main product¹. This suggests the possibility that adrenaline is demethylated during this reaction.

Conversion of adrenaline to noradrenaline *in vivo* has now been tested in several ways, since this possibility has so far been overlooked except by Lockett².

Rat liver mitochondria were shown to convert adrenaline to noradrenaline by the following *in vitro* experiment. The mitochondria (200 mgm, dry weight), prepared by the method of Schneider and Hogeboom³, were suspended in 5 ml of *M/30* phosphato buffer (*pH* 7.0), and L-adrenaline was added to bring the final concentration to 5×10^{-4} *M* and then incubated at 37°C for 1 hr. After the incubation, 2 vol. of ethanol containing 2.5 per cent (v/v) 1 *N*-sulphuric acid were added, and the mixture was kept at 3°C for 3 hr, then centrifuged and filtered. The filtrate was adsorbed with alumina at *pH* 8.5 then eluted with 0.2 *N* acetic acid. The eluate was evaporated to dryness under reduced pressure at about 30°C. The residue was extracted three times with 0.5 ml acid acetone (1 ml conc. hydrochloric acid in 100 ml. acetone) and the extract was applied to the three filter paper strips (Whatman No. 1)⁴. Phenol containing 15 per cent (v/v) 0.1 *N* hydrochloric acid⁵ was used as the mobile phase.

At the end of run (after about 24 hr.), one of the paper strips was immersed twice in benzene and hung up to dry⁴. When the strip was sprayed with potassium ferricyanide, a red spot appeared at *R_F* 0.21, which was just identical with that of noradrenaline, together with a spot of adrenaline at *R_F* 0.52. The quantity of adrenaline was found to decrease compared with controls mentioned below.

When ethylenediamine was sprayed on the second paper strip, a bluish-green fluorescent spot appeared at *R_F* 0.21 under ultra-violet light.

The zone occupied by the *R_F* 0.21 substance was cut out from the third paper strip, and was extracted with 0.01 *N* hydrochloric acid at 3°C. for 12 hr. The extract was examined both by ethylenediamine condensation and trihydroxyindole fluorescence. A part of the extract (5 ml.) was added to a mixture of 0.25 ml. 2 *M* ethylenediamine dihydrochloride and 0.5 ml. of ethylenediamine hydrate, and the mixture was heated at 50°C for 1 hr. After the addition of 2 gm. of sodium chloride, the solution was extracted with 2 ml. of *iso*-butanol, and lightly centrifuged⁶. This *iso*-butanol extract was analysed by paper chromatography in the dark, using 5 per cent crystalline disodium hydrogen phosphate, the upper layer of *n*-butanol/ethanol/5 per cent crystalline disodium hydrogen phosphate (50:25:30, v/v)⁷, or *n*-butanol-saturated phosphate buffer at *pH* 6.0⁸ as the mobile phase. In all cases, the bluish-green fluorescent spot was observed, and the *R_F* values were identical to the main condensation product of noradrenaline. This condensation product was also examined by paper electrophoresis (0.05 *M* phosphate buffer at *pH* 7.0, 1 m amp/cm of constant current¹), the mobility of the bluish-green fluorescent substance was identical with that of the main product of noradrenaline.

The extract of the zone of *R_F* 0.21 substance showed strong fluorescence when it was oxidized by potassium ferricyanide at *pH* 6.0 and then mixed with the combined reagent of sodium hydroxide and ascorbic acid according to Euler and Floding⁹.

These results confirm the identity of this substance at *R_F* 0.21 with noradrenaline.

At the same time, control experiments were carried out as follows: (1) the same amount of the mitochondria was previously heated at 80°C for 10 min., and then incubated as described above, (2) the same amount of mitochondria in the same reaction mixture was incubated at 0°C, (3) the mitochondria were incubated at 37°C with the same reaction mixture without adrenaline. They were treated just in the

same way as in the main experiment. However, no occurrence of noradrenaline was observed.

These results show that noradrenaline was produced from adrenaline by the enzymic action of the mitochondria, which suggests the possibility of the enzymic demethylation of adrenaline.

Considering the different physiological actions of noradrenaline and adrenaline, this reaction is of physiological interest.

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A Bronchodilator Alkaloid (Vasicinone) from *Adhatoda vasica* Nees

A NEW alkaloid has been isolated by us in the crystalline form from the leaves of *Adhatoda vasica* Nees (Indian Patent No. 62349 of November 21, 1957; Patent application No. 94603 of July 9, 1958). The alkaloid, which has been named vasicinone, has been found to be a much weaker base than vasicine, an alkaloid which is already known to be present in this plant. Elementary analysis gave, C = 65.33, H = 4.03, N = 13.65 per cent. The molecular weight (Rast) was found to be about 210 and the molecular formula $C_{11}H_{13}N_2O_2$. The alkaloid was found to be identical with 2,3-(α -hydroxytrimethyleno) 4 quinazoline which had been prepared earlier by the oxidation of vasicine with 30 per cent hydrogen peroxide.¹

Vasicinone showed characteristic ultra violet and infra red spectra and formed salts as well as crystalline double chlorides of gold and platinum. When chromatographed on filter paper (Whatman No. 1) by capillary ascent method using the organic phase of the solvent system obtained from *n*-butanol acetic acid: water 10:1:5 it gave a light red spot when sprayed with Dragendorff's reagent, R_F value = 0.77-0.79. Vasicine under the same conditions gave an orange red spot, R_F value 0.57-0.58.

It was found that the crude total alkaloids obtained from the leaves of the plant contained vasicine as the main alkaloid mixed with small quantities of vasicinone, but the proportion of vasicinone increased by shaking the crude alkaloids in non polar solvents like chloroform and benzene and exposing the solutions to sunlight, so much so that after a time, the vasicine in the crude total alkaloids was almost completely converted to vasicinone by auto-oxidation. Pure vasicinone could similarly be auto-oxidized to vasicinone.

Vasicinone isolated directly from the crude total alkaloids by partition chromatography (over 'Hyflo', pH = 1) was predominantly L-vasicinone and that obtained by auto-oxidation was a mixture of L- and DL-forms. Pure L- and DL-forms could be separated from this mixture. L-vasicinone showed $(\alpha)_D^{25} =$

-100 (0.5 per cent in chloroform) and melted at 200-201° C. DL-vasicinone melted at 212-213° C and a mixture of L- and DL-forms melted between 200° and 212° C. Both the L- and DL-forms of vasicinone had similar ultra violet and infra red spectra and same R_F value on paper chromatograms.

Recently an alkaloid^{2,4} has been isolated from *Peganum harmala* Linn which has the molecular formula $C_{11}H_{13}N_2O_2$ and melting point 203-4° C. We have confirmed these findings by isolating this alkaloid from the crude alkaloids of the plant and established its identity with vasicinone.

The pharmacological actions of vasicinone on the bronchial musculature were studied on the guinea pig tracheal chain on perfused guinea pig lung according to the procedure of Bhattacharya and Delaunoy⁵, and by the overflow method of Konzett and Rössler⁶ in intact guinea pigs. Vasicinone had a definite bronchodilator action on the normal lungs and a powerful bronchodilator action against the histamine induced bronchoconstriction, but its action was weaker than adrenaline. L-vasicinone was, however, stronger in action than its DL-form. Vasicinone showed a slight and transient fall in the blood pressure of a dog. On isolated perfused hearts of guinea pig and rabbit (Langendorff preparation) vasicinone had a positive inotropic action and increased the flow in the coronary vessels. Both L- and DL-forms of vasicinone displayed a bronchoconstrictor action had a negative inotropic action on the heart and also reduced the flow in the coronary vessels.

The beneficial action of the leaves of *Adhatoda vasica* Nees in respiratory disorders may be attributed to the small quantities of vasicinone, either already present or formed by auto oxidation of vasicine.

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Interfering Substances in the Determination of Glucosamine Synthesis

Previous communications have dealt with the enzymatic formation of glucosamine from glucose 6 phosphate and glutamine in cartilage.¹

I wished to test the activity of the enzyme involved in glucosamine synthesis in normal and pathological organs. The technique suggested by Castellani *et al.*² was applied to rat gastric mucosa, aorta, liver, brain, lungs, blood, testis and to rabbit cartilage.

High synthesis of glucosamine was seen when the substrates were incubated with cartilage liver and gastric mucosa homogenates. To make the determination of activity more specific the distillation method suggested by Prodi³ instead of the Schloess method, was used in later experiments. Considerably lower activity values were obtained after distillation and, moreover, the colour of our samples proved to be due in part to interfering substances as shown by their absorption spectrum. This fact led me to carry on some hexosamine determination after separation of the interfering substances by means of a cation exchange resin ('Dowex 50') as suggested by Boas.⁴

Table 1 GLUCOSAMINE AND INTERFERING SUBSTANCES FORMATION IN RABBIT CARTILAGE

| Incubated samples | | Non-incubated samples | | Glucosamino synthesized |
|------------------------|-------------|------------------------|-------------|-------------------------|
| Interfering substances | Glucosamine | Interfering substances | Glucosamine | |
| 70 | 270 | 23.5 | 140.4 | 23.4 |

Average values of six determinations. Values expressed as γ glucosamine/gm fresh tissue. Experimental conditions were those proposed by Castellani and Zambotti (ref. 1).

Still lower values of hexosamine synthesis were obtained by this method, suggesting that the high values given by the Schloss method were due to interfering Ehrlich-positive substances formed or extracted during incubation (Table 1). Part of the interfering substances seems to be due to free glucose-6-phosphate (which gives Ehrlich-positive reaction) liberated from glucose-6-phosphate (which gives Ehrlich-negative reaction), accompanied by the increase of inorganic phosphorus of the incubated samples, as compared to the control samples (450 γ free glucose/100 mgm fresh tissue liberated during incubation with liver homogenates, 150 γ free glucose/100 mgm fresh tissue liberated during incubation with cartilage homogenate). The incubation of cartilage or liver homogenates with glucose-6-phosphate only, in absence of glutamine, also leads to an apparent synthesis of glutamine.

My experiences suggest that, using the technique proposed by Castellani and Zambotti, in addition to the synthesis of glucosamine, Ehrlich-positive free glucose, liberated by a process of dephosphorylation of glucose-6-phosphate is measured.

I am indebted to Dr Luigi Tessari for advice and help during the course of the above work.

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Glycolaldehyde Trapped from Aerobic Oxidation of D-Xylose by *Torulopsis utilis*

In previous experiments on the aerobic degradation of D-xylose by living cells of *Torulopsis utilis*, we succeeded in isolating the triose-phosphate, pyruvic acid and the acetyl groups using the phenylhydrazine trapping technique. Our results have been confirmed by Heath *et al.*³, who purified from *Lactobacillus pentosus* an enzyme which phosphorolytically cleaves D-xylose-5-phosphate into triose-phosphate and acetyl-phosphate. Schramm and Racker⁴ have shown in a mutant of *Acetobacter xylinum* the presence of an enzyme which carries out the same phosphorolytic split of D-xylose-5-phosphate and cleaves also the fructose-6-phosphate into erythrose-4-phosphate and acetyl-phosphate. From the results of our preceding experiments we supposed a split of an intermediate phosphorylated ketopentose into triose-phosphate and into an unknown C-2 intermediate, both originating the acetyl group according to the formulation given in ref. 2.

The unknown C-2 intermediate was glycolaldehyde, but we were unable to separate it at that time from

the trapped intermediates. With chromatographic techniques we have now succeeded in isolating it together with the triose-phosphate, pyruvate and the acetyl group, in the same experimental conditions used in the preceding experiments.² Free glycolaldehyde was first isolated by Kaushal *et al.*⁵ from the fermentation of pentoses by *Acetobacter acetigenum*. From our results it seems that D-xylose-5-phosphate, probable intermediate of the fermentation of D-xylose³, is enzymatically cleaved with the formation of triose-phosphate and glycolaldehyde the so called 'active glycolaldehyde'. In our aerobic conditions, the acetyl group is formed from triose-phosphate by the way of the pyruvate and from the glycolaldehyde as suggested by us in a preceding paper² which deals with the oxidation of acetate to glycolate. In effect, this reaction appears to occur through the intermediate formation of an enolic form of acetyl-coenzyme A, which is transformed by hydration into glycolaldehyde, that is afterwards dehydrogenated to glycolic acid.

40 gm wet weight of living cells of *T. utilis* (Windisch strain), grown on mineral solution at 1.5 per cent of raw saccharose, were washed three times and suspended in the following medium: distilled water 1,000 ml, D-xylose (Ciba) 5 gm., disodium hydrogen phosphate, 2 gm., potassium dihydrogen phosphate, 3 gm.; ammonium sulphate, 2 gm.; crystalline magnesium sulphate, 0.3 gm. The pH was adjusted to about 5.5, and the suspension aerated in a 1,500 ml cylindrical glass flask through a sintered-glass disk at the base of the flask. Depending on the pH changes, three portions of 1 gm of the phenylhydrazine oxalate were added within 2 hr. Each portion was dissolved in 50 ml distilled water containing sodium hydroxide to pH 5.5. After 7-8 hr incubation, the medium was centrifuged and the clear liquid analysed for fixed products.^{1,2} For the separation of the glycolaldehyde, in the form of its 2,4-dinitrophenyl osazone, the centrifuged medium was treated with an excess of benzaldehyde at 70°C to free all the trapped intermediates from phenylhydrazine, except the osazone of the glycolaldehyde. The mixture was chilled and filtered to separate the precipitated phenylhydrazine of the benzaldehyde, after which the liquid was concentrated 3 l and glycolaldehyde isolated by the chromatographic method previously reported². The glycolaldehyde 2,4-dinitrophenyl osazone obtained melted at 325°C, and no depression was observed in the presence of the synthetic substance, found amounts, 10-70 mgm/l. Failure to trap larger amounts of glycolaldehyde is due to the fact that the aldehyde is degraded also in the presence of phenylhydrazine⁶.

Glycolaldehyde was trapped even in experiments on fermentation of L-arabinose by a strain of *E. coli* and one of *Lactobacillus buchneri*. This work is continuing, and a detailed report will be published elsewhere.

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Sugars of the Glycoside of the Root of *Marsdenia erecta* R Br

Marsdenia erecta is a plant which grows in Turkey as well as the Near East. Recently some of us¹ have studied the morphological and chemical properties of this plant and isolated a glycoside—marsdenin. To identify the sugar contents of this glycoside and compare with the sugars of the other *Marsdenia* glycosides, we obtained the glycoside, hydrolysed it and identified its sugars by paper chromatography.

200 gm of dry root of *Marsdenia erecta* were powdered and extracted with petrol ether, chloroform and ether as previously described by F. Korte and I. Korte², who used this method for extraction of the glycoside conduranguin. The extraction product was dissolved in 200 ml of 10 per cent methyl alcohol and filtered through an aluminium oxide column. The filtrate is dried by aeration and gave the glycoside. This glycoside is hydrolysed in 20 ml of 5 per cent sulphuric acid solution in a boiling water bath for 5 min and the aglycone fraction is separated by filtration. The filtrate is neutralised with barium carbonate decolorized with charcoal and dissolved in ethyl alcohol and evaporated; the residue is redissolved in water. The water-soluble hydrolyses were run for 24 hr on paper chromatograms, Whatman No. 1 (descending technique) using the organic layer from a freshly prepared *n*-butanol acetic acid water mixture (4:1:5, v/v)³.

These were sprayed with aniline hydrogen phthalate reagent⁴ and the chromatograms were dried in an oven at 110° C. The chromatograms showed 4 spots. The first one was dark brown and agreed with authentic specimen of glucose, the second one was brown and corresponded to conduranguinose. Third and fourth spots were dark brown and authentic for thevetose and cymatose respectively.

It seems that the sugars of both glycosides (conduranguin and marsdenin) are chromatographically the same. On the other hand the aglycone fractions of these two glycosides are different. To show the difference between these two aglycone fractions, we used different solvents as described by Zechner and Zölss⁵, and observed that the solubility of these two aglycone fractions were entirely different.

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Production of Emetic Material by Species of *Fusarium*

OCCASIONALLY species of barley and other cereals in the mid-western States of America have been infected with one of several species of *Fusarium* that cause a condition known as 'scab'. Such grain often contains an emetic principle¹ which renders it unsuitable for feeding to animals having simple stomachs.

To the best of our knowledge, there are no reports of these micro-organisms producing emetic material in artificial media. As part of an investigation into the physiology of micro-organisms associated with

grain, we have found that certain of the *Fusarium* produce emetic material when grown for at least 10 days in a suitable artificial liquid medium with agitation.

The micro-organisms investigated were *F. moniliforme* (two strains), *F. oxysporum lycopersici*, *F. graminearum*, *F. avenaceum*, *F. poae*, *F. sporotrichoides*, *F. equiseti* and *F. culmorum*. All these micro-organisms except *F. oxysporum lycopersici* produce or cause the plant to produce emetic material in grain. Those which produced emetic material in artificial media were *F. moniliforme* (one strain), *F. poae*, *F. culmorum* and *F. nivale*. All the last named, except *F. nivale*, were grown in Richards' solution². For *F. nivale*, which showed poor growth in this medium, nutrient broth was used (3 gm 'Difco' beef extract, 10 gm 'Difco' peptone, 10 gm glucose and 1 litre water). Culture filtrates were evaporated to one fifth their original volumes, adjusted to pH 9 with sodium hydroxide solution and extracted exhaustively with diethyl ether. Upon the evaporation of the dried ether solutions, the ether soluble residues were examined for the presence of emetic material by injecting an aqueous suspension of 5–10 mgm. intravenously into pigeons. A positive response was indicated by prolonged emesis. Controls prepared similarly by processing sterile media showed no activity.

Work is in progress to ascertain the chemical nature of the emetic compound(s) in these preparations and in extracts of 'scabbed' grain.

We thank Dr W. L. Gordon, University of Manitoba, Winnipeg, for some of the *Fusarium* cultures used in this investigation. Assistance from an industrial research grant from Maltng Barley Improvement Association, Milwaukee, Wisconsin, is gratefully acknowledged.

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Sterol Glycosides in Oilseed Phospholipids

STEROL glucosides (sterolins) have been shown to be present in the commercial phospholipids obtained from soybean¹, cotton seed², corn³ and groundnut⁴. Using the acetone extraction procedure already described⁴ we have now isolated similar compounds from rapeseed and linseed phospholipids to the best of our knowledge this is the first report of the existence of sterol glycosides in any part of the flax or rapeseed.

Preprecipitation with acetone of an ethereal solution of commercial rapeseed 'lecithin' yielded a crude phospholipid which contained 2.1 per cent of sterol glycoside, and a similar substance was found to comprise 2.9 per cent of linseed phospholipids prepared in a like manner. It is probable that in each case β -sitosterol is the major sterol component but minor proportions of other phytosterols may also be present; thus detailed examination of the

hydrolysis products from groundnut phytosterolin⁴ has revealed the presence of small quantities of stigmastanol and a saturated sterol

Our thanks are due to the Nuffield Foundation for their support of this work

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Isolation of the Antifungal Substance, 6-Methoxybenzoxazolinone, from Field Corn (*Zea mays* L.) in Canada

THE presence of an antifungal substance which is inhibitory to the growth of *Fusarium moniliforme* (Sheld.) and *Gibberella zeae* (Schw.) Petek, two pathogenic fungi associated with root and stalk rot of corn in Ontario, has been reported¹. The present communication reports the isolation and identification of the antifungal substance

An ether extract was prepared from 9,000 gm of corn plant tissue by the procedure reported previously. The ether was evaporated and the residue dissolved by boiling in 60 ml triple-distilled water. On cooling, buff-coloured needle-shaped crystals formed at 25°C. This crystalline material, at a concentration of 0.12 mgm per ml Czapek's agar, prevented growth of *G. zeae*, *Pyrenochaeta terrestris* (Hansen) Gorenz, Walker and Larson, *F. moniliforme* and *Diplodia zeae* (Schw.) Lévy.

The crystallization procedure and the type of crystals obtained characterized this material as 6-methoxybenzoxazolinone as reported by Loomis *et al.*² and Smitsman *et al.*³. This identification was confirmed by Dr E. Y. Spencer, Head of the Chemistry Section, Pesticide Research Institute, Research Branch, Canada Department of Agriculture, London, Canada

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PHYSIOLOGY

Urokinase-Induced Fibrinolysis of Human Standard Clots

STUDIES with human fibrinolysis, either induced by pyrogens or appearing during thoracic surgery, together with other observations, indicate that very likely the first phase of an endogenous fibrinolytic reaction in man is the release of a plasminogen activator from the tissues into the blood stream. The question whether this activator can induce lysis of an intravascular clot directly was studied *in vitro* with human urokinase, a plasminogen activator excreted with the urine, as the enzyme source and human standard clots as substrate.

Urokinase was prepared as follows. 2,500–3,000 ml of clear pooled urine was collected during the

day, filtered (from inside to outside) overnight by gravity through a Coors porcelain filtering cylinder, porosity No. 1, size 1 (pore size diam. 13.5–15 μ). The next morning, the cylinder was emptied and then eluted by forcing fluids with suction from the outside to the inside in the following succession: 20 ml of distilled water, which was discarded; 140 ml of distilled water, which elutes thromboplastic material¹; 40 ml of 1 M potassium thiocyanate, which was discarded; 120 ml of 1 M potassium thiocyanate, which elutes urokinase. This eluate was cleared by centrifugation and concentrated ten times by pervaporation in a 8 × 32-in. cellulose dialysing tubing. One end of the tubing was dialysed during the pervaporation (6 hr). Several concentrated eluates, after being cleared by centrifugation and dialysed for 2 hr against cool running tap water, were pooled and again concentrated by pervaporation (3 hr). Thus preparation, 'Uro-100x', was again cleared by centrifugation, dialysed for 90 min against distilled water and was then ready for use. The activity of the material was retained several days when it was frozen. Fibrinolysis occurred within 20–40 min. when 5 per cent 'Uro-100x' was added to human plasma and the mixture clotted with thrombin.

Standard clots were prepared as follows. Human ACD-bank blood plasma was mixed with 10 per cent 0.25 M calcium chloride, poured into the stem of a 'Klmax' protein sedimentation tube No. 46815 to exactly the 0.4 ml mark, and allowed to clot at 37°. At least 1 ml of the test solution was poured into the wide part of the tube on top of the clot filling the stem. A small glass bead was added, and the tube closed by insertion of a rubber stopper, allowing space for a small air bubble above the test solution. The tubes were chemically clean, siliconeized, and the procedure, except for the urokinase, carried out under sterile conditions. The tubes were attached horizontally to a rocking device with a cycle of 30 sec and a deviation for the horizontal of ten degrees in either direction, and placed in an incubator. The air bubble and the glass bead mixed the enzyme solution gently without touching the clot. With this arrangement, the relation of enzyme solution to the clot and its lysed product was kept constant within a few per cent during the experiment and prevented local accumulation of inhibitor deriving from the lysed clot. There was no marked progressive dilution of the test solution as in the fibrin plate method.

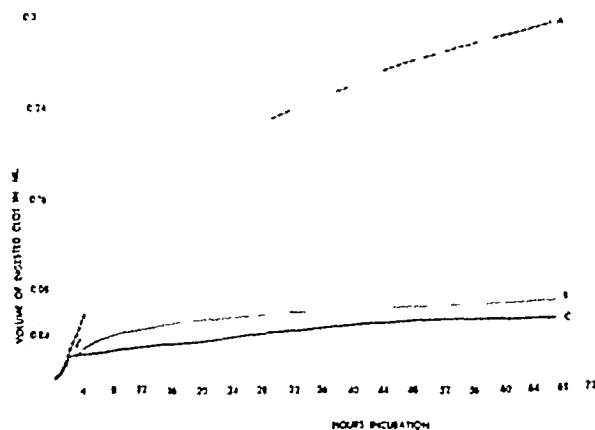


Fig. 1. Continuous fibrinolysis induced in human standard clots by human urokinase. Enzyme solutions: A, 10 per cent 'Uro-100x' in buffered saline; B, 10 per cent 'Uro-100x' in plasma; C, 10 'Uro-100x' in buffered saline, replaced after 2 hr by saline (arrow). Abscissa, incubation time (hr); ordinate, volume of clot digested.

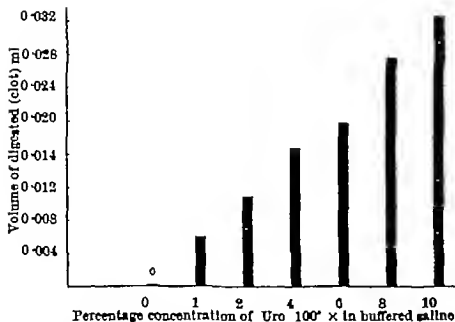


Fig. 2. Fibrinolysis induced in human standard clots by human urokinase. Urokinase replaced by buffered saline after having been in contact with the clot for 5 min. Incubation time, 72 hr. Abscissa: concentration of Uro-100x in buffered saline. Ordinate: volume of clot digested.

The progress of the fibrinolytic disintegration which started from the one enzyme-covered surface (8 mm²) of the clot was read directly in volume units of 0.004 ml and could be followed for many hours.

10 per cent 'Uro 100x' in buffered saline produced a continuous fibrinolysis of the standard clot which continued for days (Fig. 1, A). 10 per cent 'Uro 100x' in human plasma produced a progressive lysis of the clot which was less intensive and slowed down more rapidly than urokinase in buffered saline (Fig. 1, B). When the urokinase solution was removed and replaced by buffered saline alone, the clot lysis continued for many hours, but at a reduced rate (Fig. 1, C). Urokinase had to stay in contact with the clot for only 5 min, without producing any visible lysis, in order to trigger progressive fibrinolysis when it was replaced by buffered saline alone. The speed of progression was directly proportional to the strength of activity of the contacting urokinase solution (Fig. 2). Replacement of urokinase solution by non fibrinolytic plasma completely inhibits any further progression of fibrinolysis. Fresh human clots from coronary arteries, femoral veins, and other locations dissolved quickly when exposed to urokinase solutions. From the studies described, the details of which will be reported elsewhere, it is concluded (1) Urokinase penetrates the clot quickly. (2) Non retracted clots contain enough plasminogen which, when activated by human plasminogen activator, brings about their lysis. The activator itself may act on the clot *in vivo* and participate directly in thrombolysis.

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Spectral Composition of the Luminescence of the Euphausiid *Thysanoessa raschii*

We have determined the spectral characteristics of the bioluminescence of *Thysanoessa raschii*.

The crustaceans were collected in Loch Fyno, dark adapted, deep frozen, and sent to the Plymouth Laboratory, Marine Biological Association, in vacuum flasks.

For the experiments the animals were homogenized in sea water in a small beaker. The homogenate glowed spontaneously with an intensity that did not change appreciably during the experiments.

The instrument used in the laboratory observations is a telemetering bathyphotometer normally used for undersea photometric determinations. The sensor in the instrument is a R.C.A. 931-A photomultiplier tube. The signal from this tube is amplified and fed into a Leeds and Northrup 'Speedomax' recorder. The photocathode is just behind a filter holder in front of which is a collimating tube. At the distal end of the tube is an opal plastic disk with the characteristics of a Lambert collector. The beaker containing the homogenate is placed at the end of the tube. The light is collimated because narrow band interference filters are used, and their useful angle is limited to 5°. Twelve interference filters were used in the range 430-640 mμ.

The instrument measured irradiance (I), obtained from

$$n \sim LH \sim aETI\delta\lambda,$$

where n is recorder reading, E is energy of the source through the wave length interval $d\lambda$, T is measured transmission of the individual interference filter through the wave length interval $d\lambda$, and S is the relative sensitivity of the photomultiplier tube through the wave length interval $d\lambda$. The value of L was obtained from calibration of the entire instrument against a U.S. Bureau of Standards source. Irradiance values were in watts/cm², and quanta were derived from Planck's equation. The data were equated to 1.0 at the wave length of maximum emission.

All measurements were made in a dark room.

The mean of the luminescent emission from four homogenates of *T. raschii* is shown in Fig. 1. There is a sharp primary peak at about 476 mμ, and a slight secondary inflexion can be detected between 500 and 530 mμ. The spectrum is rather similar to that of *Euphausia pacifica*, the only other euphausiid for which an emission spectrum has been determined. The primary peak of the *E. pacifica* spectrum is at 472 mμ when the results are calculated in quanta, and the secondary inflexion is more pronounced than that of *T. raschii*.

Although the 1957 measurements of *E. pacifica* were made with the same instrument, a different series of interference filters was used, and the terminal glow of animals killed with ammonia was measured.

E. pacifica is an open ocean form, whereas *T. raschii* is confined to neritic habitats.

We thank Dr. Harold Barnes, Millport, for supplying us with specimens of *T. raschii*, and Dr. F. S. Russell for the hospitality of the Plymouth Laboratory.

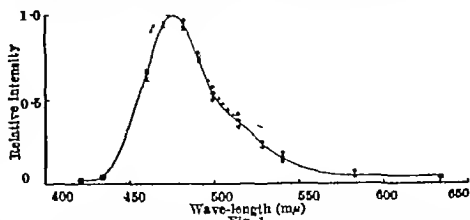


Fig. 1. Spectral distribution of luminescence from *Thysanoessa raschii* (solid line) and *Euphausia pacifica* (broken line). Data on which the curves were based are in quanta equated to 1.0 at the point of maximum emission.

tory of the Marine Biological Association, where these experiments were undertaken. This work received support from the US National Science Foundation.

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Mechanism of Autoregulation of Renal Blood Flow

It has been noted by Winton¹ and has since been confirmed many times²⁻⁵, that the renal vascular resistance is not constant but increases with increasing arterial pressure in the range 80-120 mm mercury mean pressure. The phenomenon does not depend on an intact nerve supply to the kidney but occurs in the denervated, perfused kidney. The autoregulation of renal blood flow has been considered attributable either to an active vasomotor process³⁻⁵ or, in some recent work, to a flow-dependent separation of plasma from red cells in the renal circulation. The first of these theories appears to have been developed only by the process of elimination, and the second appears no longer tenable in the light of experiments by several groups⁶⁻⁷. The oedematous kidney displays a high resistance to flow which probably results from compression of vessels by extravascular fluid. This factor has not been considered important in the function of kidneys subjected to normal arterial and venous pressure, since measurements of renal tissue pressure⁸ indicated that it does not vary directly with renal vascular resistance.

In the experiments reported here, kidneys were removed from one dog and perfused with blood from the carotid artery of a second animal. The blood was

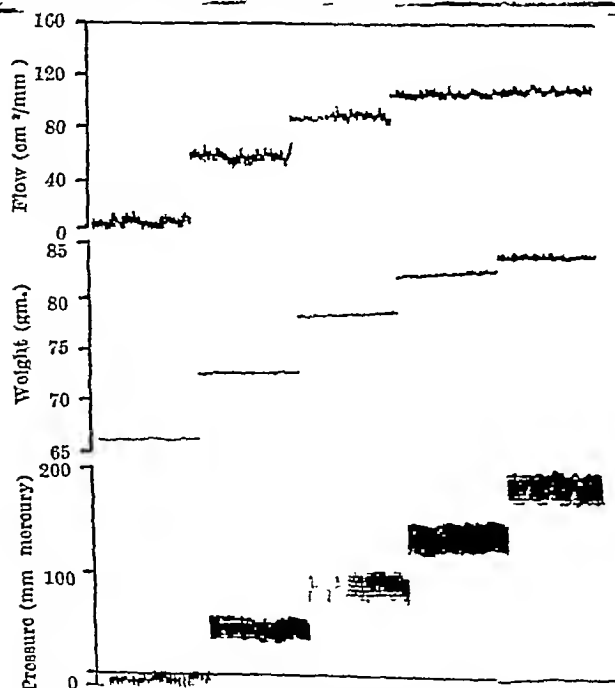


Fig 1 Responses of the kidney to step increases in pressure. Note that as the pressure is increased by a series of equal increments the flow does not increase proportionately and that the changes in weight tend to parallel the changes in flow.

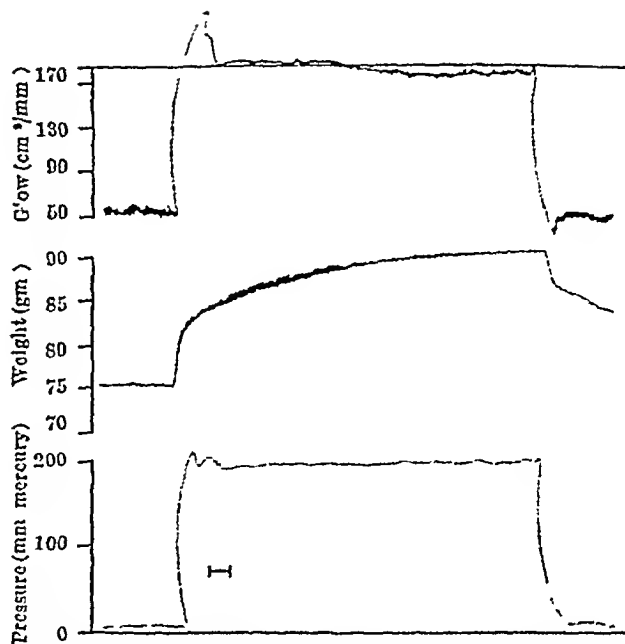


Fig 2 Results of applying a 200 mm mercury pressure step to the kidney. The weight changes rapidly at first and then slowly. These two phases are considered to result from vascular filling and filtration of the fluid out of the capillaries respectively. Flow shows an initial increase and then decreases to a final value with about the same time course as the slow pressure change. Time mark below indicates 5 msec.

returned to the second animal's jugular vein. A constant-stroke output pump was used. Its speed was adjusted through a feedback circuit, so that constant pressure was maintained. A series of stopping switches and batteries in the feedback loop made it possible to apply voltage which changed the pump speed and maintained a new pressure. Pressure was measured with a resistance pressure gauge. Flow was calculated from the pump speed and checked with an outflow recorder. Kidney volume was at times recorded by an oncometer or, alternatively, the kidney was suspended from a strain gauge and weighed.

In 24 experiments, 17 kidneys exhibited autoregulation. The flow always paralleled the renal volume (Fig 1). When the change of flow per unit pressure change in the autoregulatory range was small, the volume change per unit pressure change was also small. When the kidney was subjected to an abrupt increase in perfusion pressure in the autoregulatory range, the flow rose initially and then fell as the renal volume increased. The increase in volume exhibited a rapid (vascular filling) and a slow (filtration) phase. The equilibrium times for the changes in flow and volume were always nearly identical (Fig 2). The opposite phenomenon was apparent when the perfusion pressure was rapidly

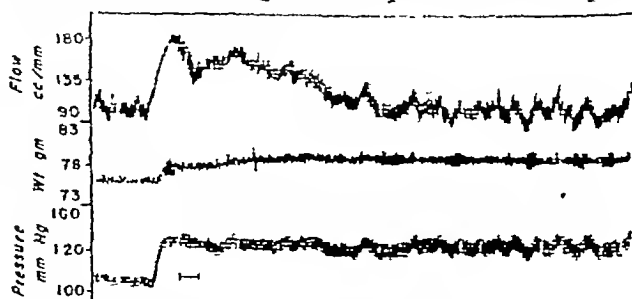


Fig 3 A step function of pressure within the autoregulatory range. Note that the vascular filling of gain in weight is not large but that it exceeds the gain in weight from filtration, that the flow decreases during the filtration phase, reaching its terminal value at about the same time as the kidney ceases to increase in weight. Time mark below indicates 5 msec.

decreased, that is, the kidney initially had a high resistance which fell as the renal volume decreased.

In some experiments the renal venous hematocrit was continuously measured by a conductivity method.⁷ As might be expected the hematocrit increased with a rise in pressure and fell with a drop in pressure. This effect was less pronounced in the autoregulatory range than below it, a finding indicating that in the autoregulatory range, the kidney does not sequester plasma as pressure increases. When autoregulation was abolished by cyanide the vascular distensibility and the distensibility of the kidney both decreased.

These results conflict with those in which intrarenal pressure did not vary with renal resistance.⁸ The fact that renal volume changes parallel renal flow changes is in accord with the possibility that the normal kidney exhibits autoregulation of flow because extravascular fluid compresses some low pressure vessels. This mechanism has previously been considered unacceptable.⁹

I would like to thank Mr O F Brown for his technical assistance.

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Carbohydrate Metabolism in Hypervitaminosis A

Excess vitamin A ingestion increases bleeding tendency,¹ depresses basal metabolism² and increases excretion of neutral 17 ketosteroids in urine of albino rats.³ The Q_{O_2} of liver slices of hypervitaminosis A rats is lower than that of control rats (Ray, Amal and Sadhu, D. P., unpublished observations), the weight of the thyroid is diminished and that of the adrenal increased.⁴ In an attempt to elucidate the mechanism of hypometabolism induced in hypervitaminosis A, liver was studied for glycogen and fat contents and diaphragm as an index of glucose utilization in peripheral tissues.

Twelve young albino rats of 55-60 gm weight were fed 30,000 i.u. vitamin A ('Arovit' Roche) daily for 10 days and were fed with twelve control rats and were killed by decapitation. A small piece from the upper part of the right lobe of the liver was taken for estimation of glycogen and fat content by a method previously described.⁵ The diaphragm was divided into two halves and each hemidiaphragm was used for studying glucose utilization and glycogen synthesis⁶ and the values compared with that of the pair fed control rats. In hypervitaminosis A liver glycogen is decreased from the control value of 16.1 \pm 1.8 (standard deviation) mgm. per gm. liver tissue to 12.2 \pm 0.93 mgm while the fat percentage is increased from control 8.1 \pm 0.71 to 10.1 \pm 0.72. Diaphragms show a decrease of glucose utilization from the control value of 0.31 \pm 0.02 mgm. 100 mgm wet diaphragm per hour to 0.213 \pm 0.05 mgm, while glycogen synthesis which is 0.163 \pm

0.024 mgm./100 mgm wet diaphragm per hour in the control rats is decreased to 0.008 \pm 0.013 mgm in the hypervitaminosis A rats.

These experiments show that the depression of metabolism is not restricted to liver alone, but that in muscles is also depressed, in spite of hyperthyroxinaemia in hypervitaminosis A.

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Effect of Thioctic Acid on Gain in Body-Weight by Turkey Poults

THIOCTIC ACID (lipoic acid, DL-6,8 dithiooctinoic acid) is known to be a component of certain enzyme systems. It is also required as a growth factor by *Streptococcus faecalis* in certain synthetic media, if this organism is to oxidize pyruvate successfully. Certain other bacteria, such as *Escherichia coli*, that oxidize pyruvate also require thioctic acid.¹ It has been tested for its ability to stimulate growth in higher animals, but the results have not been uniform. Positive results were obtained by DeBusk and Williams² with rats and chicks. In their experiments a growth response was obtained whether the basal ration was a practical corn soybean alfalfa meal type or a purified sucrose-alcohol extracted casein gelatin type. Food efficiency was also improved with both the chicks and the rats.

Briggs and Fox³ afterwards reviewed the literature up to 1957 and initiated another experiment with chicks. They could obtain no evidence of a growth stimulation when semi-purified or practical diets were supplemented with thioctic acid. These workers concluded that thioctic acid could not be considered as an animal growth factor.

Kratzer *et al.*⁴ at a later date did obtain a slight growth response to thioctic acid with turkey poults; but the response was not statistically significant. There is a possibility that the turkey poult may differ from the chick in its requirements or in its ability to synthesize micronutrients. The present experiment was set up in an attempt to clarify further the role of this factor in turkey poult nutrition.

A practical poult starter ration, currently in use at this laboratory, was supplemented with thioctic acid at a level of 7 mgm/kgm. This poult starter contained ground wheat and barley, soybean meal, fish meal, meat scrap and alfalfa meal. It was fortified with vitamin and mineral supplements in accordance with general recommendations for this type of diet. Penicillin penicillin was added at 0 mgm/kgm. Each dietary treatment was replicated

Table 1 EFFECT OF THIOCTIC ACID ON POULT GROWTH TO SIX WEEKS OF AGE

| Dietary treatment | Body weight (gm.) | |
|--|-------------------|----------------|
| | Males 1,163 | Females 908 |
| Poult starter | | |
| Poult starter plus thioctic acid (7 mgm./kgm.) | 1,160 | 971 |

six times with 18 unsexed Broad Breasted Bronze poults per replicate. The poults were randomized into the compartments of an electrically heated battery brooder. The experiment was terminated when the poults were six weeks of age.

Body-weight results for male and female poults are summarized in Table 1.

Analysis of variance showed no significant differences in 6-week body weights of male or female poults. The above results would indicate that the response to thioctic acid by turkey poults is negligible when the birds are fed a practical ration.

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A Biological Action of Deoxyribonuclease I on the Growth of *Euglena gracilis*

On realizing that the activity of the enzyme deoxyribonuclease was increased considerably in regenerating rat liver¹, we decided to investigate whether it might influence the rate of cellular multiplication by itself.

In our experiments we endeavored to maintain the enzyme at the same concentration as it occurs in regenerating tissue. Since nothing is known about permeability of cell boundaries to deoxyribonuclease we tried to compensate for any permeation difficulties. This was done by increasing the outer enzyme concentration by a factor of ten as compared with what we assumed it to be from previous experiments. In the second set of experiments we tested the dose-action relationship.

Euglena gracilis had previously been cultivated for a week in the medium of Elsasser and Adler² containing 10⁻¹⁰ gm vitamin B₁₂ per ml. 0.5 ml of this *Euglena* 'suspension' was transferred to 5 ml of fresh, sterilized medium with vitamin B₁₂ contained in 20 ml penicillin-flasks. The cultures were then incubated in a moist oxygen atmosphere at 28°C under fluorescent light (Philips TL5W). 70 hr later the total cell volume was determined after spinning down an aliquot at 1,000 g for three min. Controls were taken as 100 per cent and the difference in volume was expressed as a percentage increase. It was found that the number of cells was proportional to the total volume of cells within reasonable limits.

Clearly it can be seen from the first experiment that deoxyribonuclease in doses of the order of micrograms

will under suitable conditions double the rate of growth in *Euglena*. In the second experiment when the intensity of light is reduced the growth promoting effect is less, but the growth rate is still dependent on the dose of deoxyribonuclease.

From this experiment it is apparent that the enzyme may act as a growth promoting agent in low concentrations. It will be of interest for us to determine whether this is limited to special organisms or is rather a general phenomenon.

I thank the Deutsche Forschungsgemeinschaft for its support. I am grateful to Dr. Ilse Pendl for supplying a *Euglena gracilis* strain and to Miss A. Docter and Miss. B. Ohly for their help.

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HÆMATOLOGY

A 'New' Human Blood Group Antigen, Sw_a

In the course of compatibility tests with the serum of a patient Gu, the red cells of one donor, Swann, were found to be strongly agglutinated in all media. The patient was in crisis from auto-immune hæmolytic disease of the 'cold' non-gamma globulin type, with no free 'non-specific' antibody in the serum. Her groups were 0, cde/cde, NS/NS, M₁(a-), V_w-, M_s-, P₁+, K-, Le(a-b+), Fy(a+), Jk(a+b+), W₁(a-).

Mr Swann's groups were 0, cde/cde, E⁻-, C⁻-, V⁻-, M_s/M_s, M₁(a-), V_w-, V_r-, H_e-, M_e-, P₁+, Lu(a-b+), K-k+, K_p(a-b+), Le(a-b+), Fy(a-b+), Jk(a+b+), D₁(a-), J_s(a-), W_r(a-), Be(a-), B₃-, Le_ay-, R_m-. Negative results were also obtained with seven antisera from unsolved 'family' groups, and with over 500 Group 0 (anti-AB) sera. His saliva inhibited anti-H of human and of plant (*Ulex*) origin, anti-Le^a and anti-Le^b, but not anti-A, anti-A₁, anti-B or anti-AB. Nor was the reaction of serum Gu with his own cells inhibited with Mr Swann's saliva.

Further testing of the serum Gu revealed the presence of anti-M₁^a, anti-W_r^a and anti-B_y. The former was only weak, but the latter two antibodies were avid and powerful, and clearly separable by suitable absorptions both from each other, and from the antibody against Swann's cells. No other example of this latter antibody was found in over 1,200 normal sera, but several examples were encountered in other cases of auto-immune hæmolytic disease. In each such instance, anti-W_r^a was also present, and sometimes anti-M₁^a or anti-V_w as well. Pure antisera were prepared from all these mixtures by appropriate absorption without significant loss of avidity or titre.

It is clear from these observations that a 'new' blood group antigen is present on the cells of Mr Swann. It is proposed to name this antigen Sw_a, and the corresponding antibody anti-Sw_a. Tests of 29,487 random blood samples from adults disclosed four more Sw_a positives, two of whom were related. Tests on three of the families have shown Sw_a to be inherited as a Mendelian dominant character which

Table 1 THE ACTION OF DEOXYRIBONUCLEASE I (WORTHINGTON) ON *Euglena gracilis*

| gm. per ml. Deoxyri- bonuclease I added to culture | Increase in total cell volume or number of cells (%) | Arithmetic mean of increase | Standard deviation | Probability for (ref. 3) perfect random incidence (%) |
|---|--|--------------------------------|--------------------|--|
| 0.0 | 12 controls | ±0.0 | ±8.2 | >>5 |
| 4.2 × 10 ⁻⁶ | 12 tests | 102.7 | ±30.7 | <<<0.5 |
| 0.0 | 5 controls | ±0.0 | ±5.1 | >>5 |
| 10 ⁻⁷ | -18, -12, -11, 14, 16 | -2.2 | ±14.1 | >>5 |
| 10 ⁻⁸ | 0, 9, 9, 14, 16 | 10.8 | ±4.1 | <<<0.5 |
| 10 ⁻⁹ | 18, 21, 23, 43, 45 | 31.0 | ±12.4 | <<<0.5 |
| 3.3 × 10 ⁻⁶ | 35, 65, 82 | 60.7 | ±23.7 | <<<0.5 |

segregates independently of the ABO, Rhesus MNSs, Koll, Lewis red cell (and ABH secretion), Duffy and Kidd blood group systems, nor is the character partially sex linked.

These findings will be reported in detail at a later date.

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Glutathione Stability of the Erythrocytes in Iranians

HÆMOLYTIC reactions following the ingestion of drugs such as primaquine and the broad bean (*Vicia faba*) have been shown to be due to an inherited abnormality of the erythrocytes which can be detected by an *in vitro* glutathione stability test devised by Beutler¹. The use of this test in surveys has established that the incidence of the defect varies with peoples and races. American Negroes, Sephardic Jews and Sardinians have a much higher incidence of sensitive individuals than Ashkenazic Jews or American Caucasians. Beutler has recently reviewed the subject². Many cases of favism have been seen locally during the past few years, and it was reasonable to assume that a survey of the glutathione stability of the erythrocytes in Iranians would show the presence of the abnormality in this area.

The survey group consisted of 556 Moslems who were members of the medical nursing and ancillary staff at our two institutions. Only one member of a family was sampled. However, because consanguinity is quite common in Iran, it was impossible to be sure of eliminating children of first-cousin marriages. Persons of Jewish, Armenian, Assyrian or Zoroastrian origin were not in sufficient number for evaluation. These groups, along with various tribes are being studied and will be the subjects of later reports. The blood samples were collected into an acid citrate-dextrose solution, glutathione determinations and the glutathione stability test were performed by the standard technique usually on the same day or within 24 hr of collection. Hamatocrit values were also determined.

Since it has been shown that the gene which controls the abnormality is probably sex linked, the results

Table 1 ANALYSIS OF BLOOD GLUTATHIONE-LEVELS BEFORE AND AFTER INCUBATION WITH ACETYLPHENYLHYDRAZINE (THE GLUTATHIONE STABILITY TEST)

| | No of subjects | Range of values | | | | Mean | S.D. | S.E. |
|-----------------------|----------------|-----------------|------------|------|------|------|------|------|
| | | before | 23-2 | 70-1 | 33-9 | 8.3 | 1.4 | |
| Sensitive males | 35 | after | 0.2-10.6 | 5.1 | 4.9 | 0.8 | | |
| | 323 (257)* | before | 40.0-111.5 | 64.1 | 12.3 | 0.8 | | |
| Non-sensitive males | 12 | after | 33-104.5 | 54.6 | 12.5 | 0.7 | | |
| | 269 | before | 20.0-59.6 | 43.7 | 11.0 | 3.2 | | |
| Sensitive females | 12 | after | 0.7-27.1 | 14.2 | 0.4 | 2.7 | | |
| | 186 | before | 30.3-124.9 | 66.8 | 16.6 | 1.4 | | |
| Non-sensitive females | 132* | after | 32.8-109.0 | 60.5 | 13.2 | 1.0 | | |

All values are in mgm glutathione per 100 ml red blood cells.

The numbers in brackets are the number of samples tested both before and after treatment with acetylphenylhydrazine; the remainder of the non-sensitive persons were tested only after treatment with acetylphenylhydrazine.

Table 2 DISTRIBUTION OF GLUTATHIONE LEVELS (IN MG. GLUTATHIONE PER 100 ML. RED BLOOD CELLS) AMONG SENSITIVE PERSONS AFTER INCUBATION WITH ACETYLPHENYLHYDRAZINE

| Range of values | 0.1-5.0 | 5.1-10.0 | 10.1-15.0 | 15.1-20.0 | 20.1-30.0 |
|-----------------|---------|----------|-----------|-----------|-----------|
| No of males | 22 | 8 | 3 | 2 | 0 |
| No of females | 2 | 3 | 1 | 0 | 6 |

were calculated independently for the two sexes. Using as the criteria of sensitivity to the glutathione stability test all values of less than 30 mgm glutathione per 100 ml red blood count after incubation with acetylphenylhydrazine¹, there were 35 sensitive males out of 358 (9.8 per cent) and 12 sensitive females out of 198 (6 per cent). This difference of incidence between the males and females in this series is not statistically significant ($P > 0.10$). Table 1 gives an analysis of the levels of glutathione in the erythrocytes before and after incubation with acetylphenylhydrazine and Table 2 shows the distribution of post incubation glutathione levels among the sensitive individuals. As previously described by other workers¹ sensitive males gave lower post-incubation glutathione levels than females.

Having thus established an overall incidence of 8.6 per cent of sensitive individuals the subjects were analysed according to place of birth. The results were as follows: Shiraz area 275 rest of Fars (the province in south west Iran of which Shiraz is the chief town) 89 Bushire 5, Teheran region 53, Azarbaijan 8, Caspian sea area 12, Kholirasan 15, Korman 4, Kurdistan 12, Bandar Abbas 1, Khuzestan 18, Yazd 26, Isfahan and province 31 born of Iranian parents outside Iran 7. Of the total of 47 sensitive persons, 26 were born in Shiraz (that is, an incidence of 9.5 per cent in this area), 10 were born in the rest of Fars and 11 were born in the rest of Iran. Though the number of subjects born outside Shiraz constituted slightly more than half of the series, they were too spread out over Iran to allow comparison with the Shiraz group. However it appears that persons sensitive to the glutathione stability test are to be found in the Moslem population throughout Iran.

At the same time as this survey was performed a number of other genetically determined characteristics were also examined. A statistical analysis of the ABO and Rh data revealed that the survey group represented a good random selection of individuals. The results of these and other blood anthropological studies will be presented later.

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Hæmoglobin Pattern of the Cyclostome *Pteryomylon planeri* during the course of Development

Two hemoglobin components have been demonstrated by starch gel electrophoresis in both larval and adult forms of *Pteryomylon planeri*. Although the components are most clearly separated by electrophoresis in starch gel separation has also been

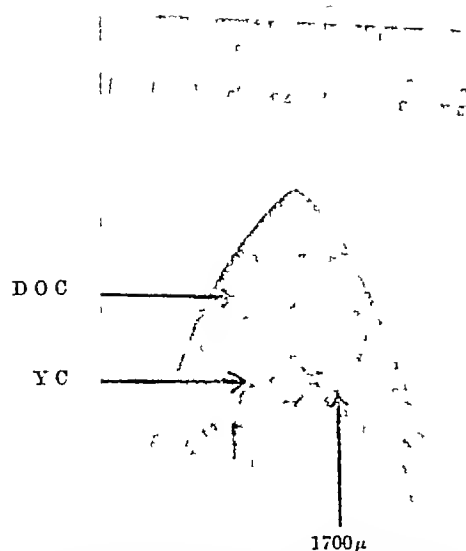


Fig 1 Tooth N1 half natural size DOC, deep olive colour YC, yellow colour, 1700 μ , maximal thickness of manganese covering

dentine disappeared and the manganese dioxide layer was much thicker than on the surface—up to 1 cm. But the results of Pettersson's work are scarcely applicable to this part of the manganese dioxide layer; he investigated the surfaces of nodules, and the rate of formation of the manganese dioxide layer inside the deposits cavity is a separate problem to be solved by special investigation. To determine the age of the teeth, we take the lowest rate of nodule formation and the greatest depth of covering only.

The colour of the main part of the front side of tooth N1 resembled the light-coloured yolk of a hen's egg varying from barite—yellow to buff—yellow, or apricot yellow and pale orange according to Ridgeway⁴. It is seen clearly on a photograph as a light field surrounded from the top and sides by a dark stripe and spots, deep olive in colour, which is characteristic of fossilshark teeth found in the ground and from the ocean bottom deeply embedded in manganese dioxide. Yellow seems to be a natural colour and indirectly shows that this tooth is geologically young. The manganese dioxide layer was preserved in several small spots only, the thickest of which is 1,700 μ . Using the minimal Pettersson's rate—0.15 mm in 1,000 years—it will require 11,333 years for deposition.

Tooth N2 is much darker than the first one, the deep olive colour of the fossil predominating, the yellow (cream buff) colour occupying a noticeably smaller surface, which on the front side formed rather

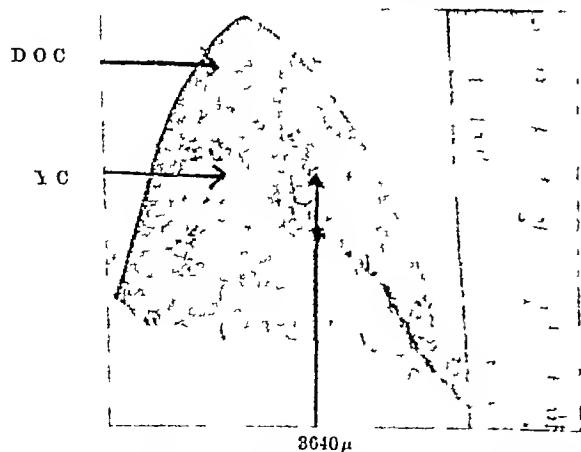


Fig 2 Tooth N2, half natural size DOC, deep olive colour, YC, yellow colour, 3640 μ , maximal thickness of manganese covering

a small triangle in the middle. The maximal thickness of the manganese dioxide covering is 3,640 μ . The minimal rate gives an age of 24,206 years. This means that *Carcharodon megalodon* became extinct in the latest Pleistocene or even survived until the Holocene period. To prove this, let us imagine that *Carcharodon megalodon* was really extinct in the middle Pleistocene—about 500,000 years ago. Then even the minimal rate shows that its tooth must be covered with a manganese dioxide layer about 75 mm in thickness. Or let us imagine that the tooth in 500,000 years was covered with a coating of 4 mm. only. Then the rate of manganese nodules growth will be literally microscopic, that is, 8 μ in 1,000 years. This small, quite speculative figure sharply contradicts all the results of Pettersson's experimental work.

Recognizing the relation between the age of the fossil and the thickness of the manganese dioxide covering, we can also determine the rate of nodule growth on the basis of the age of enclosed fossil. Up to 40,000 years, the carbon-14 method gives very exact results, but it needs a rather large quantity of organic material. This method is therefore more suitable for such big deposits as whale carbones, covered with a manganese dioxide layer in the same manner as a shark tooth.

Knowing the age of the bone, we could estimate the overall rate of growth of the surroundings at different points and particularly in the deposit cavity.

I am grateful to Dr J D H Wiseman of the British Museum and Prof J E Smith, head of the Department of Zoology, Queen Mary College, for their help and advice during this work and to Mr. S V N Casey for the photographs.

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Distribution of Sodium in Compact Bone, as Revealed by Autoradiography of Neutron-Activated Sections

RECENT work has emphasized the heterogeneous composition of compact bone. According to X-ray absorption, young osteons contain less calcium than the others¹. Histological methods indicate that the mucopolysaccharides of the ground-substance are different in the preosseous layers, in the incompletely calcified osteons, and in the fully mineralized structures².

The distribution of sodium in compact bone was investigated in the same respect. Since histochemical methods are deficient in sodium, an attempt was made to identify this element after its activation in a nuclear reactor.

Pieces of ribs or tibiae were taken from humans during surgical operations. They were kept in 96 per cent ethanol. It is obvious that part of the sodium, not firmly attached to the tissue, escaped in the fluid. Bones were cut in transverse sections with a saw, and these were ground down and polished by hand with emery paper.

The sections were submitted for six hours to a flux of 3.5×10^{11} neutrons/cm²/sec in Trico (Triga Reactor supplied by General Atomic to the Government of Belgian Congo). It has been demonstrated³

that, after 3 hr, nearly all the radioactivity induced in bone originates from sodium ^{24}Na . R. Loos, of the Department of Physics confirmed this fact for our material by γ -spectrography.

After this delay the sections were sandwiched between two Maximum Resolution plates (Kodak Ltd). When exposed for about 40 hr, the plates were developed in D 178.

Microradiograms of the sections were then obtained in 10 min by exposure at a distance of 25 mm from the tube of a Philips apparatus set at 5 kV and 1.8 mA.

Fig. 1 shows an autoradiogram (A) and a microradiogram (B) of the same region of a human rib in transverse section. The darkening of the autoradiogram is not uniform. On the left a large area which is not radioactive corresponds to an absorption cavity. Smaller white spots on the autoradiogram indicate Haversian canals as seen on the microradiogram. Besides these empty spaces which could be expected to be devoid of sodium, one may observe that the osseous substance itself is not uniformly radioactive. More precisely, the osteons not yet fully calcified and thus appearing gray on the microradiogram, have given a weaker imprint on the autoradiogram. No doubt they are poorer in sodium than the completely calcified tissue.

Some sections were decalcified in ethylenediamine tetracetic acid others were thus treated before neutron activation. The former produce much paler images on the autoradiographic emulsion, the latter give the same pictures as untreated bone. It is thus confirmed that most of the sodium is linked in the mineral portion of bone tissue.

These observations show that the load of sodium at least of sodium remaining in ground sections of bone fixed in alcohol parallels the load of calcium as indicated by X rays. The concentration of sodium is lower in young osteons than in old ones, just as it is lower in the skeleton of young rats than in that of old rats. It seems that an osteon reaches saturation nearly at the same time for both calcium and for sodium.

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Dimorphism and Size Distribution in *Veella* and *Physala*

Woodcock¹ attributed right- and left handedness in *Physala*, the Portuguese man of war to a selective advantage in avoiding entrapment in windrows of *Sargassum* weed and floating debris. This selective advantage was presumed to be due to differences in sailing patterns through convection cells in the surface water of the northern and southern hemispheres. The absence of *Sargassum* from the South Atlantic and the paucity of debris in the barren, blue waters in which *Physala* is characteristically found would seem to invalidate this hypothesis. On the other hand Woodcock's arguments concerning food concentration by the convection cells and sailing patterns are more convincing. Woodcock² continued to favour the hypothesis that there are significant differences in abundance of the two forms between the northern and southern hemispheres. Other authors^{3,4} have commented on this problem however, none has pointed out that the more extensive literature on *Veella* long known to be dimorphic⁵, shows no statistically reliable difference between the abundance of the two forms in the northern and southern hemispheres.

The fact that Agassiz⁶ found only left handed specimens present in more than two thousand *Veella* collected along the shores of the north west Atlantic while Chun⁷ found 71 left-handed and 6 right handed *Veella* off Africa in the north-east Atlantic would indicate an east-west or zonal difference. Chun⁸ findings are confirmed by the results of Moser⁹. In a recent paper Savile¹⁰ reported left and right handed specimens of *Veella* from the north west and south west Pacific. Of more than 250 specimens examined by the author from the north east Pacific all were left handed. Thus if there is an east-west difference in relative abundance of the two forms, the results available to date indicate that the situation in the Pacific is the reverse of that in the Atlantic.

Savile¹⁰ advances a hypothesis that appears to solve this problem. In the northern hemisphere left handed specimens of *Veella* move to the left of the wind direction due to the anticyclonic wind circulation over the ocean. The left-handed specimens are therefore concentrated along the outer edges of the distribution. The right handed *Veella* move to the right of the wind direction and are concentrated in the centre of the distribution. Thus one should find the left handed specimens near shore. In the anticyclonic wind circulation of the southern hemisphere the left handed *Veella* are concentrated in the centre of the distribution with the right-handed specimens more abundant along the borders of the distribution. The only results which weaken this argument are the exclusively left handed specimens taken by me off California. Many of these were collected more than 300 miles off shore.



Fig. 1. Transverse section of a human rib. Correlation between autoradiogram after neutron activation (A), where darkening is related to sodium concentration, and microradiogram (B) where white areas indicate the greatest amount of calcium. The absorption cavity (on the left) and the Haversian canals are not radioactive. The less calcified osteons contain less sodium than the others. ($\times 25$)

Savilov* found large specimens of *Veleva* most abundant in the region of 40° N lat in the Kuroshio Extension. Young and larval forms were common in the south and far western parts of the Pacific. He attributed this size distribution to the wind and current patterns. An alternative explanation follows.

My studies of *Veleva* off California, extending over a period of six years (unpublished results), show a marked seasonal appearance of *Veleva* at the surface. This is confirmed by a careful examination of the previously published literature. The post-larval specimens first appear at the surface in very late December or early January and continue to reach the surface through the spring. The largest specimens are found in late autumn and early winter.

Examination of the track of the *Vityaz* shows that the stations in the Kuroshio Extension were occupied from July to November when neither larval nor very young forms would be present. The southern and far-western stations were occupied in December, January, February, July and August when the largest specimens are rare if present at all. Larval and young specimens would be present in December, January and February. Thus the size distribution Savilov describes in general terms can be more easily explained by seasonal differences. The data he presents do not allow a more precise analysis of the problem. One might also expect to find mean length differences between local populations because of different sea surface temperatures. However, these would be much smaller than those due to seasonal appearance and growth.

From the above it is apparent that the origin and occurrence of the different sizes and morphological forms of *Veleva* and *Physalia* are not yet satisfactorily explained. Of the several variables that appear to be involved, seasonal appearance and growth have not been properly considered in previous reports.

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Penetration of the Liver-fluke, *Fasciola hepatica* into the Snail, *Limnaea truncatula*

THE life-history of *Fasciola hepatica* has been recounted in nearly every text-book of zoology or of parasitology since it was elucidated by R. Leuckart (1881-82) and A. P. Thomas (1881-83). In spite of this and much original work by other investigators our knowledge of (a) the form which penetrates the snail host and (b) the manner of its penetration is misconceived. For example, in the modern account given by G. Lapage¹ it is stated that once a snail has been found, the miracidium "applies the papilla at its broadest, anterior end to the soft skin of the snail and, spinning by means of its cilia on its long axis, it drives the papilla into the snail and penetrates the snail's body". Other writers have introduced something between this sort of statement and the more correct idea, succinctly expressed by Faust², that penetration "is accomplished by the secretion of digestive enzymes elaborated in the so-called

'penetration glands' which discharge the secretion at the anterior end of the miracidium". It is difficult to prove that 'digestive secretions' are produced, or even to demonstrate the cytological effects produced by a penetrating larva which is smaller than some ciliated protozoa. It is here shown, for the first time by means of photomicrographs, that the miracidium creates a perforation in the snail's integument by the loosening, cytolysis and abstraction of epithelial cells, an action which appears to be chemical rather than mechanical and is probably the result of onzyme activity. It will be shown also that, because the miracidium loses its ciliated epithelium and is in other ways transformed before penetration is effected, it is an early sporocyst and not a miracidium which enters the snail.

The miracidia of *Fasciola hepatica* are not as efficient in locating and penetrating snail hosts as some studies of their tropistic behaviour lead us to suppose. In the immediate vicinity of a snail many larvae swim to and fro without ever attacking, and many more encounter the snail but do not succeed in adhering to it, much less penetrating it. When contact is established, however, the miracidium butts the snail several times, and it is this action which has given the false impression that the rotating larva is boring like an auger into the snail when in fact it is merely trying to attach itself. Early adhesion is so light that no matter how carefully snails are examined and prepared for sectioning, the larvae fall off. Attempts to adhere often fail and the larvae swim away to try again elsewhere. After several unsuccessful attempts of this kind miracidia seem to be exhausted, their swimming movements become erratic and eventually they die. Some such moribund larvae lose their ciliated epithelium, however, and undergo partial metamorphosis into ovoid sporocysts. According to Mattes³, the anterior posterior 'Klebdrüsen' are concerned with adhesion. Careful study has not so far revealed these unicellular glands, although their large nuclei, their position beneath the first and second epithelial cells of the miracidium should make them conspicuous. Early attachment is more probably brought about by suctional action of the anterior papilla which, by its introversion, presses the first epithelial cells hard against the snail's integument, mucus assisting adhesion. Once attachment is established, retraction of the papilla would create a saucer-like space between the anterior nonciliated end of the larva and the snail's integument, and this would serve for the reception of secretions of the gut and the unicellular pharyngeal glands. Not until marked cytolytic effects have been produced in the epithelium of the snail does the anterior papilla of the miracidium penetrate into this layer (Fig. 1, A1, A2).

Complete penetration of the larva into the snail takes only about 30 minutes from the time of adhesion. During this period the larva is a sac-like object which occasionally contracts and relaxes but which certainly does not rotate. At the end of the period when failure to penetrate seems likely, the larva suddenly disappears into the snail. Sections indicate that about the middle of the period the anterior papilla is only slightly extended and is approaching the sub-epithelial tissues of the snail, amidst the debris of loosened and cytolysed epithelial cells (Fig. 1, A2).

As the larva presses into the cytolytic mass, the edges of these cells are heaped externally at the rim of the opening (Fig. 1, A1). At the same time the larval epithelial cells are becoming detached, although

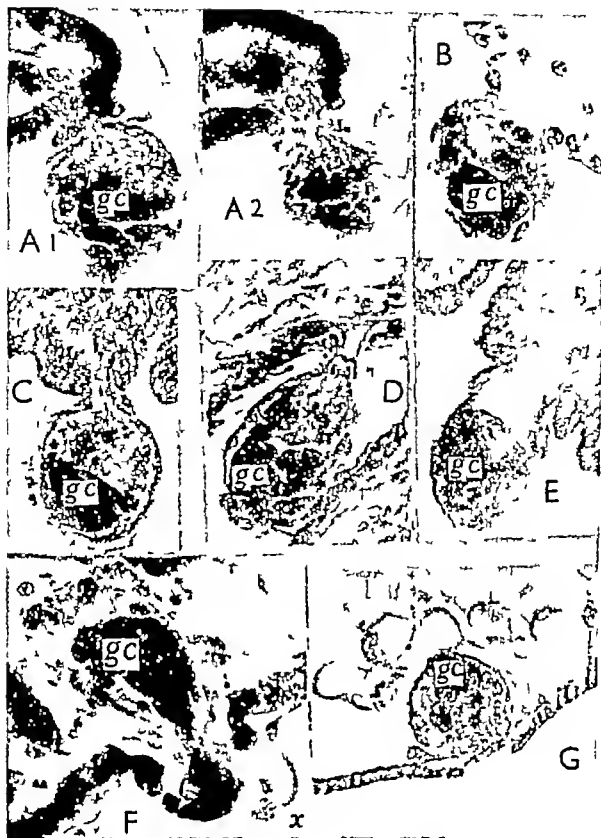


Fig. 1 A-E attached metamorphosing miracidia. F penetrating sporocyst. G entered sporocyst. A1 and A2 are adjacent sections of germinal cells. (Various magnifications. D and F oil immersion; the remainder 1 in. objective)

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The anterior ends of the first tier cells are trapped in the raised margin of the opening. Cytolysis is very evident when attachment is to the mantle, which has a shallow epithelium nuclei standing out starkly (Fig. 1 B) and the papilla is seen to be retracted in anterior action.

The papilla is now becoming attached to the sub-epithelial layer of the snail (Fig. 1, C and D) and damage to this tissue soon becomes evident. As the larva draws its anterior end further into the cytolyzing host cells it presses aside the damaged epithelium forming the rim of the opening, which is thus enlarged. The larva then contracts momentarily inside a kind of sac formed partly of cytolyzing cells and partly of its own discarded epithelium, together with some mucus (Fig. 1, E). This stage immediately precedes the swift final thrust which takes the extending larva into the body of the snail. Available sections show the thrust in several phases, the larva becoming constricted at different levels along the antero-posterior axis progressively as it squeezes through the opening. Only one stage is shown here (Fig. 1, F) and in this, the cytolyzed sub-epithelial

tissue (x) is being pressed out through the opening as the larva enters the snail. As the larva completes its entry, the damaged cells at the rim of the opening are drawn inwardly, partially sealing the opening (Fig. 1 G). The posterior end of the larva is seen as a zone of dense tissue produced by intense contraction.

The larva which enters the snail is certainly not a miracidium although it retains the eyes, the gut and other organs and also the germinal cells, it is a young sporocyst covered by what was formerly sub-epithelial tissue, carrying with it into the snail some epithelial and other debris. The miracidium may be regarded as a form which serves to implant the sporocyst in the body of the snail host by what appears to be an elaborated process of external digestion. A fuller account of this work, with more adequate discussion, will be published soon. My thanks are due to Mr. A. T. Green, for making the photographs.

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Production of Seedless Hops by Interspecific Pollination

THE difficulty in inducing hop cone formation through the application of growth-stimulating substances has been well illustrated by Seeley and Wain¹ who found that, at best, it was possible to achieve only temporary stimulation of cone growth in experiments using some 22 growth-stimulating substances, as well as pollen extracts.

In order to test the stimulation produced by foreign pollen, a small-scale experiment was conducted using the cultivated variety Late Clusters (of the species *Humulus lupulus* L.) and crossing this with the wild hop, *Humulus japonicus* Sieb. and Zucc. These two species, *H. lupulus* and *H. japonicus*, are very distinct. The former is a perennial with a chromosome number^{2,3} of 20 and the latter an annual of 17 chromosomes in the male, 16 in the female⁴.

Table 1 contains measurements, based upon 30 samples, from unpollinated and pollinated cones.

Table 1

| | Average length (mm) of bracts | Average length (mm) of bracteoles | Average length (mm) of internodes | Average No. of nodes |
|--|-------------------------------|-----------------------------------|-----------------------------------|----------------------|
| Pollinated with <i>H. japonicus</i> pollen | 12.9 | 14.7 | 1.5 | 8.4 |
| Unpollinated | 10.1 | 11.3 | 1.0 | 11.1 |

The stimulation of bracts, bracteoles and internodal length in the cone of Late Clusters produced by pollen of *H. japonicus* is very noticeable, though it is unquestionably less than that produced by pollen from the male plants of Late Clusters. Fig. 1 shows pollinated (*H. japonicus* pollen) and unpollinated cones collected at the same stage of maturity.

Early workers, including Salmon and Amos⁵, had shown the importance of pollination (by pollen of the same species) upon increasing yield. Their results indicated, as in this experiment, that pollination decreased the number of nodes formed, though they did not discuss this effect which is based upon the indeterminate growth of the cone apex. Pollination brings this apical growth to a halt. The length of time during which such growth continues without pollination varies with variety, being longer in a variety such as Late Clusters than Fuggles. These facts help to explain the difference among varieties in the influence of pollination upon yield. In some varieties the smaller size of bracts and bracteoles in unpollinated cones is offset by a continued growth of the apex, and a resulting increase in their number. Conversely, in those varieties in which apical growth ceases early, pollination is vital for the stimulation it produces upon bract and bracteole size.

As with normal pollination, the effect of interspecific pollination is to reduce greatly the critical 'burr' stage, when the cone is so susceptible to disease.

Following interspecific pollination, the ovary is stimulated at the same time as the internodes, bracts, and bracteoles. However, since fertilization does not occur, due to the difference in chromosome number between the species, no embryo, endosperm or seed develops. The matured pistil, much smaller than the normal product of pollination, remains empty.

It is not possible to draw conclusions regarding the commercial usefulness of such interspecific pollination in hop cultivation. Extensive experiments would be necessary to determine the extent to which such pollen will effectively carry by wind, the practicability of



Fig. 1 Cones pollinated with pollen from *H. japonicus* on left, unpollinated cones of late clusters on right. Scale in mm.

growing the weed hop in cultivated fields and the desirability of the cone, formed without seeds but containing abortive pistils. This does, however, illustrate a principle which may prove of some importance, namely, that stimulation may be produced in hops by pollination which cannot lead to fertilization, and consequently, seed formation. Moreover, it suggests that the triggering mechanism for stimulation of cone growth in hops must occur at the time of pollination, with fertilization providing only a secondary boost, if any boost at all.

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Vein Anastomoses in the Leaves of Long Shoots of *Ginkgo biloba*

It has recently been found that four types of vein unions occur in the leaves of *Ginkgo biloba* L. and that long shoots have a significantly higher average per cent of leaves with anastomoses than short shoots¹. In the present examination of 2,249 leaves collected from 164 long shoots from 16 trees it was found that the leaves from the median portion of the long shoots have a higher per cent of anastomoses than either the basal or apical leaves. It was also found that considerable variation existed in the percentage of leaves with anastomoses in the samples taken from various trees. An average of 33 per cent of the 2,249 leaves had one or more anastomoses, but the range in the individual 16 trees extended from a low of 7.3 per cent to a high of 71.2 per cent.

By collecting the leaves in a manner so that the position of each leaf on its shoot was known, the percentage of leaves having anastomoses could be determined for each leaf position. Because of multiple anastomoses occurring in many leaves, the total number of anastomoses at each leaf position is best expressed as an anastomosis index, which is derived by dividing the total number of anastomoses by the total number of leaves at a given leaf position. In Fig. 1 results are presented which show the relationship between anastomosis index and leaf position. The median leaf positions (10-13) show an anastomosis index more than double that of the most basal (1-5) and the most apical (19-20) leaf positions.

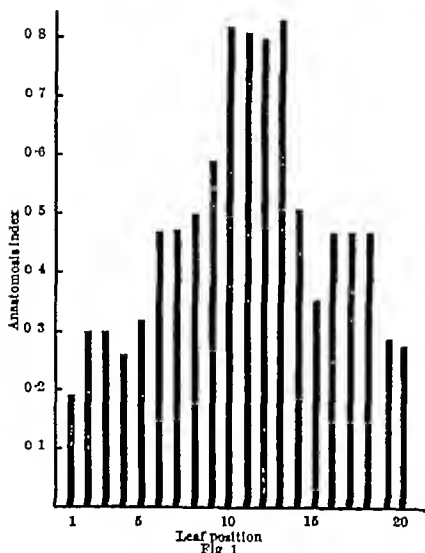


Fig. 1

The number of leaves studied at each leaf position averaged 112 and varied from 164 at leaf position 9 to 18 at leaf position 20. The first 13 leaf positions were represented by a minimum of 121 leaves each, while those from 14-20 were represented by an average of 41 leaves. The number of leaves from the apical leaf positions is lower because many of the long shoots studied had less than 15 leaves. Leaves above leaf position 20 which were few in number, were not included in this study.

While surveying the literature on *Ginkgo* some striking similarities in the pattern of auxin distribution and that of anastomosis frequency were noted. The nonunity of these distribution patterns can be elucidated by the hypothesis that the percentage of anastomoses in the leaves of long shoots of *Ginkgo biloba* is in some way correlated with the amount of auxin present in the shoot at the time of leaf differentiation. The similarity of the pattern of auxin production and anastomosis distribution in the long shoots of *Ginkgo biloba* can be seen by comparing the data results above with those of the auxin diffusion experiments of Gunkel and Thumann¹. They found that in very young long shoots "the peak of auxin production lies in the middle or toward the base of the shoot."

Poster², and Gunkel and Wetmore³ report that there is no fundamental difference in the organization of the apical meristems of long and short shoots. Gunkel and Wetmore³ report that the early stages of growth and differentiation in long and short shoots are indistinguishable. Gunkel and Thumann¹ compared the amounts of diffusible auxin in 'putative' long and short shoots during early ontogenetic development. They found that in both shoot categories the amount of auxin increased to a peak and then decreased during the early stages of bud expansion. In short shoots auxin production continues to diminish, however, in long shoots auxin production undergoes a further and much higher, increase as the shoot begins to elongate. Results collected during this work show that in leaf positions

1-5 the average anastomosis index is 0.28 whereas in leaf positions 6-18 the anastomosis index averages 0.61. A tentative explanation for this anastomosis distribution is that approximately the first five leaves of a long shoot are produced under a 'short shoot regime', a regime which is apparently exactly the same as that of a short shoot both in morphological differentiation and in auxin production. The more median leaves of long shoots, however, are differentiated under a 'long shoot regime' during which auxin production is higher and the shoot is elongating. The higher anastomosis index of these leaves is in harmony with the data on auxin diffusibility in long shoots given by Gunkel and Thumann¹ and again tends to support a correlation between anastomosis frequency and auxin.

At present no experimental evidence is available which tests a hypothesis linking auxin concentration and anastomosis frequency in *Ginkgo*, however, experiments which may shed some light on this relationship are now under way.

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ENTOMOLOGY

Pentachlorocyclohexene as a possible Intermediato Metabolite of Benzene Hexachloride in Houseflies

STERNBERG and Kearns¹ have reported that both γ benzene hexachloride (γ BHC) resistant and susceptible houseflies can dehydrochlorinate γ BHC to pentachlorocyclohexene (PCCH). Their evidence relied on the formation of 1-chloro 2,4-dinitrobenzene when the method of Secheater and Hornston² for the determination of γ BHC was applied to flies treated with the insecticide. This method involved the reduction with zinc and acetic acid of unchanged γ BHC and PCCH to benzene and chlorobenzene followed by nitration to form *m*-dinitrobenzene and 1-chloro 2,4-dinitrobenzene respectively. Bradbury and Standen³, working with a different strain of resistant and susceptible houseflies used an isotopic dilution technique to determine any γ PCCH present after γ BHC treatment but failed to find the large amounts reported by Sternberg and Kearns.

Work has been carried out at this laboratory on a strain of dielidrin resistant (*R* strain) and susceptible *Musca domestica* obtained originally as pupae through the kindness of Dr. J. R. Busvine. The dielidrin resistance of the *R* strain has been built up to a high level by exposure of the larvae to dielidrin alone. The same insects have however become highly resistant to γ BHC. Studies of the resistance mechanism have been made using the α , γ and δ isomers labelled with carbon 14. Preliminary experiments were made using the technique of Sternberg and Kearns. Flies were treated with 2 μ g of the radioactive BHC isomers in acetone solution 2 μ l. of the solution being applied topically to the dorsal thorax of each fly. After 3 hr at 25°C the flies were ground under acetic acid and subjected to the Secheater-Hornston reduction and nitration procedure. The 1-chloro 2,4-dinitrobenzene was separated from the *m*-dinitrobenzene by chromatography on paper impregnated with castor oil⁴ and detected radioactively.

Table 1 PRODUCTION OF COLICINES BY COLICINOGENIC STRAINS IN SIMMONS'S CITRATE AGAR

| Type of colicine produced | No. of colicinogenic strains | No. of strains producing colicine in Simmons's citrate agar |
|---------------------------|------------------------------|---|
| I | 30 | 0 |
| E | 12 | 5 |
| E+I | 11 | 5 |
| V | 4 | 4 |
| K | 4 | 4 |
| A | 3 | 3 |
| B | 1 | 1 |
| D | 1 | 1 |
| A | 1 | 1 |
| F | 1 | 1 |
| G | 1 | 0 |
| C | 1 | 1 |
| H | 1 | 1 |
| S ₂ +I | 1 | 1 |
| S ₆ | 1 | 0 |
| Total | 73 | 28 |

colicines B, D, A, F, G, C, H, S₂+I and S₆, finally, a very strong, non-typed colicine, produced by the strain *Mutafior* of Prof Nissle, largely produced in Germany by the A G Hageda for the treatment of 'Dysbakterie', is defined as colicine X

Strains producing colicine I, a part of strains producing colicine E, or colicines E+I simultaneously, and type cultures producing colicines G, H, and S₆ did not produce any inhibition zones on the strain sensitive to the indicator (Table 1)

Strains producing colicines V and K, some of the strains producing colicines E or E+I, and type cultures producing colicines B, A, C and S₂+I, gave smaller inhibition zones of the indicator in Simmons's citrate than in nutrient agar

Finally, the type cultures producing colicines D and F, and the cultures producing colicine X gave very large inhibition zones in the synthetic medium

This observation can be of practical value in the typing of the colicinogenic strains. This typing was found to be important in epidemiological studies of infantile diarrhoea due to *Escherichia coli*¹. A large number of colicinogenic *E. coli* isolated from epidemics produce colicine I² or colicine I together with another colicine (unpublished results)

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Lysogeny in the Genus *Proteus*

A LYSOGENIC strain of *Proteus* species was detected by Fejgin in 1924¹ but no systematic attempt has ever been made to ascertain the prevalence of such strains. We have investigated the incidence of lysogeny using 23 *Proteus* strains for which we have previously isolated lytic phages from sewage², media used have been previously described³.

The Fisk technique⁴ using overnight broth cultures gave uniformly negative results, and other methods of induction were then used. The 3 methods used, details of which will be published elsewhere were (1) individual cultures of the 23 strains were grown in broth for 10 days at 37°C, (2) ultra-violet irradiation according to the method of Gots and Hunt⁵, (3) all possible combinations of pairs of the 23 strains were grown together in broth for 10 days according to the Scholtens' method⁶.

Cultures thus obtained were centrifuged to clarity, kept at 56°C for 45 min to inactivate remaining

bacteria, and then tested for phage activity by a modification of the agar layer technique². Using 49 different *Proteus* strains as indicators, 12 of the 23 strains were found to be lysogenic. The three induction methods apparently possess a degree of species specificity, in that not all lysogenic strains were induced by all three methods, and the strains induced by method (3) were all *mirabilis* species, while 4 of 5 induced by method (2) were *vulgaris* species. In only one instance did a phage derived from a *vulgaris* act on a *mirabilis* species. The host range of most temperate phages isolated was restricted to one strain, in contradistinction to the sewage phages isolated².

Some phage suspensions appeared to contain mixtures of phages. This is being investigated. It is possible that if a greater variety of methods of induction and a wider range of indicator strains had been used more lysogenic *Proteus* strains would have been detected.

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Influence of Carotenoids on the Infra-Red Spectrum of Bacteriochlorophyll in *Chromatium*

ALTHOUGH it is well known that the infra red maxima in the absorption spectrum of *Chromatium* exhibit considerable variability, the basis of this phenomenon has remained obscure. Wassink *et al.*¹ described in detail the variations which they observed in the infra-red spectrum of both the organisms and colloidal extracts. After considering several explanations, these authors took the view that all these infra-red maxima represent one pigment, namely, bacteriochlorophyll bound to different proteins. More recently, Duysens² also has claimed that each of the infra-red peaks represents bacteriochlorophyll, however, he has not tried to explain the existence of more than one peak. Work in this laboratory has led to a hypothesis of the ultra-structure of the bacterial chromatophore³. It was postulated from this model that the transfer of energy from carotenoids to bacteriochlorophyll has spatial requirements which are met only when the chromatophore is in a suitable environment and further that the complexity of the infra-red spectrum is related to the interaction between these two pigment systems. At this time both postulates have received experimental support. Variation in the concentration of inert solute in the suspension medium has pronounced effects upon the efficiency with which quanta absorbed by the carotenoids are used for photophosphorylation by isolated chromatophores⁴. The loss of the ability to transfer energy is also correlated with specific changes which appear in the infra-red spectrum. These changes which appear in the infra-red spectrum of isolated chromatophores are comparable to the differences which are observed in organisms with differing carotenoid content.

In Fig. 1 the changes in light absorption which accompany the 'uncoupling' between the carotenoids

and bacteriochlorophyll in the chromatophore are compared with the changes which occur when carotenoid deficiency is induced by diphenylamine treatment⁶. The infra red spectrum of the isolated chromatophores in which the two pigments are 'coupled' is identical with the spectrum obtained *in vivo*, similarly the activity of the carotenoids for photophosphorylation in such preparations is comparable to the activity *in vivo* for carbon dioxide fixation⁴. Both 'uncoupling' and carotenoid deficiency are associated with an increase in absorption in the 800 m μ maximum and a disproportionate decrease of the maxima at 850 and 890 m μ , respectively. In addition the latter two peaks tend to shift to lower wave lengths. A similar family of curves (Fig 2) results with the spectra obtained *in vivo* from normal cultures which differ in carotenoid content. These changes are remarkably similar to the alterations produced by the interaction between certain dyes for example, chrysophenine G and sky blue FF⁶. Although these observations are consistent with the view that bacteriochlorophyll contributes to the absorption in the infra red, they indicate that the fine structure of the infra red spectrum is determined by more subtle effects which are related to an interaction between bacteriochlorophyll and the carotenoids. An analysis and theoretical evaluation of this phenomenon will be presented in detail elsewhere.

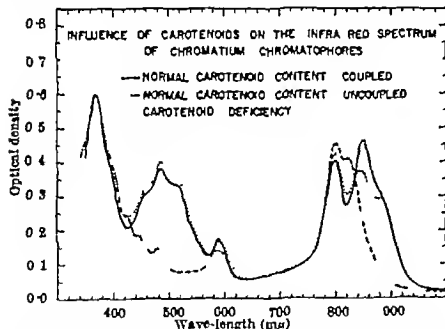


Fig 1. The chromatophores containing the normal amount of carotenoids were prepared from a 48-hr old culture. The coupled chromatophores were isolated and suspended in 0.5 M sucrose buffered to pH 7.8 in 0.1 M Tris. The uncoupled chromatophores were isolated and suspended in 0.5 M glucose at the same pH (ref. 5). The carotenoid deficient chromatophores were prepared in the sucrose medium from cells grown in the presence of diphenylamine (ref. 6). The spectra are compared using the Soret peak at 370 m μ as a reference.

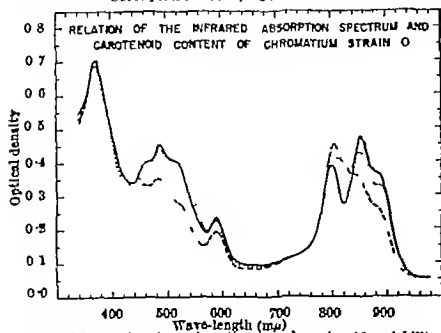


Fig 2. The spectra above show the normal carotenoid variability found in cultures of differing age. Opt. glass was used to minimize scattering produced by the cells.

This work was carried out at the Brookhaven National Laboratory under the auspices of the U.S. Atomic Energy Commission.

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Release of Compounds containing Diaminopimelic Acid from *Vibrio metchnikovii* treated with Antibody and Complement

THERE is now much evidence supporting the suggestion that it is the peptido-amino sugar complex of the walls of Gram-negative bacteria which is responsible for the rigidity of the surface 'envelope'. Loss of these components from the cell either by direct enzymic digestion as with lysozyme or by the metabolic disturbances brought about by penicillin action or diaminopimelic acid deprivation, results in a weakening of the wall and a transformation to spherical cells¹. We have been interested in the possible similarity between the events responsible for immune bacteriolysis and those leading to the formation of spherical cells during lysozyme treatment and penicillin action.

When fresh guinea pig complement was added to cell suspensions of *Vibrio cholerae* and *V. metchnikovii* sensitized with their specific antisera, the cells became distorted and were eventually transformed into spherical cells of fairly uniform appearance. The conversion to spherical cells was virtually quantitative within 1-2 hr at 37° C after the addition of the complement. To determine whether any release of compounds containing diaminopimelic acid accompanied these morphological changes, thick suspensions of cells of *V. metchnikovii* were incubated with the appropriate amount of antibody and complement which effected the transformation to spherical cells on incubation for 2 hr at 37°, and the supernatant fluids were examined for the presence of diaminopimelic acid. Control suspensions with antibody alone, complement alone and neither antibody nor complement were incubated under identical conditions. A small proportion of spherical transformations occurred in the control series. Cells were removed by centrifugation and the supernatant fluids were de-proteinized by the addition of trichloroacetic acid to a final concentration of 5 per cent w/v. The material soluble in trichloroacetic acid was extracted with ether to remove the acid, dialysed and then hydrolysed with N hydrochloric acid for 16 hr at 105° C and the diaminopimelic acid contents were estimated by the colorimetric method of Wark² after separation on paper chromatograms using the solvent system of Rhuland *et al.* The amount of diaminopimelic acid released in the form of a non-dialyzable compound soluble in trichloroacetic acid during treatment with the antibody-complement system is compared with the control series in Table 1. The cell wall of *V. metchnikovii* contained 0.5 per cent diaminopimelic acid and if it is assumed that the wall accounts

Table 1 EFFECT OF ANTIBODY AND COMPLEMENT ON THE RELEASE OF SOLUBLE COMPOUNDS CONTAINING DIAMINOPIMELIC ACID FROM *Vibrio metchnikovi*

| Treatment | Diaminopimelic acid released from 200 mgm dry weight cells (μ gm) |
|--|--|
| Cells incubated with antibody and complement | 104 |
| Cells incubated with antibody alone | 30 |
| Cells incubated with complement alone | 36 |
| Cells alone | 34 |

for 20 per cent of the weight of the cell, the amount of diaminopimelic acid released on treatment with antibody and complement would represent half the cell wall diaminopimelic acid (if the wall accounted for a smaller fraction of the whole cell then of course the proportion of the wall diaminopimelic acid released will be greater)

These results make it clear that the morphological changes occurring during immune bacteriolysis with antibody and complement are accompanied by a release of soluble, non dialysable components containing diaminopimelic acid. The cell constituents released are almost certainly derived from the bacterial cell wall. Thus, it is reasonable to conclude that the spherical transformation occurring during immune bacteriolysis (Pfeiffer's phenomenon) is explicable in terms of an enzymic (?) release of the cell wall peptide which in the normal cell provides the wall with a rigid structural framework. Amano *et al*⁴ have suggested the possibility of enzymic disintegration of the cell wall playing some part in immune bacteriolysis and the results reported here contribute experimental evidence in general accord with this view. From light microscopic studies, Amano *et al*⁴ infer the complete disintegration of the wall by complement and antibody. However, our experience with isolated walls of *V. metchnikovi* incubated with complement and antibody indicated no appreciable lysis. Whether the complement acts enzymically or activates an enzymic system normally present in the cell cannot be said at the moment.

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Group- and Type-specific Polysaccharides of Group D Streptococci

MCCARTY¹ showed that in group A streptococci the serologically group-specific polysaccharide (Lancefield's "C substance") is a major component of the bacterial cell wall and contains glucosamine and rhamnose. The type-specific proteins ("M substance") are located at the surface of the cell wall from which they may be detached by proteolytic digestion.^{2,3}

Recent work here has shown that in group D streptococci, which include the predominant intestinal streptococci of mammals and birds, a different situation exists. The results of this work are summarized in Table 1 from which it will be seen that

Table 1 CHARACTERISTICS OF TWO POLYSACCHARIDES FROM GROUP D STREPTOCOCCI

| Probable location in Streptococcus | Serological specificity | Component sugars |
|------------------------------------|-------------------------|------------------------|
| Cell wall | Cell specific | Hexosamine Rhamnose |
| Cell counts | Group specific | Glucose |

the cell-wall polysaccharides of group D are serologically type-specific instead of group-specific as in group A. Acid hydrolysates of these cell-wall polysaccharides from five different serological types of group D streptococci contained hexosamine (probably glucosamine), rhamnose and glucose.

The group-specific polysaccharide in group D appears to be situated deep within the streptococcus from which it may be extracted by shaking with glass beads in a Mickle disintegrator. A preparation made in this way from Lancefield's group D strain 'C3' (*Str. durans*) was partially purified by high speed centrifugation to remove most of the cell-wall material followed by digestion with proteinases and nucleases. The final product after dialysis contained approximately 20 per cent (w/v) total carbohydrate and 0.6 per cent hexosamine. In precipitation tests it reacted strongly with group reactive antisera made against group D strains of heterologous type but reacted only weakly with homologous type specific antiserum. From the same streptococcus a cell wall preparation, serologically type specific, contained approximately 10 per cent total carbohydrate and 8.0 per cent hexosamine. Allowing for contamination of the group preparation with residual cell wall material estimated at between 5 and 10 per cent of the total serologically reactive carbohydrate, it may be inferred that the group specific polysaccharide probably contained no hexosamine. Indeed, glucose was the only sugar found when acid hydrolysates of the group polysaccharide were submitted to paper chromatography. By contrast, hexosamine accounted for approximately 80 per cent of the cell-wall type specific polysaccharide isolated from the same strain of streptococci.

Clearly, these results need confirmation with more highly purified material, but the present evidence suggests that the type specific antigens in group D are the structural and chemical counterparts of the group-specific polysaccharide in group A streptococci. Although the evidence is not conclusive it seems likely that in group D streptococci the group specific polysaccharide is situated deep within the bacterial cell. The difference in location and chemical constitution of the group specific antigens in group D and group A may account for the greater difficulty generally experienced in making 'grouping' antiserum with group D streptococci and would help to explain Shattock's⁴ observation that, for inducing the formation of group specific antibodies in rabbits, a vaccine consisting of disrupted group D streptococci is more effective than one consisting of intact micro-organisms.

A more detailed account of this work will appear elsewhere. My thanks are due to Dr R. C. Lancefield for cultures of her 4 'type' strains of group D streptococci and corresponding antisera. This work was supported in part by a grant from the Helen Hay Whitney Foundation, New York.

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TAXATION OF LEARNED AND PROFESSIONAL SOCIETIES IN BRITAIN

DURING the past two decades, the professional and learned societies have encountered increasing financial difficulties. The major institutions no longer possess the intimate and social character that once was theirs, and this may well be one factor that has encouraged the proliferation of specialist societies with only a limited range of interests. Nevertheless, even those with a membership of several thousands have encountered difficulties in maintaining the publication of professional periodicals, and this is a matter to which the Nuffield Foundation has given some attention since 1955, in co-operation with the Royal Society for scientific periodicals, and the British Academy for periodicals in the humanities. Moreover, there appears to be a marked reluctance on the part of younger scientists and technologists to join the more general societies; the tendency is to support institutions the membership of which constitutes a professional qualification.

It is probably too early to assess as yet the effect of the concession made in the Finance Act last year which allowed fees and subscriptions to professional bodies, learned societies etc. not of a mainly local character to be claimed as expenses against income tax. When this clause was considered in the House of Commons on June 17, 1958, the Financial Secretary to the Treasury explained that while there was no logical reason to exclude the local societies, to include them would place an administrative burden on the Inland Revenue out of all proportion to the relief to the taxpayer. It was estimated that the national societies alone probably numbered about 3,000, and since the subscriptions to the local societies were usually small, the cost to the general body of taxpayers was not consonant with any relief to the individual.

During the past year, the Inland Revenue has examined the activities of the national societies in the light of the new clause, and most of the societies have already been able to notify their members that they are in a position to claim relief. If it could be shown that the membership of these societies has appreciably benefited from this concession, it might be reasonable to re-open the question of the local societies and, with the position of the national societies already clarified the Inland Revenue should not find it an unreasonable task to deal with the local learned societies.

To the professional and learned societies, however the effect of this concession is unlikely to be great; its main benefit is to the individual member. The concession is important, so far as the societies are concerned in helping to offset a number of adverse factors against which most of them have been struggling: stationary or declining membership (in spite of the increasing numbers of scientists and technologists); mounting costs of printing and pub-

lication, and the steady rise in postal charges. Some of these factors could be offset by a measure of rationalization, and the pilot survey of the publishing and distribution practices of the learned periodicals carried out by Mr Robert Lusty on behalf of the Nuffield Foundation may be regarded as a step in this direction.

A much more serious matter for the learned societies and professional institutions is, however, the complexity of rulings about the payments they make to local authorities in the form of rates. During the past three years or more, the Parliamentary and Scientific Committee has made repeated representations to the Government on this matter, submitting, for example, a comprehensive memorandum to the Minister of Housing and Local Government directing attention to anomalies in the rating of both scientific societies and research associations. During the second reading debate of the Local Government Bill in the House of Commons on December 9, 1957, the Minister announced that he intended to set up a committee to give special consideration to the rating of charities and similar organizations, and the chairman of the Parliamentary and Scientific Committee was eventually informed that the terms of reference of this committee would be wide enough to permit consideration of the special position of scientific institutions.

This committee was, in fact, appointed on January 22, 1958, under the chairmanship of Sir Fred Pritchard, "To review the present treatment for rating of hereditaments in England and Wales occupied for purposes of a charitable nature or for other similar purposes (other than hereditaments to which Section 7 of the Rating and Valuation (Miscellaneous Provisions) Act, 1955, applies); to consider in particular the provisions of Section 8 of the Act of 1955 and of the Scientific Societies Act, 1943, and to advise on the proper treatment for rating of the hereditaments within these terms of reference." The Parliamentary and Scientific Committee submitted a memorandum on the general lines of that previously submitted to the Minister of Housing and Local Government and was later invited to submit oral evidence. Only the Royal Society also gave oral evidence.

The report of this Committee*, which was presented to Parliament in August 1959 is of considerable general scientific interest, quite apart from the specific recommendations and their effect on scientific or professional societies. It should be remembered that rates are the main source of revenue within the direct control of local authorities, and it is the occupier rather than the owner of a hereditament

* Report of the Committee on the Rating of Charities and Kindred Bodies, Pp. iv+80 (Cmd. 531) (London: H.M. Stationery Office, 1959) 6d net.

who is ratable in respect of it. The earliest general enactment still extant which exempts a specific class of hereditament from rates is Section 1 of the Scientific Societies Act, 1843, which covers societies instituted for the purposes of science, literature or the fine arts. This section exempts such societies from rates if these societies are supported wholly or in part by annual voluntary subscriptions and do not make any dividend or bonus to their members. It would seem that in granting such exemption, Parliament intended to do no more than put the buildings of such societies on a par with buildings dedicated to public purposes.

The commonest ground for loss or refusal of exemption has been failure to comply with the condition about support by annual voluntary contributions, and in reviewing the working of the Act, the Committee gives most attention to this condition, which has led to a good deal of litigation and is still not entirely clear. It appears that income from invested voluntary contributions is not itself an annual voluntary contribution and, in consequence, a society which depends almost entirely upon voluntary contributions but accumulates trust funds for prizes, exhibitions or scholarships could ultimately be disqualified because the investment income from contributions, although undoubtedly voluntary, was too large in relation to current activities. Moreover, the Committee could often see no difference between societies within and those without the exemption, and several societies now exempt appear to be fundamentally different from the kind of institution which members of Parliament who supported the Bill in 1843 appear to have had in mind.

The Committee was agreed that the provision could not be left unchanged, and because wherever the line were drawn there would be anomalies at the margin and any re-drafting of the conditions precedent to exemption would give rise to fresh litigation, the Committee invited the Royal Society and the Parliamentary and Scientific Committee to give oral evidence. The Committee was not, however, satisfied that any of the societies had a better claim to exemption than other charities. Most of them would be entitled under the Committee's other recommendations to 50 per cent mandatory relief as charities and, accordingly, the Committee recommended that the Scientific Societies Act of 1843 should be repealed.

Nevertheless, the Committee, like the Sorn Committee which reported in September 1954 on the Scottish rating system, recognizes that to withdraw abruptly the exemption under the Scientific Societies Act, 1843, might cause undue disturbance to the finances of the bodies concerned. It suggests, therefore, that in the first full financial year after the repeal of the provision, none of the societies which was a beneficiary under it at the date of repeal should be liable for rates in respect of hereditaments which were exempt at that date. In the second year, the rates which, apart from the transitional arrangements, would have been payable by the societies concerned should be abated by four-fifths, and in the third year by three-fifths, in the fourth year by

two-fifths, and in the fifth year by one-fifth. A scientific society would thus not be liable for the full 50 per cent until the sixth and subsequent years, while if it was not a charity it would pay 20 per cent in the second and 40 per cent in the third, rising to full rates in the sixth and subsequent years.

The Committee shares the general view of its witnesses that Section 8 of the Rating and Valuation (Miscellaneous Provisions) Act, 1955, which governs the rates payable by charitable and other organizations, is unacceptable as a permanent provision, and it sees no justification for giving permanent rate relief to all organizations in so wide a field. It considers that the time has come to introduce a measure of uniformity and certainty into the rating relief enjoyed by bodies within its terms of reference, and that a satisfactory scheme should be simple and economical to administer and should not add materially to the rates borne by other classes of rate-payer. Its essential basis should be mandatory relief for the great majority of the classes of organization which in the past have enjoyed some measure of relief.

It recommends accordingly that charities should have mandatory relief and that, although the decision as to the amount must be to a considerable degree arbitrary, relief of 50 per cent strikes a reasonable balance. It does not consider that there is any need to re-define the term 'charity' for rating purposes only, and in the White Paper outlining its policy on Charitable Trusts in July 1955, the Government rejected proposals for a new definition for general purposes. The Committee recommends that organizations on the fringe of the field of charity should be eligible for relief at the discretion of the local authorities, but it does not recommend that charities in general should be excluded from relief on the ground that the body is national or that it is in receipt of Exchequer grant or fees or because its voluntary income is small. The position of the universities was specially considered, but the Committee does not consider that, on balance, the exclusion of all university institutions would be justified by the evidence or arguments presented.

Representations were made to the Committee that a new statutory relief of 75 per cent should be allowed to industrial research associations, and on this also oral evidence has been heard from the Parliamentary and Scientific Committee. The Pritchard Committee, however, submits reasonably enough that research associations are much more akin to the research establishments of individual firms than to charities, and that the relief considered appropriate for research establishments conducted by individual firms within the curtilage of their industrial hereditaments should be extended to the premises of industrial research associations. This view is in accordance with that expressed in evidence by the Department of Scientific and Industrial Research.

No pronouncement has yet been made by the Government regarding its acceptance or otherwise of the recommendations of the Pritchard Committee, this matter of rating relief is only one way in which Section 8 of the Rating and Valuation (Miscellaneous

Provisions) Act, 1955, has touched the scientific and other learned societies very closely. Under the Local Government Act, 1948, valuation officers of the Board of Inland Revenue became responsible for valuation rating on February 1, 1950, with the object of securing uniform standards of valuation, and this, of course, precluded the continuation of the practice of sympathetically undervaluing hereditaments occupied by charities and kindred bodies. Section 8 of the Rating and Valuation (Miscellaneous Provisions) Bill introduced in March 1955 was intended to avoid the substantial increases in liabilities for rates which such bodies would otherwise have incurred, and it was quite clear in the debates on the Bill, which received Royal Assent on July 27, 1955 that the Government fully appreciated the difficulties of the scientific and learned societies.

The Pritchard Committee in its report emphasizes that this Section of the Act provides the first statutory relief from rates for charities as such, and the first endorsement by Parliament of the relief previously given extra statutorily by local government in various ways. Further, this element of mandatory relief was introduced by the Government not, initially, as a matter of Government policy, but in deference to the wishes of the House of Commons after a provision relying entirely upon local discretion had been criticized from all quarters. Moreover, this particular enactment was designed as a holding provision and never intended as a permanent arrangement.

These observations are important, as they indicate clearly the line which should be taken by scientific societies and professional organizations which may be unfairly affected in the new situation. It follows, moreover, that legislation to provide some reasonable permanent arrangement is not merely probable but almost inevitable, and that it is in the debates on such legislation that the needs of the scientific and learned societies and professional organizations should be clearly and effectively presented to Parliament.

When in 1950 the valuation officers of the Board of Inland Revenue assumed responsibility for valuation for rating, they did not disturb the exemptions in the old lists unless they were asked to do so by the rating authorities, but in preparing the new valuation lists which came into force on April 1, 1950 they applied strictly the provisions of the Act of 1843 as recently interpreted by the courts. In consequence some societies which had been exempt became liable for rates on assessments based on full current rental values, and only some of those which challenged this liability in the courts succeeded. Further, the Board of Inland Revenue has suspended the income tax rebate which the learned societies enjoyed on seven year covenants entered into by their members, and for some of them has finally withdrawn the relief.

This is the second aspect of the situation which deeply concerns the professional associations and learned societies and other bodies, and may affect some of them much more seriously than the concession made regarding subscriptions to such bodies in Clause 14 of the Finance Bill, 1958. Indeed,

although the situation is complex and is still being argued between various bodies and the Inland Revenue, sometimes in the Court of Appeal, it would appear that those bodies which have lost the right to tax rebates on subscription income guaranteed from covenants are likely also to lose rating relief and the advantage of their members being able to claim subscriptions as expenses against income tax. Probably it is not too much to say that some of the societies have only been able to meet post-war costs through the rebates in covenantal subscriptions and relief from rates which they have hitherto enjoyed.

The Pritchard Committee argues lucidly and cogently for a mandatory and uniform system of rating relief. It does not suggest that all anomalies will be removed or that there should be no discretionary relief. It is difficult to refute the argument of an eminently sensible report but before adopting the legislation to which the report points, Parliament might reasonably re-examine the fundamental question what is a charity for tax purposes and especially the full and wide implications of what could not unfairly be described as an assault on learned societies launched by the Board of Inland Revenue. Parliament, at least, should be concerned not so much with the benefits and advantages, to particular institutions and their members, of taxation or rating relief, but with the extent to which the public interest is served by such bodies. A recent survey of leisure and learning in Bolton and Rochdale pointed to the value of such societies in the world of to-day; quite apart from their place in the dissemination of knowledge and the maintenance of professional standards, and to their need of assistance in the maintenance and equipment of premises. The place of the scientific and learned society in the world of to-day could be appropriately re-examined in the light of all the implications of the situation on which the Pritchard Committee has now reported.

KEW, PAST AND PRESENT

The Royal Botanic Gardens, Kew
By W. B. Turrill. Pp. 256 + 16 plates. (London: Herbert Jenkins, Ltd., 1959.) 25s. net.

"KEW" to botanists, horticulturists and admirers of plants the world over is the Royal Botanic Gardens Kew, Richmond, Surrey, England. Like many other famous places or institutions the exact day of its founding is uncertain. This summer, however, the Royal Botanic Gardens celebrated a birthday of approximately two hundred historic, profitable, eventful and beautiful years. At this occasion grateful botanists paid tribute by manuscript letter or personal visit. Few have honoured Kew as well though, as William Bertram Turrill does in this book. It is a devoted tribute to the Gardens the author knew and served for forty nine years until his retirement in 1957.

"The Royal Botanic Gardens, Kew" is both a historical account of the development of the Gardens and laboratories and a detailed description of their current contents. The book is readable, but the historical portion and that of the staff are written so

that one longs for greater emphasis on the personality and procedures of the men who made Kew and contribute to its reputation to-day. The Royal Botanic Gardens have served as a training ground for many scientists, explorers and gardeners, but Dr Turrill is almost reluctant in admitting the contributions of these men. Procedures, ideas and even the architecture developed at Kew were taken by students to distant lands, and one sees the influence of Kew in some aspect of every major herbarium and botanic garden of the world. A single chapter of a scant fourteen pages describes the current scientific research of nearly eighty-five people. Three pages are devoted to "Plant Introductions via Kew", and nearly half of this concerns the story of quinine. One wishes Dr Turrill had elaborated more the credit which is due to the activities and leadership of Kew, and in basic research and practical horticulture.

The remaining chapters, particularly those on "Economic Botany and the Kew Museums", "The Greenhouses" and Kew at various seasons, charmingly describe a tour of the exhibits, living and preserved, in infinite detail. The book will serve as a guide, supplying, where appropriate, the personal exposition of a tour leader on how trees grow or manufacture food, or how plant products are used, or where particular plants can be found. One familiar with museum and garden exhibition techniques visualizes in Turrill's account both the display and the information on the labels. At the same time, the casual reader may be unaware that chapters of a basic text-book of botany have been paraphrased to present briefly and clearly the reasons for the exhibit.

A chapter on "Wild Life at Kew" exemplifies the detail of the book in relating much information, including the introduction of the American grey squirrel and its destruction, the amount of myxomatosis in the rabbits of Kew during the year 1955, the types of weeds in the lawn or the record-sized fish caught in a Kew pond and its present location. Throughout this and other chapters are the intimate stories one gets in a personally conducted, leisurely tour by a guide who knows and loves the Royal Botanic Gardens, Kew.

Sixteen excellent plates illustrate the men and women responsible for Kew's past, the present buildings, and scenes from the Gardens. Appendixes give details on the climate, the rules and regulations, the physical plant, the composition of the staff and the chronology of the curators and keepers of the Herbarium, Library and museums. A bibliography of sixty-six titles relating to Kew, an index and a grid map, referred to frequently in the text, complete the book.

As one enjoys a garden at many hours of many seasons, so I recommend to past, present and future friends of Kew a leisurely and frequent reading of this book.

RICHARD A. HOWARD

JET PROPULSION

Jets and Rockets

By A. Barker, T. R. F. Nonweiler and R. Smelt. Pp. xiv + 268 (London: Chapman and Hall, Ltd., 1959) 35s. net.

THE history of this book prior to publication was unusually rich, and Mr Nonweiler recites it with relish in his candid preface. The book was begun by Mr Smelt in 1945, and then passed to Mr Nonweiler after the former 'went West to the States',

finally Mr Barker brought it up to date and completed it. Although a few authentic touches of antiquity survive, most of the book has been satisfactorily modernized, and the reader need have only occasional qualms on this score.

The book is intended as an introductory text-book on all forms of jet propulsion, rocket, ramjet, turbojet, pulse-jet and various hybrids, and on the whole, it achieves this purpose well. The authors describe clearly the main features of each power plant, and preserve a fair balance; they do not delve very deeply into the specialized problems of each engine, but this cannot be expected in a 250 page book so wide in its scope. The chemistry of rocket combustion and the thermodynamics of the various engines—the theory underlying the calculation of thrust coefficient and fuel consumption—are presented in adequate detail, and the methods of calculating drag and the design of air intakes are also thoroughly discussed. One of the best features of the book is its emphasis on the close links between the internal thermodynamics of an engine and its external aerodynamics. This emphasis is particularly valuable because many text-books on propulsion tend to ignore the external aerodynamics, although minimizing drag can be just as important as maximizing thrust, especially at supersonic speeds.

Unfortunately, the book is marred by lack of attention to detail. Several of the formulae are in error (e.g., equations 5.13 and 5.15), some of the graphs lack units, the spelling is erratic, misprints abound and there are many stylistic lapses. Chapter 15 is in places sadly out of date—it gives the impression that the V2 was the ultimate in rocket missiles and that space vehicles are virtually impossible. Indeed, throughout the book, German war-time engines, now museum-pieces, are too often quoted as examples, thus giving the false impression that the accompanying text is equally obsolete. On one point of detail the book is excellent: there are more than 120 diagrams and photographs, most of them pertinent, clear and informative.

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NUCLEAR FUEL TREATMENT

Chemical Processing of Nuclear Fuels

By Dr F. S. Martin and Dr G. L. Miles. Pp. x + 242 (London: Butterworths Scientific Publications, New York: Academic Press, Inc., 1958) 40s., 7.50 dollars.

ALTHOUGH this book is intended mainly as an introduction to the problems of chemical processing of nuclear fuel after irradiation in a reactor, its scope extends much further. In Part I, which deals with "Nuclear Considerations", the three main systems uranium-235, uranium-238-plutonium and thorium-uranium-233 are considered separately and the reactions occurring under thermal neutron irradiation shown diagrammatically.

The several highly developed solvent-extraction processes employed in nuclear processing are described and decontamination factors listed. The requirements of a process for purifying the plutonium product of primary separation are also enumerated and the value quoted for the overall recovery of plutonium (99.4 per cent) in one process shows how highly developed this particular technology has become.

In the middle chapters the authors survey other processes which have been considered (and in some cases developed) for the separation of heavy nuclides from fission products. The range covered is sufficient to indicate the amazing volume of research which has been carried out on both sides of the Atlantic in this field—ion-exchange separations, metal distillations, halide volatilizations, extractions by molten metals, purification by slagging processes, extraction by fused chlorides as well as the more conventional (and historically important) processes of separation by precipitation.

There is also a section in the book dealing with the disposal of effluents and fission product recovery, a field which has received much attention from authors, both knowledgeable and otherwise, in recent years. It is sufficient to say that the treatment here is brief and chemically factual and scores on both these counts.

A criticism which may be advanced, perhaps, is that the reader is not given very clearly to understand which are the most important separation processes described. The dominant position now held by solvent extraction processes and the resultant commercial difficulties in the way of any competing technology are not brought out very fully. But such an appreciation is not necessarily a function of this book; it is abundantly clear that it represents a valuable and important contribution to chemical literature. It should find its way not only to those science and engineering graduates with some acquaintance of nuclear reactor development but also to that much wider reading public of chemists and chemical engineers who would like to read and have by them an authoritative and interesting work on the applied chemistry of nuclear power. J. E. LITTLEWOOD

FOOD ANALYSIS

The Chemical Analysis of Foods and Food Products
By Dr Morris B Jacobs. Third edition. Pp xxiv+970. (Princeton, N.J. D Van Nostrand Company, Inc. London. D Van Nostrand Company, Ltd., 1958.) 103s. 6d.

THE 970 pages of this book include more material than the title indicates. The text includes information on the make-up of several types of food. For example, the chapter on sugar foods and carbohydrates begins with a useful summary of the types of carbohydrates found in foods; the chapter on meat gives definitions of meat products and tables of typical compositions; the chapter on oils and fats contains in tabular form information on 24 fatty acids; the chapter on quality measurement includes a general introduction on flavour acceptance; while the chapter on milk comprises more than a hundred pages and includes detailed information on composition, on cheese and other products, and on adulterants.

Essentially, however, the work is a practical book for use at the bench. The book begins by describing general chemical and physical methods that are used in the analyses of food products. Directions are given for analysing constituents of all common and some less common foods. The book also includes chapters on undesirable materials in food. For example, one chapter deals with filth, and includes working directions for estimating the amount of rodent excreta, maggots, rancidity, and decomposition

in fish and other foods. There are also chapters on pesticide residues, radiochemical determinations, food poisoning and preservatives. The detection of horse meat in presence of other animal tissues is discussed. Chapters are included on artificial sweetening agents and on colouring matters. Instructions are even given for such details as how to count the pits in preserved cherries from which the pits have ostensibly been removed.

In a few respects—for example, in spectrophotometry, in absence of mention of methyl cellulose in determination of tocopherols and of carotene in lack of reference to paper chromatography—the book is not up to date, but it would be impossible for so large a work to be kept up to the minute by one author. The book has been produced in the United States and is primarily concerned with codes of practice and food laws in that country, but in nearly all cases the information has general application. The book is indeed a useful compilation.

V. H. BOOTH

A FLORA OF THE ARCTIC

Circumpolar Arctic Flora

By Nicholas Polunin. Pp xxvii+514. (Oxford. Clarendon Press, London. Oxford University Press, 1959.) 126s. net.

TWO problems immediately confront those who write on arctic plants: first, the difficulty of defining the limits of what one proposes to term 'the Arctic'; and secondly, the even greater difficulty of providing an adequate and up-to-date account of that vast and virtually inaccessible area lying east of Finland and west of the Bering straits. Dr Polunin with his extensive experience of the arctic and arctic vegetation faces up boldly to the first problem and can no doubt furnish weighty arguments in favour of what appears to be a curiously involved indeed almost tortuous, delimitation. As regards the second problem, the author freely admits that our knowledge of the Soviet arctic is inadequate, and that, in present circumstances, no Western or American botanist can hope to compile a detailed and critical circumpolar flora. Some may feel this being so, that any attempt to deal with the flora of the area is bound to be promiscuous and unsatisfactory. The number of flowering plants and vascular cryptogams occurring in the Arctic is so small that the critic has some right to expect a minute and detailed analysis, and to be more exacting in his demands than if the author were attempting a survey of some tropical region with a richly diversified flora. If the reader approaches Dr Polunin's book in this frame of mind he will find much to criticize, for the very frequent use of the tell tale abbreviations *agg.* and *s.l.* after the scientific names shows how much has still to be done before the last word can be written on this subject. But half a loaf is better than no bread, and the less exacting will be glad that Dr Polunin has had the energy and enterprise to give us a concise, lavishly illustrated and, for practical purposes, a tolerably complete account of those northern plants.

British botanists, whose thoughts turn not infrequently to those epochs when much of Great Britain lay buried under ice and snow, will be intrigued to see how many truly arctic species still survive from those bygone glaciations, and (bearing in mind recent

records of *Koenigia*, *Diapensia* and *Artemisia norvegica*) some may choose to ruminate on the number and likely identity of species yet to be discovered here. Palynologists, geologists and archaeologists will also find, in these pages, the sort of information that can save hours of exhausting work in the identification of doubtful grains or fragments. Two features that will certainly not be commended by botanists are the absence of author citations in the main body of the text, and the invention of popular names, some of which (for example, "Boreal Blinking-chickweed") would, in a less august environment, raise a laugh. It is a pity, too, that space should have been devoted to derivations of generic names, such learning is scarcely called for in a book of this sort. The illustrations, though uneven in quality, are on the whole very pleasant to look at, and sufficiently detailed to give us a very fair idea of each plant. Printing and format are excellent, though the regrettably high price must necessarily put the book beyond the means of many who would be happy to possess it.

R. D. MEIKLE

NEW IDEAS FOR INDUSTRY

Investment in Innovation

By C. F. Carter and B. R. Williams. Pp. ix+167. (London: Oxford University Press, 1958) 15s net.

THIS book is in effect a supplement to the same authors' work on industry and technical progress, being in the main a by-product of the case studies which were undertaken in connexion with the writing of that book under the auspices of the British Association and the Conditional Aid scheme. It is a detailed investigation, based upon case material, of the reasons why firms invest or do not invest in technical innovations. Perhaps the only brief statement that can be made about its conclusions is that it shows the enormous range of difference between firms and industries in the nature of the incentives to investment. Thus, for example, it is made clear that, in some cases, keener competition at home or abroad is an incentive to investment while in other cases protection from competition will have this effect. The effect of excess demand manifesting itself in long order books is also noted as one of the factors that have been important in some cases in recent years, and there is a careful discussion of the effect of fiscal changes in stimulating either new investment or quicker replacement of plant. The general factors which are regarded as likely to promote accelerated investment in innovations most effectively, however, seem to be the supply and wide diffusion through industry of scientifically literate people and the improvement of recruitment and training for management. It is essentially effective access to information about new technical possibilities and the willingness and ability to introduce change without creating insuperable opposition that seem to be key factors in determining the rate of industrial progress.

Not very much attention is given by the authors to the supply of capital as a factor limiting investment of the relevant kind, though they found some cases in which shortage of risk capital had been important. Their investigation, however, throws more light on the old question whether interest rate is an important controlling factor governing industrial investment. In general, they conclude from their field studies that with interest rates varying over the normal range

their direct influence is slight—investment projects are either so attractive that a difference in interest rate between, say, 2 and 6 per cent will have little effect upon them or so unattractive that they will not be undertaken at any interest rate however low. The authors think, however, that there is an intermediate class of projects to which the rate of interest is critical even as things are, and that this class might be much bigger if interest rates were capable of going higher than in fact they have gone in advanced countries in modern times.

Altogether this is an extremely valuable and stimulating book belonging to the select but growing class of contributions to economics which seek answers to the really fundamental questions from direct investigation of industrial life.

A. J. BROWN

THE FUTURE OF THE ETRUSCANS

Ciba Foundation Symposium on Medical Biology and Etruscan Origins

Edited by G. E. W. Wolstenholme and Cecilia M. O'Connor. Pp. xii+255. (London: J. and A. Churchill, Ltd., 1959) 45s net.

THE publication of a Ciba Foundation symposium is always an interesting event. This volume has a stimulating title, the synthesis attempted is an innovation of some significance, and it will be viewed from many quarters with a critical eye, in order to assess the value of its application to populations other than the Etruscans.

The Foundation must be congratulated on having drawn together a group of eminent scientists and Etruscologists, and on the clear layout and attractive presentation of the volume. The illustrations show evidence of a care not always extended to the maps. The first five papers presented at the symposium give the evidence of archaeology, religion and linguistics, and some space is given to discussion of the varying theories on the origins of the Etruscans which this evidence permits. As Prof. Banti points out, no one theory can be held dogmatically on the basis of the present information from these fields, and for this reason if for no other, much might be expected of the contributions of the scientists to this meeting. If, in the conclusions which may be drawn from it, the second section falls short of the reader's expectations, it must be borne in mind that the value of scientific work to such studies has only recently been appreciated, indeed, this is made clear in the discussions, in which it is admitted that skeletal material has received cavalier treatment in the past. The main value of this meeting of scientists and archaeologists lies in its promise, and in the opportunity it has provided to discuss mutual requirements, many interesting possibilities are outlined by the various speakers, not the least of which is that of the blood grouping of skeletal remains. Several speakers discuss the serology of the modern population of Etruria, a feature the impact of which is somewhat spoilt by the failure of the historians to show that this region has remained genetically isolated since the Etruscan period.

This book presents an intriguing approach to an old and fascinating problem, and much can be gained from its careful outline of the requirements and pitfalls of such studies. It is likely to become a useful reference book.

MADELINE SMITH

Khami Ruins

Report on Excavations undertaken for the Commission for the Preservation of Natural and Historical Monuments and Relics, Southern Rhodesia, 1947-1955. By K. R. Robinson. With Reports by G. Bond and E. Voce. Pp. xvi+192+28 plates (Cambridge At the University Press, 1959) 40s. net

IT seems likely that iron working agriculture and the manufacture of well made pottery reached Central Africa at the same time and as elements of the same culture complex, within a century or two of the beginning of the Christian era. The event marks the beginning of the history of the Bantu speaking peoples in the area and forms a most important field of pre- and proto-historical research. None the less it is a sadly neglected field of study and much credit must go to prehistorians working on this period in Southern Rhodesia.

Miss Caton Thompson's work on Zumbabwe is well known, and earlier this year Roger Summers produced a most important book on the terraces and ruins of Inyanga. Keith Robinson's excellent book on the Khami ruins now enables us to make some sense of the third of the great ruins sites of Southern Rhodesia.

The book is an excellent objective study of the ruins based on many years of intimate study backed by carefully selected excavation. It is attractively set out with good illustrations, and in Chapter 5 the conclusions are logically and clearly presented. The overriding weakness in all three of the works mentioned is the lack of conclusive dating evidence. This is no fault of the writers concerned and is entirely due to the difficult nature of the evidence. Radiocarbon dates are urgently needed.

It is to be hoped that the future will see a continuation of the excellent work now being done in Southern Rhodesia, perhaps we may add, with rather more emphasis on the crucial earlier phases of the Rhodesian Iron Age. R. R. INSKIP

Rock Pressure in Mines

By E. de St. Q. Jaaneon. Pp. x+313 (London: Mining Publications, Ltd., 1958) 45s.

SEVENTY FIVE years ago Fayol published results of his investigations into ground failure. While his conclusions were valid at shallow depths, it was found that at deeper levels stresses, which had little significance near the surface, began to play an ever increasing part. During the past thirty years many workers have investigated the problem, and in "Rock Pressure in Mines" we have a comprehensive account of the theoretical and practical principles that govern the behaviour of pressure in underground workings. The author who is in charge of the Rockburst Research Unit of the Kolar Gold Mines devotes the first four chapters to theoretical considerations, dealing with elastic stresses and strains, elastic stresses in isotropic rocks around differently shaped excavations, the behaviour of rock stressed beyond the elastic limit, and modifications due to departures from homogeneity. He then applies these considerations to the planning and lay out of workings. In a chapter on rock bursts he shows how strain energy may be built up. He considers that good planning coupled with destressing should substantially reduce the danger of rock bursts. Descriptions and criticisms of several occurrences are given. Finally some of the instruments suitable for measurement of stresses and strain underground are described. The book is

well planned and pleasingly written. There are 135 simple line-drawings and some plates. References to standard text books and technical papers are adequate. It is a book which will be invaluable to all who are concerned with problems of rock pressure.

J. K. L. GRAHAM

Plant Nematodes

Their Bionomics and Control. By Dr. Jesse R. Christio. Pp. xi+256 (Gainesville, Fla.: Agricultural Experiment Stations, University of Florida, 1959) 3.75 dollars.

NEMATOTOLOGY as a separate discipline is a relatively recent development and, as a result, the information on the bionomics and control of plant parasitic nematodes is spread widely through technical journals and bulletins. This literature has not only been surveyed and compiled by the author but is also presented in a clear and logical manner. The author of this relatively small book has succeeded admirably in fulfilling his declared intention of writing a work for specialists which is also understandable to others generally interested in agriculture and horticulture. Thus he has done in fourteen chapters of which the first is a general introduction to nematodes and nematology, while the second is a general discussion of the principles of nematode control. Each of the remaining chapters deals with one group of related nematodes and each is laid out in the same sequence, so far as the subject matter will allow. First, the taxonomy of the parasite, then the life-history and habits, the injury caused to the host, a list of hosts, the parasites' known distribution and methods of spread, and, finally, methods of control. Five tables, in an appendix, list the parasites and their distribution, under the crop plants attacked, control measures, details of hot-water treatments, the common names of plant parasitic nematodes, and in the fifth table a list of scientific names of nematodes attacking plants and their synonyms, is given. The symptoms resulting from nematode attack are illustrated by photographs which are generally of a high standard. The book should form a useful source of reference to experienced workers as well as a text book for the student. W. G. INOLIS

Acetophenetidin

A Critical Bibliographic Review. By Prof. Paul K. Smith (Monographs of the Institute for the Study of Analgesic and Sedative Drugs, No. 4). Pp. x+180 (New York: Interscience Publishers, Inc.; London: Interscience Publishers, Ltd., 1958) 45s.

P. K. SMITH'S book on acetophenetidin is the fourth in a series of monographs reviewing the literature on individual drugs. It deals with 520 references on the clinical uses, pharmacological properties, metabolism and side-effects of acetophenetidin (phenacetin) and its metabolite *N*-acetyl-*p*-aminophenol. The book throws an interesting light on the history of the use of antipyretics, and reflects the changes in medical thought on disease during the past seventy years. If the purpose for which the drug is employed has changed, its popularity has stood the test of time, and justifiably so, since acetophenetidin is not only efficacious but virtually free from harmful side-effects. Pharmacological work on the substance will continue, as we are far from understanding the reasons for its pain-relieving action. MARTIN VOGT

A NEW EXPERIMENTAL TEST OF SPECIAL RELATIVITY

By J. P. CEDARHOLM

IBM Watson Laboratory

AND

PROF. C. H. TOWNES

Columbia University, New York

EXPERIMENTS which have tested special relativity have usually been forced to rely on great delicacy and precision in order to detect or examine the small differences between predictions of special relativity and those of alternate theories. This is because these differences appear multiplied by a very small quantity $(v/c)^2$, where c is the velocity of light and v is some relative velocity which is generally much smaller than c . While giving a clear-cut support to special relativity over some other theories such as a simple ether, experiments have not generally measured the small terms in $(v/c)^2$ with impressive fractional accuracy. Michelson and Morley's first experiment¹, for example, was of remarkable precision. But it was searching for a change in light-path of only about one part in 10^8 due to the motion of the Earth about the Sun on the basis of the then current ether theory, and was able to set an upper limit no less than $1/40$ of this, or an ether drift of about one sixth the orbital velocity of the Earth. Subsequent very refined experiments² of a similar type succeeded, a half-century later, in setting an upper limit on any ether drift of $1/20$ the velocity of the Earth around the Sun. Others³ even suggested the existence of an ether drift as large as about one-fifth of the orbital velocity of the Earth. The advent of very high precision atomic clocks suggests that still more exacting experimental tests may now be made, one such, which is now more or less completed, is reported here.

The experiment compares the frequencies of two maser oscillators⁴ with their beams of ammonia molecules pointed in opposite directions, but both parallel to a supposed direction of motion through the ether. If both masers are rotated 180° , and their frequencies again compared, a change in relative frequency should be found due to motion of the masers through the ether, assuming the molecular vibrations are unchanged by such motion. A precision of one part in 10^{12} has been achieved in this frequency comparison, and failure to find a frequency change of the predicted type allows setting the upper limit on an ether drift as low as $1/1,000$ of the orbital velocity of the Earth. This precision also provides a test for some other effects which will be discussed below.

The effect on the frequency of a beam-type maser oscillator of motion through the ether was first worked out by Møller⁵. A brief, somewhat intuitive explanation of this shift follows. In this device, ammonia molecules in an excited state travel at thermal velocities along the axis of a circular cylindrical cavity, giving it energy. If the cavity is stationary in the ether, the standing waves may be considered to be made of travelling waves with wave-fronts nearly parallel to the axis. As the molecule moves along the axis, there is then no Doppler shift

If the apparatus is moving axially through the ether at velocity v , the wave fronts must tilt at an angle $\alpha = v/c$ in order to follow this axial velocity. Hence, molecules travelling at velocity u through the cavity produce a frequency shifted by the Doppler effect of an amount $uv\alpha/c = uvv/c^2$. Here v is the molecular frequency. Since uvv/c^2 depends on the relative direction of u and v , two masers with oppositely directed beams should have frequencies which differ by $2uvv/c^2$ due to this effect. If each is rotated 180° , the total change in their frequency difference is $4uvv/c^2$.

A more precise derivation of this effect is obtained from the fact that special relativity predicts the same result as does an ether theory, provided that the FitzGerald contraction $\sqrt{1 - \frac{v^2}{c^2}}$ is introduced for

any length parallel to the motion v through the ether, and also that the proper time of any clock or oscillator is modified by the same factor $\sqrt{1 - \frac{v^2}{c^2}}$ due to

this motion. In other words, any effect due to motion through a simple ether is just compensated by appropriate changes in scale for length and time which correspond to the Lorentz transformation. If, then, an ether theory is used without FitzGerald contraction and time dilation, the expected shift in frequency may be computed from an examination of the effects of these changes of scale for length and time.

Consider first the FitzGerald contraction. Its effect on the frequency of maser oscillation is very small and may be neglected because this frequency is rather insensitive to the dimensions and resonant frequency of the cavity⁴.

The time dilation, however, produces the effect we seek. If the cavity moves through the ether at a velocity v and the molecule through the cavity at velocity u , then the molecular velocity through the ether is $V = u + v$, and the molecular time will be slow, for an observer in the framework of the ether, for the factor

$$\sqrt{1 - \frac{(u+v)^2}{c^2}} \approx 1 - \frac{u^2}{2c^2} - \frac{uv}{c^2} - \frac{v^2}{2c^2}$$

But time in the actual laboratory framework, which is fixed with respect to the cavity, is slow by the factor

$$\sqrt{1 - \frac{v^2}{c^2}} \approx 1 - \frac{v^2}{2c^2}$$

Hence the molecule would appear slow to an observer in the laboratory by the difference between these two, or by the factor

$$1 - \frac{u^2}{2c^2} - \frac{uv}{c^2}$$

The first small correction is the well known transverse Doppler effect, and is independent of ether drift. The second small correction is the discrepancy uv/c^2 which would occur if we were to accept a simple ether and no time dilation in the proper oscillation of the molecule, as postulated in Moller's original discussion¹.

The above derivation makes it clear that failure to see any change in time equivalent to the small fractional amount uv/c^2 may be explained away by the assumption of a time dilation for those who wish to adhere to an ether with such peculiarities. Hence the experiment is more closely related to the Kennedy-Thorndike experiment² than to that of Michelson and Morley. A null result in the latter needs, of course, only a Fitzgerald contraction for an explanation in terms of an ether theory.

For performance of the present experiment, two ammonia beam masers were mounted with oppositely directed beams on a rack which rotated about a vertical axis. The frequencies of these oscillators are near 23,870 Mc/s. The thermal velocity $u = 0.6$ km/s for NH_3 at room temperature. If the orbital velocity of the Earth is assumed to be the rate of motion through the ether then $v = 30$ km/s and the frequency change $4uv/c^2 = 20$ o/s when the masers are rotated 180° from an initial east-west position at noon or midnight.

During a small fraction of a second the relative frequency of the two masers fluctuates randomly about ± 5 o/s. Over somewhat longer periods such as those required for measurement before and after rotation, the average frequency difference does not vary more than about ± 5 o/s or one part in 10^{12} . Hence the 20 o/s variation expected on an ether theory would be very easily detected. Variation of about 1 o/s on rotation of the two masers was in fact observed. However, this variation could be eliminated by magnetically shielding the masers, and without shielding it remained constant to within about ± 5 o/s as the Earth rotated throughout a 24 hr run. This shows that no more than about ± 5 o/s shift could be attributed to an ether drift.

The experiment involving rotation of the two masers was carefully done for the first time on September 20, 1958.³ No proper effect as large as ± 5 o/s was found. Hence, since the orbital velocity of the Earth of 30 km/s would have given an effect of 20 o/s the ether drift could not have been larger than $1/1,000$ of this value, or 30 m/s. It is, of course, possible for the motion of the Earth to be just cancelled by the motion of the solar system through the ether at some particular time of the year. The experiment has now been repeated at the Watson Laboratory during 24-hr runs at approximately three month intervals throughout the year. In none of these runs was any effect as large as ± 5 o/s found.

The present experiment sets an upper limit on an ether-drift velocity about one-fiftieth that allowed by previous experiments. This is in part because the effect measured is linear in the ether drift velocity v . An experiment of the Michelson-Morley type is designed to detect a fractional change of the form $\frac{1}{2}v^2/c^2$, which is an order of magnitude larger than the term uv/c^2 discussed here. An upper limit of $1/400$ of $\frac{1}{2}v^2/c^2$ has been set by the very careful

experiments of Joos⁴ with a Michelson interferometer. However, since this term is second order in v , the upper limit given for the ether-drift velocity is one twentieth of the orbital velocity of the Earth, or 1.5 km/s. The present experiments have the advantage that the expected effect is linear in v , and also that two clocks can now be compared with much greater precision than can two distances. This experiment, involving a comparison of two maser oscillators to an accuracy of one part in 10^{11} may perhaps represent the most precise experiment so far reported.

For most physicists, a confirmation of the fundamental postulate of special relativity that no absolute motion can be detected comes as no surprise, and a more precise experimental test may not even seem important because this postulate is so intuitively satisfactory and firmly accepted. It should be noted however, that the positive detection of an effect in the present experiment could give some new information without necessarily contradicting the general principles of relativity. The motion of the Earth involves velocity relative to other parts of the solar system, as well as to the fixed stars and external galaxies. Hence this relative motion might, in principle, produce some anisotropy in space and some shift in relative frequency of the two masers when they are rotated by 180° .

Dicke⁵ has suggested that an effect due to motion with respect to fixed masses in the universe should be present which is of the order of the fine structure constant, α , times the effect due to ether drift. This would correspond to a frequency shift in the present experiment of the order of $\frac{1}{2}c/s$. Reasons given by Dicke why such a shift might occur are speculative but very interesting. The present results allow no shift larger than ± 5 o/s, which gives some indication against a term of the order $4\alpha uv/c^2$.

Optical maser oscillators⁶ should also lend themselves to interesting experiments on relativity since they will probably be capable of examining changes in length as small as one part in 10^{11} . An optical maser oscillator could be constructed with a resonance between two étalon plates which is narrower in frequency than the atomic resonance supplying energy. In this case the frequency would depend primarily on the spacing between the plates rather than on the atomic frequency. It is estimated that the oscillation would be monochromatic to about one part in 10^{11} . This suggests an experiment in which the oscillations of two optical masers are beat together in a photocell. One of the masers may be rotated about a vertical axis. On the basis of an ether theory, the beat frequency should then vary by an amount $\pm v^2/2c^2$, for the same reasons that the Michelson-Morley experiment was expected to show a variation of path length. The fraction v^2/c^2 is 10^{-8} so that its presence could probably be tested with excellent precision.

¹ Michelson A. A. and Morley E. W. *Amer. J. Sci.* **34**, 333 (1887).

² Joos G. *Ann. Phys.* **7**, 335 (1930).

³ Miller D. C., *Rev. Mod. Phys.* **3**, 203 (1933). See, however, Shankland R. S., *Cusack R. W.*, *Leone F. C.* and *Kuerti O.* *ibid.* **27**, 167 (1955).

⁴ Gordon J. P., Zeiger H. J. and Townes C. H. *Phys. Rev.* **99**, 1261 (1955).

⁵ Moller O. *Nuovo Cimento* **6**, Supp. 381 (1957).

⁶ Kennedy R. J. and Thorndike E. M. *Phys. Rev.* **42**, 400 (1932).

⁷ Cedarholm J. P., Bland G. F., Havens B. L. and Townes C. H. *Phys. Rev. Letters* **1**, 842 (1953).

⁸ Dicke R. H. *Proc. Symp. Quantum Electronics*, Columbia Univ. Press (to be published).

⁹ Schawlow A. L. and Townes C. H. *Phys. Rev.* **112**, 1940 (1958).

ECHO-LOCATION AMONG COLLOCALIA

By LORD MEDWAY

Department of Anatomy, University of Birmingham

IT is known that a number of species of the swiftlets (*Collocalia*) of south-east Asia are able to fly in total darkness in the caves in which they nest. When on the wing in the dark or in poor light they utter a series of click-like calls in very rapid succession so that the final effect is a staccato rattle. Novick¹ has recently demonstrated that this call is essential for oriented flight in darkness by *Collocalia brevirostris unicolor*, a swiftlet found in Ceylon.

A similar call is heard from *Collocalia maxima lowi*², which nests in a number of caves in Sarawak³. In 1957, recordings of this swiftlet were made for the Sarawak Museum with the assistance of staff of Radio Sarawak. Successful recordings were made both under natural conditions in Meraja cave, Bau⁴, known to be inhabited only by *C. maxima*, and of individuals of the same species flying singly in the dark-room of the Sarawak Museum, which measures 11 ft by 16 ft by 12 ft high and has interior walls finished in rough plaster and distemper.

The recording apparatus used was a Philips hand microphone type 9564/10 with an EMI portable battery-operated recorder, type L2B. Parts of the tape were later played into the 'Sonograph' sound spectrograph to give a plot of frequency spectrum against time. They were also played back into an oscillograph which was photographed on moving film. From these films the spectrum was calculated by carrying out a Fourier transform of the waveform.

Although blindfolding and deafening experiments were not performed, there are several features of the rattle call of this swiftlet that emphasize its function in dark orientation, many of those listed below are discernible on the tape recording. (Copies of the edited tape, with commentary, are held in Kuching, at Cambridge and by myself.)

(1) Birds approaching the cave from outside are heard rattling while still some distance from the mouth, but those leaving the cave by day in direct flight are silent well within it when in sight of the mouth. This has already been noted and discussed by Novick (*op cit*). By night, however, outgoing birds continue to rattle beyond the mouth.

(2) In imperfect darkness the rattle is not continuous but intermittent, clearly its use is not obligatory and, for example, in the dim light near the cave mouth, it is employed only in dark corners where eyesight fails.

(3) In complete darkness the rattle is continuous, although it tends still to be somewhat spasmodic when the bird is on a familiar flight line through a large chamber. The highest rate of steady rattle recorded on the tape is six clicks per sec, but when a bird approaches its nest site, or if it is frightened in the dark, the rate may be higher still.

(4) In dark regions of the cave away from the nest sites, where all birds are in passage to or from the mouth, only the rattle call is heard and never song or other vocalization, apparently the two types of call cannot be uttered simultaneously. This sug-

gests that the mechanism is syringeal, however, the rattle sound is so unlike any other call that a different mechanism may be involved.

(5) Roosting or nesting birds do not utter the rattle call, a bird flushed from the nest is silent for the first yard or two of flight. For this reason attempts to record at the nest sites were unsuccessful.

(6) The rattle call appears late in development, and well-grown fledglings which are forced to fly prematurely often do so silently, and are then totally disorientated in darkness.

In the Museum dark-room, five birds were flown singly. In every case the rattle call was 'switched on' the instant the electric light was switched off, when the light was turned on again it ceased less abruptly, tending to die away slowly into short well-spaced bursts or single clicks. Such brief outbreaks of rattle are heard in the field from swiftlets flying near cliffs or mountain tops, or diving to drink (on the wing) from the rivers. Chason⁵, in an account of weather movements of mixed swift and swiftlet flocks in Malaya, records the rattle call far from any cave.

In caves the rattle is never heard from birds at roost and usually ceases the moment they alight on the nest, but occasional clicks or brief outbreaks of rattle were heard from the caged swiftlets in transit from Meraja cave to the Museum. It seems likely that in unfamiliar surroundings or when close to solid (or liquid) surfaces the rattle call may be used tentatively to supplement eyesight even in full daylight.

Analysis was applied to three recordings: a single bird flying in the cave, a single bird flying in the dark-room, and very many birds rattling simul-

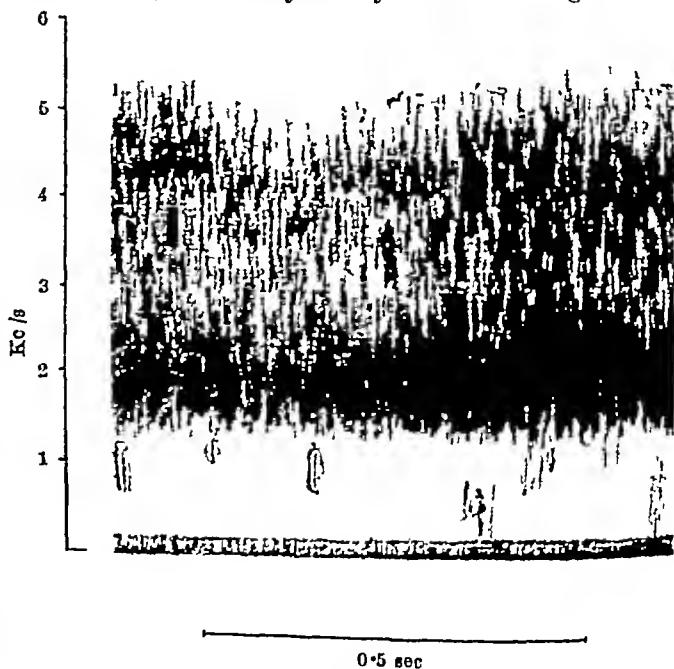


Fig 1 Spectrum of many birds sounding simultaneously in the cave

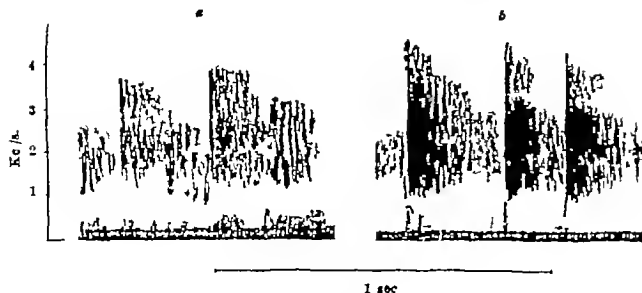


Fig 2 a and b Two different birds recorded separately in the museum dark room

taneously in the cave mouth by night. Results show that the single click is very brief, lasting approximately 2.5 msec. The spectrum of the crowd of birds sounding together is continuous from 1.5 to 5.5 kc/s, with peaks at around 2 and 4.5 kc/s (Fig 1). Isolated bursts of sound from individual avifauna all fall within the same frequency range (Fig 2) and successive clicks are more or less similar although they show no exact correspondence of wave form. The Fourier analyses of the wave forms correspond well with the sound spectrograms. The single clicks of different birds (Fig 2a and b), however, show different distributions of frequency peaks within the characteristic range; this variation might assist each bird to identify the echo of its own call among a crowd although in most circumstances the coincidence in timing between emission and echo would be quite sufficient to discriminate against the calls of other birds. For example, it can be shown that if the bird neglects all echoes returning more than 10 msec after emission (that is, reflected from more than 5 ft away) it may be able to infer the presence of an obstacle with 90 per cent certainty, even though there may be twenty other birds within a radius of

20 ft. This calculation assumes that the echoes from only three successive clicks are noted; if a greater number can be utilized the discrimination increases correspondingly.

The only other avian genus known to echo navigate is the oil bird *Steatornis*.⁴ This utters a similar call, but the mean frequency is considerably higher (7.3 kc/s) and the range (8–10 kc/s) does not overlap with that of *Collocalia maximo* which is shown to rely for sonic navigation on lower frequencies than any other bird, bat or dolphin so far investigated. Other *Collocalia* in Sarawak also utter the same call; one species (*C. esculenta*) lacks it. As part of a survey of the life and habits of the genus in Borneo at present in hand it is hoped soon to extend investigation of the use of echo navigation and of the physiology of the mechanism involved.

I am grateful to Mr. Tom Harrison, curator of the Sarawak Museum for the opportunity to work in Sarawak, for encouragement in the study of *Collocalia* and for criticism of this communication before publication to the staff of Radio Sarawak whose interest and help made these recordings possible and to Dr. K. E. Machun of the Department of Zoology, Cambridge, for the analysis of the recordings and for the discussion on the identification of a bird's own call.

- ¹ Novick, A. (in the press). Also vide Grimm, D. R. "Listening in the Dark" 291 (1959).
- ² Delgman, H. G. *Dull Birds. Orn. Cl.* 75, 92 (1955).
- ³ Smythies, B. B. *Sarawak Mus. J.* 7 (24) 823 (1957).
- ⁴ Graphically described, though not named by Lake, Wan, Tin, and Grimm (ref. 1, p. 292).
- ⁵ Chasen, F. N. "The Birds of the Malay Peninsula" 4, 115 (1939).
- ⁶ Grimm, D. R. *Proc. U.S. Nat. Acad. Sci.* 39 (5) 831 (1953).

IONIZATION PHENOMENA IN GASES

THE fourth International Conference on Ionization Phenomena in Gases took place at Uppsala, Sweden, during August 17–21. The very wide programme included sections on plasma physics, as well as on fundamental processes and other applications of electric discharges and attracted a representative gathering of about 800 scientists from research organizations active in this field in twenty-five different countries. This number of delegates represented a considerable increase when compared with the previous Conference at Venice in 1957 and reflects the increasing world interest in this subject. After a short opening address by the honorary president, the Rector Magnificus of the University of Uppsala, Prof. Torngy Sgerstedt, the general pattern of the Conference followed closely that of previous conferences in the series¹, in that part of each day was devoted to plenary sessions at which general survey papers were read while for the rest of the time the Conference split into four parallel sessions taking place simultaneously. The titles of

these sessions were: (1) Fundamental Processes, (2) Different Types of Discharges and Their Application, (3) Theoretical and Experimental Studies in Plasma Physics; and (4) Production, Confinement and Heating of Plasmas. Since there were, altogether, about 250 papers presented, considerations of space make it impossible to give a complete coverage in this report; instead, a selective review of the papers given in the plenary session together with those in the related sessions which can be regarded as having the most general interest is given, but this inevitably means the omission of mention of many papers.

Fundamental Processes

W. L. Fite (San Diego) presented a paper surveying recent advances in the study of collision processes in gases, in which he first discussed the results obtained for the cross section for scattering and electron exchange using modulated crossed beam techniques, work with which he himself has been associated for a

the diamagnetism of the plasma during its acceleration and after removal of the radial electric field were discussed.

R. F. Post (Livermore) reviewed recent progress on mirror machines where investigations have been concerned primarily with (a) studies of injection methods, (b) investigation of diffusion and non-adiabatic loss processes, and (c) further attempts to analyse the energy spectrum of trapped and heated plasma particles. The experimental difficulties being encountered at this stage in the project were outlined. Results were given of measurements of the radial distribution and rate of diffusion loss of the high-energy electron component of a heated plasma, produced by magnetic compression.

The present state of the *DOX* experiment was reported by A. H. Snell (Oak Ridge) and difficulties being encountered in providing a suitably energetic injection system were analysed. The paper discussed, among other things, observations on the spreading of the trapped ions, life-times of trapped particles, the density of the trapped plasma and an assessment of the factors that may be limiting this density. Another, earlier paper by J. S. Luce (Oak Ridge) had discussed in more detail the trapping of high-energy ions within the walls of a hollow vacuum arc. This wall prevents neutral atoms from reaching the trapped ions and therefore reduces charge exchange losses. New arc techniques were described which include plans for 15 in diameter discharges.

Contributions from the United Kingdom were presented by G. Francis (Harwell), G. B. F. Niblett (Atomic Weapons Research Establishment, Aldermaston) and D. R. Chick (Associated Electrical Industries, Aldermaston). Progress reported from Harwell included the recent identification of Alfvén waves in a high-current toroidal discharge, an earlier paper by D. F. Jephcott (Harwell) had discussed measurements of the velocity and damping of these waves. Other fields of investigation have included experiments with linear pinch and inverse pinch systems (which have shown that in the inverse pinch case the current sheath remains stable for a longer time than in the straightforward pinch system) and some further work on *Zeta*.

Much of the work on devices such as the thiotatron (azimuthal current) carried out at the Atomic Weapons Research Establishment, Aldermaston, had been reported in other papers, so that the review by G. B. F. Niblett was confined to a discussion of attempts to produce very large rates of current growth, by the design of very low inductance systems, and some very recent studies of dissociation phenomena in the hydrogen molecule. Rates of current rise of 6×10^{12} amp/sec, with peak currents of 3×10^6 amp, were reported for the parallel spark gap condenser bank known as *Maggie*. Again, because of many earlier papers from other members of the AEI team, the review by D. R. Chick was confined to a description of the design and engineering of the machine to be known as *Sceptre IV*, and an outline of the proposed experimental programme.

Although members of the USSR delegation delivered papers during this plenary session, there were no review papers in the sense of those presented by the United States and the United Kingdom. Because of this, the papers from the USSR will be discussed in those sections of this report to which they were directly related. Two other papers concerned with thermonuclear investigations were pre-

sented in plenary sessions. W. B. Thompson (Harwell) considered fine scale magneto-hydrodynamic behaviour in plasmas, where the effects of the finite ion Larmor radius may be important, by use of the collision-free Boltzmann equation. A consistent series expansion of this equation was used to derive first order magneto-hydrodynamics, and the magneto-hydrodynamic shock was studied as an application of this technique. "Recent Progress in Shock Wave Research" was the title of a paper by A. C. Kolb (Washington), and in it he described the spectroscopic study of temperature and density in shock wave fronts. Very high-ionization densities had been achieved and there was strong evidence for high temperatures, and thus considerable ionization, ahead of the travelling wave-front, probably produced by a radiation process. In the general paper sessions, those concerned with plasma physics were divided into two: (a) theoretical and experimental studies in plasma physics, and (b) production, confinement and heating of plasmas. These two sections will be briefly reviewed individually.

Theoretical and Experimental Studies in Plasma Physics

The topics in this section were transport phenomena, interactions involving electric and magnetic fields, microwave radiation measurements and spectra from plasmas.

An interesting theoretical approach to transport phenomena was described in a paper by M. N. Rosenbluth and N. Rostoker (San Diego), where, in a fully ionized plasma, all field particles are considered to be in equilibrium except for one 'test' particle. The resultant reaction on this test particle, due to its interaction with the field particles, consists of a frictional drag and a random force that produces acceleration and diffusion in velocity space. A systematic procedure for determining these effects with no magnetic field and in the presence of a constant magnetic field has been developed.

The topic "Interaction involving Electric and Magnetic Fields" produced the largest number of papers of any at the Conference. Among them was a paper by Derimkhanov, Gavarkov and Popov (Moscow) on "The Interaction of a Beam of Charged Particles with a Plasma". This paper described the investigation of plasma oscillations created by a continuously injected electron beam. It was shown that the maximum intensity of plasma oscillation is produced when the electron beam passes through the plasma. Electromagnetic fields with the same plasma frequencies were also found outside the plasma column, the intensity of these oscillations as a function of the density of the plasma was investigated and found to be the same as that inside the plasma column. Detection of these oscillations was possible because of the considerably increased sensitivity of the recording apparatus compared with that used by previous workers. Another paper on this topic was that by Khazhenko and others (Moscow), in this case an electron beam was modulated by oscillations in a plasma through which it passed and afterwards detected in a resonant cavity.

Other papers of interest included one by J. A. Wesson (Associated Electrical Industries, Aldermaston) on the effect of runaway electrons on the heating of a plasma, where it was shown that, for

constant electric field, runaway electrons set a limit to the temperature which can be efficiently achieved by ohmic heating; but for constant current density, if the fraction of the current carried by the runaways is small this fraction will decrease as the temperature increases. A paper by I B Bernstein and I N Rabinowitz (Princeton) considered the velocity distribution of plasma electrons in an external magnetic field when the ions are assumed to be infinitely massive, and electron-electron interaction is suppressed. These assumptions produced equations which could be solved numerically on a computer, and results indicated that, with an initially Maxwellian distribution, the distribution functions do not develop the double humped character which oscillation theory indicates to be unstable.

J E Allen and F Magistrelli (Rome) described experiments on the plasma sheath transition in the presence of a magnetic field. Using an azimuthal magnetic field which could be applied in the 'pinch' or 'anti pinch' direction, they showed that a magnetic field in the pinch direction reduced the directed energy of the positive ions leaving the plasma and a magnetic field in the anti pinch direction increased this energy. The result was shown to be in accord with theoretical predictions.

S O Brown (Massachusetts) in his review paper on "High Frequency Waves in Ionized Gases" considered the various types of electromagnetic waves that are set up in an ionized gas due to the application of a magnetic field. There are six natural frequencies, three being cyclotron frequencies and three plasma frequencies. Because the magnetic field is a vector the resultant oscillations in the plasma can be parallel or perpendicular to the field and thus a very large range of possible oscillations exists. The paper discussed some basic properties of these waves.

A fascinating combination of plasma and microwave physics was presented in a paper by G S Kino and B Ludovici (Stanford). The paper discussed a plasma parametric amplifier based on the principle that if electromagnetic waves of three frequencies ω , ω_1 and ω_2 such that $\omega = \omega_1 + \omega_2$ can be propagated through a lossless non-linear medium with propagation constants β , β_1 , β_2 , strong interactions will take place between these signals if $\beta \approx \beta_1 + \beta_2$. If ω is of large amplitude there will be a power transfer to ω_1 and ω_2 . This principle has been confirmed in a mercury vapour discharge with $\omega = 800$ Mc/s, $\omega_1 = 500$ Mc/s and $\omega_2 = 300$ Mc/s. Both ω_1 and ω_2 have been observed to increase in amplitude by a few db in travelling from one end of the positive column to the other.

The broadening of spectral lines by Stark effects was discussed by H Margenau (Yale). Equations for the calculation of half widths were given for three different cases: (i) when both electrons and ions can be treated by impact theory, (ii) when the electrons can be treated by impact theory but the ions have to be considered statistically, and (iii) when both electrons and ions can be treated statistically. Physical conditions to which these equations are applicable were discussed. Improved methods of calculating Stark broadening of spectral lines were presented in a paper by H R Griem (Maryland) and A C Kolb (Washington). It was shown that the calculated line profiles depend only slightly on temperature and can therefore be used to deduce electron densities in dense plasmas from measured profiles with much improved accuracy.

Production, Confinement and Heating of Plasmas

This section, as with the other sections of the Conference, was split into sub sections which were (a) the longitudinal pinch, (b) mirror machines and the azimuthal pinch, (c) shock waves, and (d) further methods of production and confinement.

In a paper by D W Allan (London) consideration was given to the detailed behaviour of the simple unstabilized pinch in respect of the inward movement of the current sheet. He concluded that evidence favours the free particle piston model and the shock wave model rather than the snow plough model. Whether the behaviour follows more closely the free particle model or the shock wave model depends on the effective mean free path.

Two papers by S A Colgate, H P Furth and others (Livermore) discussed the linear and toroidal hard-core or inverse pinch. Small-scale instabilities in the linear case have been shown to be of non-hydrodynamic origin. A toroidal version of the hard-core pinch has been attempted using a magnetic field to levitate a ring conductor inside a toroidal shell. This device will be used to study the nature of these small scale instabilities and also to study the stability of near vacuum field hard-core configurations and to determine if this stability leads to an improved containment of the plasma energy. 'A Dynamically Stable Current Column' was the title of a paper by V S Komelkov and others (Moscow). The formation and development of a current cord appearing during the movement of a plasma jet were examined by means of advanced high speed photographic techniques. Measurements were made of the current distribution in the moving plasma jet and showed that the current in the cord had remained stable throughout the half period of the discharge. The existence of a radiation continuum the appearance of which coincided with the appearance of the current cord had also been demonstrated.

A Kantrowitz and others presented a paper on the use of collision free shocks to study dissipation mechanisms in collision free plasmas. At high temperatures, collisional dissipation in plasmas is slow, and losses due to magnetohydrodynamic turbulence become important. Preliminary experiments show that it is possible to produce shock waves that obey the required theoretical condition that the shock thickness is less than the mean free path, and that observations on these thin shocks can provide a powerful tool for the study of dissipative mechanisms in collision free plasmas.

Finally, L Högberg, K Siegbahn and K Bookstam (Uppsala) described an apparatus for the electrodeless generation and acceleration of plasma rings. A single turn primary winding placed close to the end wall of a 'Pyrex' tube induces a ring discharge which is accelerated as a function of the gas current and the magnetic field. Ion velocities in the range 10^4 - 10^7 cm/sec have been observed with this technique.

Conclusion

During the Conference, visits to the Institute of Physics and the Institute of High Temperature Research at Uppsala and the Nobel Institute of Physics in Stockholm were organized, a full social programme for members and their wives was also arranged. All those concerned with the organization of the conference and particularly the hard working secretary Dr Åke Nilsson of the Institute of Physics Uppsala

are to be congratulated on the excellence of the arrangements which enabled such a large conference to run so smoothly throughout

It is no reflexion on this organization to comment that these conferences, including as they do such a wide range of topics, are becoming too large and unwieldy, one possible solution would seem to be to divide the subject-matter into two groups, one devoted to ionization phenomena and gas discharges and the other to controlled thermonuclear research and plasmas. If these groups were arranged to run

consecutively it would give those with interest in both fields an opportunity to attend more of the lectures in which they are interested, while considerably reducing the total number of delegates present at any given time

The next conference in this series is to be held in Germany, probably at Baden-Baden, during 1961

J. DUTTON
D. HARCUMBE
E. JONES

¹ Garton, W. R. S., and Latham, R., *Nature*, 180, 700 (1957)

RADIO ECHO OBSERVATIONS OF VENUS

By J. V. EVANS and G. N. TAYLOR

Jodrell Bank Experimental Station, University of Manchester

DURING September 1959 an attempt was made to observe radio echoes from the planet Venus using the 250-ft radio telescope at Jodrell Bank. The radar equipment used with the telescope operated on a frequency of 408.00 Mc/s. The transmitted power was 50 kW, pulse-length 30 msec and pulse repetition rate 1 per sec. The receiver had a noise figure of 4.6 db and a bandwidth of 60 cps. The overall losses in the feeders amounted to 2.5 db, and the polarization of the transmitted wave was right circular. Observations were made with the telescope in continuous motion to follow the planet across the sky, with alternate periods of transmitting and receiving. The length of these periods was approximately equal to the time of travel of the radio pulse to and from the planet (5-6½ min).

No echoes were observed with this equipment stronger than the noise-level in the receiver. An analysis of the signals for echoes which were weaker than the noise was made with an integrating equipment, which added together receiver noise powers corresponding to the same range-intervals on successive sweeps of the time-base. With this system eight adjacent range-intervals were examined. These were made equal in width to the transmitter pulse (30 msec) and their distance along the time base was controlled in order to compensate for the change in range of Venus, so that any echo would remain in the same 30 msec time-interval. It was also necessary to provide compensation for the Doppler shift of the echo relative to the transmitter frequency.

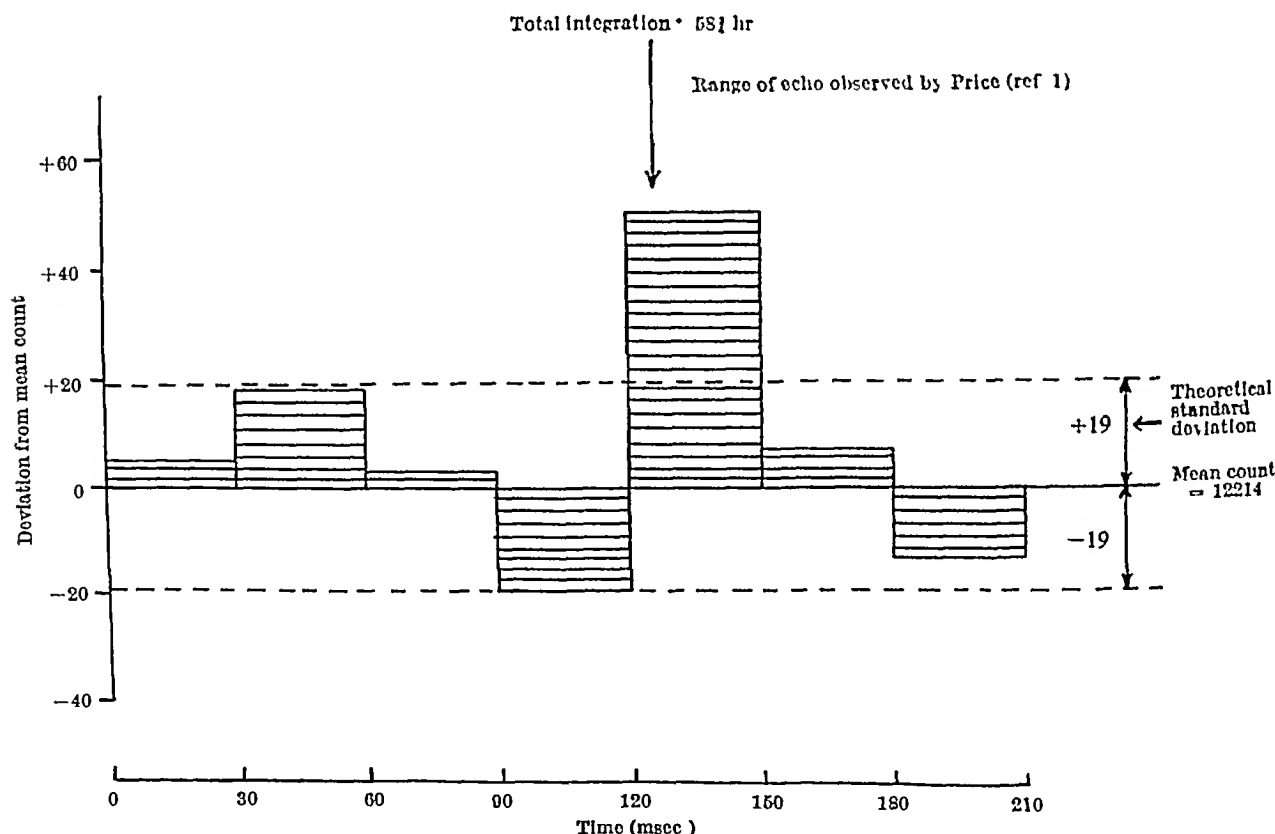


Fig. 1 The deviations of the counters in the Integrator system from their mean is plotted as a histogram. Different positions of the eight gates along the time base were employed and only seven range intervals were common to all the periods of observation. Hence there are only seven counts shown in the histogram.

Exhaustive checks were made to confirm that the integrated noise counts in the eight range channels showed statistical fluctuations which agreed with theory, and that no systematic errors were introduced by, for example, the operation of the transmitter or the telescope. Such systematic errors were unlikely because the transmitter and receiver operated alternately for 5-6 min. intervals.

A total of 58½ hr useful operating time was obtained before the range of Venus had increased to a point where further work was not considered worth while. The addition of all the periods of observation is presented as a histogram (Fig. 1) where one of the eight range intervals shows an excess count of 2½ times the standard deviation. The addition of many samples of noise by the integrating equipment gives a Gaussian distribution of counts, hence there is an 8 per cent chance that noise alone will produce a count 2½ standard deviations greater than the mean in one of eight channels. If the high count is caused by the planetary echo, then the range observed gives a value for the solar parallax of 8.8020 ± 0.0005 sec of arc. This value is in agreement with that obtained by Price *et al.*¹ using the Millstone Hill Radar Station operated by Lincoln Laboratory of the Massachusetts Institute of Technology (8.8022 ± 0.0001 sec of arc). The likelihood that, by coincidence, a high count should appear in the range interval predicted by the Millstone Hill result is 1 per cent.

The signal to noise ratio required to produce an excess count of 2½ standard deviations has been estimated by applying to the receiver signals which

are weaker than the noise by a known amount and is -23 ± 2 db. This is within 6 ± 2 db of that expected on the basis of a model for Venus in which it was assumed that the scattering is similar to that observed for the Moon² and that the period of rotation is of the order of 20 days. However the result is not in agreement with the work reported by Price, which suggested that the radar cross-section of Venus was equal to the physical area presented by its disk. If this were the case a signal to noise ratio of about -5 db should have been observed. This discrepancy of 18 db in signal strength might be accounted for in two ways: (a) if the rotation period of Venus is much faster than once every 20 days the Doppler broadening of the echo will cause some of the received power to fall outside the 60 c.p.s. bandwidth limit of the receiver, (b) if the echo is subject to large rapid changes in intensity then because a square law detection system was employed at Millstone Hill, a false estimate of the average signal to noise ratio would be obtained. Such fading could not have been caused by Faraday rotation in the Earth's ionosphere because circularly polarized radio waves were used in both experiments.

We are indebted to our colleagues at Millstone Hill for their interest and co-operation particularly in producing for us predictions of the range and Doppler corrections which were applied to select the received signal.

¹ Price R., Green P. E., Jon Gobllick T. J., Kingston R. H., Kraft L. O., Jans, Pittenill G. H., Silver R. and Smith W. D. *Science* 129 751 (1959).

² Evans J. V. *Proc. Phys. Soc. B* 70 1105 (1957).

OBITUARIES

Prof M. Caffrey

THROUGH the death of Prof M. Caffrey, which occurred on September 17 at the age of seventy Ireland has lost an outstanding personality in the field of agricultural science and one who took an active part in the Faculty of Agriculture in the National University of Ireland.

Michael Caffrey was born at Lughill, near Monasteran, Co. Kildare. He received his early education at the local national school and at the Christian Brothers' School, Monasteran. He entered the Albert Agricultural College, Glasnevin, in 1908 and in the following year was awarded an agricultural scholarship into the Royal College of Science, Dublin. After a distinguished undergraduate course, he gained the diploma of the latter institution in 1912, and was appointed as assistant to Dr H. Hunter in the Plant Breeding Section of the Department of Agriculture, Dublin. The studies and work he then undertook under the able guidance of Dr Hunter formed the basis of his later successful career in plant breeding, lecturing and teaching. When Dr Hunter resigned after the First World War, Caffrey became head of the Plant Breeding Section of the Department of Agriculture, and when a Faculty of Agriculture was established in the National University of Ireland in 1927, the University made him lecturer in plant breeding, and afterwards in 1938 appointed him to fill the newly established chair of plant breeding, a post which he occupied until his death.

Throughout his career, Prof Caffrey remained in close contact with the Department of Agriculture, which he kept supplied with nucleus stocks of leading

cereals and grasses. These in turn became available to the various county committees of agriculture by which they were tested and reported on in due course. Prof Caffrey was also in close contact with plant breeding stations abroad, and he introduced many foreign cultivars of wheat, oats and barley. They were tested against cultivars commonly grown in Ireland and numerous crosses made with the most promising sorts. During four decades he produced not only varieties of wheat suitable to local soil and climatic conditions, but also improved varieties of oats and grasses. In crossing and breeding, Prof Caffrey was particularly interested in the reaction of the hybrids to disease resistance, and one outstanding case of his work on this aspect may be quoted here. At Glasnevin year after year, the most common and serious disease of wheat has been yellow rust (*Puccinia glumarum*). To combat this, Caffrey produced the cultivar Glasnevin Rosa, a wheat which was immune to yellow rust for seven years, a period which is about usual for varieties bred immune or resistant to rust diseases before they become attacked by new strains of the pathogen which develop in the meantime.

Close co-operation always existed between the Plant Breeding Division and the Plant Pathological Division at Glasnevin, and down the years the latter Division has been indebted to Prof Caffrey on many occasions for directing attention to outbreaks of disease and to the appearance of new pathogens on cereal crops.

Although Prof Caffrey's entire professional career was devoted to plant breeding he had a wide interest in all agricultural subjects. He was a founder Council

member of the Irish Grassland Association, a member of the Agricultural Commission appointed by the Government to examine agricultural development in the late 'thirties, and in general he identified himself with many agricultural developments. He was equally at home with students and scientific audiences, and as a lecturer on behalf of the Royal Dublin Society he became intimately acquainted with and highly appreciated by a wide range of farmers all over the country.

Prof Caffrey's outspoken manner, genial personality and hearty laugh will long be remembered by all who knew him. He was predeceased by his wife some years ago, and he is survived by three sons and three daughters, for whom the greatest sympathy is felt.

R. MCKAY

Dr E J Holmyard

ERIC JOHN HOLMYARD was born on July 11, 1891, at Midsomer Norton, Somerset, and all his life he was a faithful man of Somerset. He was a scholar of Sidney Sussex College, Cambridge, and after graduation he served as a sixth-form science master at Marlborough College during 1917-19. He then became head of the Science Department at Clifton College, an appointment which he filled with signal success for the twenty years 1920-40. It was at Clifton that his best work was done. In 1941 he became editor of *Endeavour*, retiring in 1954 to live at Clevedon, Somerset. Among his other activities, he was chairman of the Society for the Study of Alchemy and Early Chemistry and co editor of a "History of Technology" in five volumes.

Holmyard, as a teacher, well knew the capacities of young pupils at school, and his books on inorganic and organic chemistry of this standard have deservedly been very popular. They are written in a lucid and attractive style and many readers of this notice must owe their introduction to chemistry to them. In collaboration with F. A. Philbrick, he wrote a more advanced book on theoretical and inorganic chemistry which has also been very successful. All these books present the basic facts of chemistry as an experimental science, relating them to general principles in a way which gives them significance and interest, but the theory is kept in proper proportion, so that those who gained their knowledge from them in the past will now have very little to unlearn.

Dr Holmyard, who was a member of the Royal Asiatic Society, will probably be best remembered for

his profound studies of Muslim chemistry. He was well equipped with a knowledge of Arabic, and in this field he was a recognized authority. He made a special study of Jābir ibn Ḥayyān and the writings attributed to him. He published some Arabic texts, brought to light some little-known works of Jābir, and re-interpreted some which had previously been studied. More recent research has shown that the problem of Jābir is very difficult and much remains to be cleared up, but Holmyard's pioneering work has a permanent value. He showed that the theory which dominated alchemy and early chemistry, that metals are composed of mercury and sulphur, was taught by Jābir, who derived it from a statement in the "Meteorology" of Aristotle.

In collaboration with his pupil at Clifton, Mandeville, Holmyard published the Arabic text and a translation of a work known in Latin as by Avicenna and showed that it is, in fact, part of the genuine *Shifā'* of Ibn Sīnā. This text, which denies the transmutability of species and stigmatizes alchemical gold as fraudulent, was a puzzle in the Middle Ages, when it was thought to be part of the "Meteorology" of Aristotle. Holmyard also edited and translated an alchemical text of Abū'l Qāsim al-'Irāqī. In all these studies he made much use of the writings of Jildakī, available only in manuscripts, and established their value as a source of information on Muslim alchemy. The work in this field by Holmyard completely changed the outlook on Muslim chemistry which prevailed when he began.

Holmyard wrote some excellent small books on the history of chemistry, the best known being his "Makers of Chemistry" and his recently published "Alchemy". These are accurate and authoritative, and it is to be regretted that he did not write a general survey of Muslim chemistry which he was so well qualified to undertake.

Holmyard was modest and unassuming, ready to put his knowledge at the disposal of those who asked it, with a cool and critical outlook in scholarship, expressing himself concisely and avoiding polemics. His learning sat lightly upon him, and for all he cared it could remain unknown in circles incapable of understanding it. He was open and friendly and in whatever company he found himself his quiet charm and delicate sense of humour, wholly free from malice, endeared him. He was a member of Clevedon Golf Club. He died at Clevedon on October 13, and among those who valued his knowledge and friendship his death leaves a vacant place which it will be hard to fill.

J. R. PARTINGTON

NEWS and VIEWS

Royal Society Award of Royal Medals

H.M. THE QUEEN has been graciously pleased to approve recommendations made by the Council of the Royal Society for the award of the two Royal Medals for the current year as follows: to Prof. R. E. Peierls, professor of mathematical physics in the University of Birmingham, for his distinguished work on the theoretical foundations of high energy and nuclear physics, to Prof. P. B. Medawar, Jodrell professor of zoology and comparative anatomy at University College, University of London, for his distinguished contributions in the field of tissue transplantation immunity and acquired tolerance.

Geological Society of London: Foreign Members

THE Geological Society of London has elected to foreign membership the following distinguished geologists: Academician V. V. Belousov, of the Academy of Sciences, Moscow, in recognition of his studies on sedimentation and geotectonics, Prof. J. A. Broggi, of Lima, Peru, for his work in the advancement of geological science in Peru and his contributions to Peruvian geology, Academician D. V. Nalivkin, of the Academy of Sciences, Moscow, in recognition of his contributions to the geology of the Soviet Union and especially of his part in the preparation of the recently published geological map

of that country, Academician N S Schatsky, of the Academy of Sciences, Moscow, for his work on tectonics, stratigraphy and economic geology, Dr F Prantl, vice-president of the National Museum Prague, in recognition of his distinguished researches in palaeogeography, stratigraphy and palaeontology Prof Norman D Newell, of the American Museum of Natural History New York, for his contributions to invertebrate palaeontology and his work on reef deposition

British Broadcasting Corporation Science Unit

A SCIENCE UNIT has been established by the British Broadcasting Corporation with the object of providing a more extensive coverage of science in sound programmes. The senior member of the Unit is Dr Archie Clow, who joined the B.B.C. in 1945 and has produced many science series and individual talks notably the two weekly series 'Science Survey' and 'Who Knows?', in which leading experts deal with all kinds of scientific developments in a non technical way. The Unit is also responsible for 'Science Review' and Third Programme science talks and discussions. Recently, Mr David Edge joined Dr Clow in the Talks Department. Both received their earlier education at Aberdeen, the former at Aberdeen Grammar School and the latter at Robert Gordon's College. Mr Edge did research work in radio astronomy for three years after taking his degree in physics at Cambridge in 1955.

A third member of the Corporation staff who is contributing to the expansion of science broadcasts is Mr C L Boltz, who is now attached to the News Division as science correspondent (*Nature* 183 1231; 1959). He formerly worked for seven years in a similar capacity in the B.B.C.'s European Service. Succeeding Mr Boltz in the European Service is Mr Bryan Silcock, who was born in Liverpool in 1933 and has since 1957 been an assistant editor of *Nature*. He went to Dartington Hall School in Devon, and after National Service in the West Yorkshire Regiment and the Royal Artillery, to Jesus College, Cambridge graduating with honours in natural science.

British Commonwealth Education Liaison Committee

In a written answer in the House of Commons on November 12, the Minister of State for Commonwealth Relations, Mr C J M. Alport, stated that in accordance with the recommendations of the Commonwealth Education Conference representatives of all member countries in the Commonwealth met in London on October 27 under the chairmanship of Sir Henry Lintott. It was proposed to establish a Commonwealth Education Liaison Committee, comprising one representative of each member country and of Nigeria and in addition the United Kingdom would appoint a member to represent the other Colonial territories. This Committee would follow up and record progress on the schemes of assistance agreed at the Oxford Conference and would also consider suggestions for the further improvement of Commonwealth co-operation in education, and, in particular, it would prepare material for submission to the next Commonwealth Education Conference, to be held in India in the winter of 1961-62, at the invitation of the Government of India. The chairman would be Sir Philip Morris, and under the general direction of the Liaison Committee there

would be a Commonwealth Education Liaison Unit consisting initially of a director (who would also be secretary to the Committee) and one administrative assistant. The Unit would supplement normal direct dealings between the countries of the Commonwealth on education, and would deal on request with inquiries from education authorities in Commonwealth countries and generally act as a reference centre. The cost of the Unit would be shared between member countries of the Commonwealth.

United States and Great Britain to exchange Data on Advanced Gas-cooled Reactors

THE UNITED STATES Atomic Energy Commission and the United Kingdom Atomic Energy Authority have signed a five-year agreement to exchange technical information on advanced gas-cooled reactors. The exchange, effective as from November 16 will be carried out under the terms of the agreement between the two countries for co-operation in the civil uses of atomic energy, which has been in effect since 1955. Data will be exchanged on development, design, construction and operation, as well as on related research and development, of the advanced gas-cooled reactors being built at Windscale, England and on the U.S. experimental reactor project of this type at the Oak Ridge (Tennessee) National Laboratory. Information exchanged under this agreement will be made available to British and American industry.

British Book Exhibition in Moscow

A LARGE exhibition of British books and periodicals sponsored by the British Council and the Soviet Ministry of Culture is opening in Moscow on November 21 for a fortnight. A similar exhibition of Russian books and periodicals will be shown at the Festival Hall in London next February. This will be the largest exhibition of British books and periodicals to have been shown in the U.S.S.R. at any time so far as is known. Between three and four thousand books will be exhibited together with six hundred periodicals, a display of posters and large photographs. The exhibition will be shown in the main lecture hall of the Lenin Library, one of the largest libraries in the world. The books selected by the British Council have been provided free of charge by British publishers through the co-operation of the Publishers' Association. The main emphasis lies on science and technology, although there are important sections dealing with the arts and the humanities. Under the terms of the agreement made with the Soviet Ministry of Culture, there are no sections on religion, politics or economics. Two thirds of the periodicals are on medical and scientific subjects. At the end of the exhibition all the British material will be handed over to the Soviet Ministry of Culture for use in Russian libraries and cultural institutions.

New Zealand Research on Weed Transportation

WEED species are sometimes inadvertently introduced into one country from another, but it is not always possible to establish the means by which this occurs. A J. Healy, of the Botany Division, Department of Scientific and Industrial Research, Christchurch has given some particular instances of introduction of foreign species into New Zealand (*New Zealand Journal of Agricultural Research* 2 No 2, April 1959). The first example is a straw envelope from a whisky bottle picked up in a rubbish

heap on a North Canterbury farm. The envelope contained a flowering stem of bindweed, *Calystegia sepium*, portions of an inflorescence of tall oat grass, *Arrhenatherum elatius*, and a bent grass, *Agrostis* sp. Such containers when discarded are generally thrown on rubbish heaps and other sites suitable for weed establishment. A plate-glass container from an English source, examined in the Wellington district, contained wheat straw in which was found portions of Californian thistle, *Cirsium arvense*, cleavers, *Galium aparine*, willow weed, *Polygonum*, fruiting material of *Beta* sp., nipplewort, *Lapsana communis*, and a hemp nettle, *Galeopsis* sp. This straw was being used locally both for compost heaps and in racing pigeon cages, which would further serve to disperse the weeds throughout the country. An examination of the trouser cuffs of a tourist returned from a trip through Spain, France, Switzerland and Italy revealed fruits of Gramineae and Compositae.

University News

Birmingham

THE title of reader in mathematical physics has been conferred on Dr J G Valatin, senior lecturer in mathematical physics. The following appointments have been made to lectureships: Dr H B Griffiths (pure mathematics), Dr J K Brown (chemistry), Dr M E Davies (botany), Dr Nancy Montgomery (botany), Brenda Manly (zoology), J Cohen (zoology), C R Sladden (biology in the department of zoology), Dr D J Blundell (geology), I R Smith (electrical engineering); K B Haley (engineering production), Dr V G Jenson (chemical engineering), K A Redish (computing in the Department of Mathematical Physics), N A Dyson (physics), N A J Rogers (chemistry).

The annual lecture of the Institute of Education is to be named "The Raymond Priestley Lecture" in recognition of the help which Sir Raymond Priestley gave to the Institute of Education when the Institute was established.

Preliminary plans have been approved for a building for highway and traffic engineering as an addition to the new Civil Engineering Building.

Oxford

THE following research grants are announced from European Research Associates, Brussels, £1,200 for one year from September 1, for research on acetylene chemistry being carried out in the Dyson Perrins Laboratory under the direction of Prof E R H Jones, from the Department of Scientific and Industrial Research a grant not exceeding £3,400 for the year ending July 31, 1960, for the maintenance of the 140 MeV synchrotron for nuclear physics research in the Clarendon Laboratory, from the Colonial Medical Research Council a grant not exceeding £2,500 for a further two years ending August 31, 1961, for the study of the sensory neuro-histological changes in skin infected with leprosy, being carried out in the Department of Human Anatomy under the direction of A G M Weddell, reader in human anatomy, from the Smith, Kline and French Research Institute a grant not exceeding £1,500 for research on the electrophysiology and pharmacology of smooth muscle to be carried out in the Department of Pharmacology by E Bulbring, from the United States Public Health Service a grant not exceeding 30,600 dollars for the year beginning September 1, 1959, for research in the Department of Biochemistry under the direction of Sir Hans Krebs.

Announcements

PROF C F CARTER, Stanley Jevons professor of political economy and Cobden lecturer in the University of Manchester, has been appointed a member of the Council for Scientific and Industrial Research, in succession to Prof E A G Robinson, who retires on completion of his period of service. Prof Carter's interests are in the field of applied economics. He is the author of "Industry and Technical Progress" (with Prof R B Williams), published in 1957, and "Investment in Innovation", 1958, he is chairman of the Science and Industry Committee of the Royal Society of Arts, the British Association for the Advancement of Science and the Nuffield Foundation.

THE Metallurgical Society of the American Institute of Mining, Metallurgical, and Petroleum Engineers, in association with Interscience Publishers, Inc, has announced the publication of a new series of books entitled "Metallurgical Society Conferences", each volume being the proceedings of a technical conference sponsored by the Society through one of its technical committees. It is hoped by these means to provide for co-ordinated and comparatively rapid publication of scientific and engineering papers of interest to metallurgists. The first volume in the series, "Flat Rolled Products, Rolling and Treatment", can be ordered from Interscience Publishers, Inc, 250 Fifth Avenue, New York 1, New York (price 3.75 dollars).

THE Population Council Incorporated of New York is making grants totalling 89,348 dollars over three years to the National Institute for Research in Dairying. The award is in support of researches on cervical mucus with particular reference to the control of fertility, to be carried out in the Physiology Department under the direction of Dr S J Follev.

INDUSTRIAL AND TRADE FAIRS, LTD, announce that a conference on New Engineering Materials and Design will be held in conjunction with the first Engineering Materials and Design Exhibition at Earls Court, London, during February 22-26, 1960. Among the subjects selected for discussion at the conference will be safety factors and the appearance in design. Further information can be obtained from the Secretary for the Conference on Engineering Materials and Design, Drury House, Russell Street, Drury Lane, London, WC 2.

At the annual general meeting of the Photobiology Group, held at the National Physical Laboratory, Teddington, on November 6, Dr D Vimec, of the Department of Horticulture, University of Reading, was elected honorary secretary in succession to Dr E M F Roe.

THE sixth National Symposium on Reliability and Quality Control in Electronics will be held at the Statler Hilton Hotel, Washington, D C, during January 11-13, 1960. Further information can be obtained from Mr R Brewer, The Research Laboratories, The General Electric Co, Ltd, Wembley, Middlesex.

ERRATA. In the communication entitled "Effect of Sorbitol on the Urinary Excretion of some B Vitamins in Man" in *Nature* of September 19, p 911, the numerical values of the ordinates have been inverted; thus, reading from below upwards, the values for riboflavin should be 150, 200, 250 μg , those for thiamine, 10, 20, 30 μg , those for N-methylnicotinide, 2, 3 μg .

ASSISTANCE FOR UNDER-DEVELOPED COUNTRIES

THE Queen's speech at the opening of Parliament on October 27 referred to the Government's urgent concern to improve conditions of life in the less developed countries of the world and its intention to promote economic co-operation and support plans for financial and technical assistance. This was warmly welcomed in both Houses in the subsequent debates. Lord Stoneham asked for further information on this matter and, emphasizing its urgency, stressed the need to seek international agreement to stabilize basic commodity prices, the fall in which in 1958 had cost the under developed countries 2,000 million dollars. Only urgent and increasing financial and technical assistance can avert the human suffering implicit in the two thirds increase forecast in the population of Asia in the next fifteen years. The Marquess of Lansdowne was unable to specify the exact increases but assured Lord Stoneham that the Government intended to increase considerably contributions in the various fields of aid to under developed countries. Lord Home also expressed the view that the foundation of peace probably lies in bringing the standard of living of the under-developed nations nearer to that of the industrial nations. In replying on the debate, the Lord Chancellor said that under the Colonial Development and Welfare Acts, £140 million would be available for the Colonial territories during the next five years, with up to £100 million more by way of Exchequer loans. External private investment of all kinds averaged £90 million a year, two thirds being from the United Kingdom, and it was estimated that the United Kingdom's financial contribution to the Colonial territories averaged £100 million a year in 1956-58. Economic and technical assistance to all overseas countries and territories from United Kingdom public funds rose by a third in the past financial year to about £100 million, and is expected to increase similarly this year, exclusive of military assistance and certain emergency and miscellaneous expenditure amounting to about £30 million. Subject to agreement on the constitution for the new International Development Association, Parliament would be asked to put £50 million into the new Association.

In the House of Commons, Mr J. Harvey, referring to the growing awareness of the need to give greater assistance to the under-developed territories suggested that the Government might take some initiative in stimulating such interest so as to enlist voluntary contributions in addition to Government funds for this purpose. Mr W. Owen suggested the Co-operative movement as a possible source of experience, knowledge and enterprise in this connexion, and Sir John Barlow advocated use of the International Monetary Fund to stabilize world production and prices of such primary commodities as tin and rubber. Mr H. A. Price pointing out that we are already devoting more than 1 per cent of our national expenditure to the under-developed countries, thought that we could do much more and that these territories offer great potentialities for the production of increased wealth. The President of the Board of Trade, Mr R. Maundling referred to our need to increase our balance of payments position if we are to play our full part in helping the development of these countries and Mr J. Arbutnot sug-

gested that reduced taxation in these countries would greatly assist in the creation of the conditions for development.

Mr Anthony Head emphasized the vital importance of giving adequate attention to the backward, dependent and under developed countries during the next five or ten years. He directed attention more particularly to the educational problem, and urged that here the West needs to overhaul its whole approach, and that co-ordinated effort is imperative. In this he was supported by Mr K. Zilliacus, who pointed out that economic co-operation and the provision of financial, economic and technical assistance to backward countries internationally through the United Nations represent the support of constructive and modernizing forces. Sir Henry d'Avigdor Goldsmid and Mr J. Grimond spoke strongly in the same sense, Mr Grimond referring also to the importance both of the type of government which is established in the newly independent territories and of education, including technical education. Mr Philip Noel Baker was somewhat critical of the magnitude of our present contribution. Although our contribution to United Nations Technical Assistance has risen from 2.5 to 3.0 million dollars, the Commonwealth has every year received far more from Technical Assistance than it has paid in, and against the increase in our contribution to the United Nations Special Fund from 1 to 5 million dollars should be set the scheme, costing 15 million dollars, for work in the Commonwealth already submitted by the Colonial Office to Mr P. Hoffman. Moreover, the £1,000 million loan to the under developed countries by the International Bank during the first twelve years of its existence was less than one tenth of the extra capital required during the following ten years to achieve Mr Hoffman's objectives.

Replying on the debate, the Minister of State for Foreign Affairs, Mr J. Profumo, recognized the importance of the struggle for man's minds and the part which the Chancellor of the Duchy of Lancaster has to play in that connexion. He also took up the point about education which had been stressed separately in the Queen's speech in a reference to the introduction of legislation to implement recommendations of the Commonwealth Education Conference, which had been warmly welcomed by Mr E. Gardner and, in the House of Lords by Lord Hastings. Lord Home noting that the presence of 42,000 overseas students in Great Britain put a considerable strain on our universities and technical colleges, welcomed Lord Hastings's reference to the importance of education nevertheless he thought that the task of equipping youth to meet the intellectual, physical and moral challenge of the time will strain our resources to the full. Apart from a reference by Mr P. Wall on November 2 to the way in which the under-developed countries in Asia, Africa and the Middle East are beginning to realize the importance of European capital and European technicians, there was no further reference to the under developed countries in the debate on the Address although others besides Mr Wall stressed the importance of education when the position in Central Africa was discussed at some length on November 2.

NEW RESEARCH LABORATORIES FOR THE CAMBRIDGE INSTRUMENT COMPANY, LTD.

By DR. M. C. MARSH
Head of Research Department

ON October 14 a new block of research laboratories for the Cambridge Instrument Company, Ltd., was opened by Lord Adrian, Master of Trinity College and until recently Vice-Chancellor of the University of Cambridge. Following the opening, about 120 distinguished guests were entertained to lunch by the Directors of the Company, and they afterwards had an opportunity to inspect the new accommodation. On October 16 an open day was arranged for shareholders and for guests from the University and from several research establishments in the neighbourhood of Cambridge. About four hundred guests availed themselves of this opportunity. On both occasions the guests were received by Dr P. Dunsheath, chairman of the Board of Directors, and Mr H. C. Pritchard, managing director of the Company.

This new building is the result of a decision to expand greatly the research and development facilities of the Company. It provides about three times the previous floor area and permits the whole of these activities, which before this were dispersed in various parts of the works, to be brought under one roof, together with a design and drawing office.

The new laboratories are situated in Chesterton Road, adjacent to the Cambridge factory. They have a very fine view over the River Cam and over Jesus Green and provide accommodation suited to the work to be undertaken. As will be seen from Fig 1, the clean, modern appearance of the building is emphasized by large windows that run the length of the first three floors and also by the colour contrast afforded by the light buff brickwork of the side walls and the dark green of the slate panels beneath the front windows. The building, which has a floor area of approximately 20,000 sq ft, has four storeys and is provided with a three-storied entrance block and a rear link block giving access to the factory buildings. The mode of construction gives a clear area on each floor entirely uninterrupted by columns or beams, and extensive use has been made of modern building materials and fittings, such as red thermoplastic flooring, heating coils embedded in the structure, double-glazed windows and acoustic panels.

The entrance block is distinguished by a spacious entrance hall, which is decorated in contemporary style and contains an instrument showroom and a reception area. The block also houses offices and a lift serving all floors.

The laboratory block consists of four floors approximately 100 ft long and 40 ft wide. On the ground floor is the mechanical engineering laboratory with its

offices, stores and constant-temperature room. Instrument makers' benches and experimental benches are arranged mainly beneath the front windows, and the remaining floor space is taken up by precision machine tools and mechanical laboratory equipment. The first floor is devoted to physics and electronics. It has a large and airy main laboratory, offices, dark room and optical laboratory, standards room and electronics workshop. The second floor houses the physical chemical laboratory which, in addition to offices, has special rooms for balances, glass-blowing and for chemical preparations. Polythene and 'Vulcatlono' fittings are used in a special system for draining chemical waste from this floor. The top floor is taken up by design and drawing offices. Excellent lighting is provided by a number of roof-lights in addition to windows running the entire length of both walls. Along the front of this floor is a covered balcony, edged with flower-boxes.

In designing the laboratories, great stress has been laid on versatility. With this in view all the services are laid in trunks of ample size, and it would be an easy matter to add any facilities not originally provided. Besides the usual supplies of gas, water and electricity, there is a special low-voltage electrical supply for portable apparatus. At 18 places there are boards containing four terminals and an appropriate switch. From a central control board it is possible to feed to these terminals a three-phase and neutral supply of any required voltage, single-phase a.c. of any voltage up to 250 volts at frequencies between 25 and 60 c/s, a.c. stabilized against changes of voltage and frequency and d.c. between 0 and 250 volts. These supplies are obtained from trans-

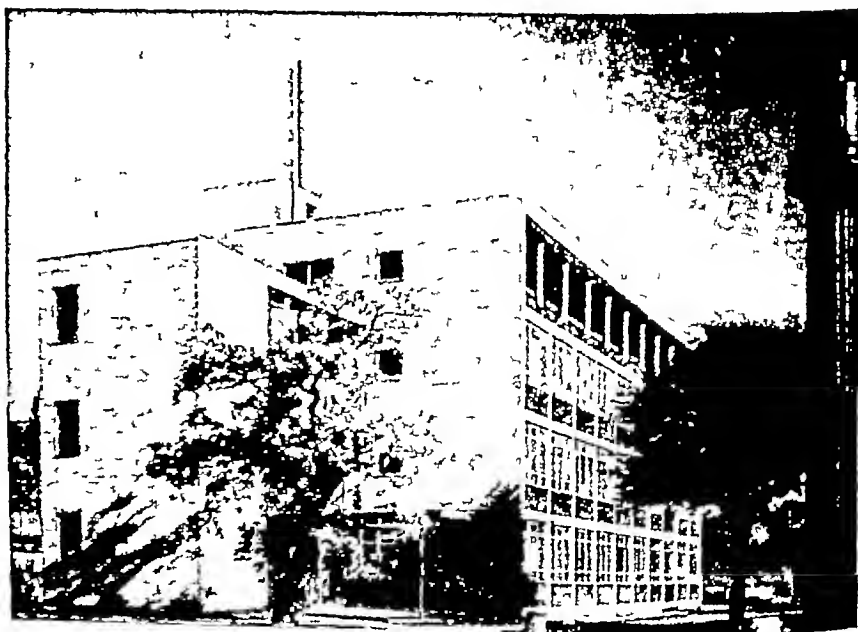


Fig 1 Research Laboratories of the Cambridge Instrument Company, Ltd

formers, stabilizer and a Ward Leonard set with a connected motor alternator. The last two are situated in a cellar but are controlled from two points in the laboratories. On the third floor a large glass de-aerator of special design has been fitted in order to supply oxygen free water for researches on boiler feed water problems. Compressed air of high and low pressure is supplied to all laboratories, with an extra high pressure supply in the mechanical laboratory.

The building was completed in the remarkably short time of just under one year by Messrs J Jarvis

and Sons, Ltd. (London and Manchester), to the design of the architects, Messrs Edward D Mills and Partners. Light oak furniture with oak tops has been supplied to all the laboratories by Messrs Baird and Tatlock (London), Ltd.

These laboratories are now fully occupied and with an expanding staff, a large programme of research and development work is being undertaken. This programme relates to improvements to instruments which are already being manufactured, as well as to a number of entirely new projects in which the Company is interested.

CARBON-DATING CONFERENCE AT GRONINGEN

SEPTEMBER 14-19, 1959

ON the invitation of Prof. H. de Vries (Natuurkundig Laboratorium) and Prof. H. T. Waterbolk (Archaeologische-Biologisch Instituut), of the University of Groningen, a small conference of scientists from carbon-dating laboratories was held in Groningen during the week September 14-19. It was similar in character to the conferences held in Copenhagen, Cambridge and Andover, Mass., already reported in *Nature*^{1,2} and *Science*³. Twenty-two dating laboratories were represented, some well established and others just getting into their stride, from twelve countries. We were happy for the first time to welcome Russian colleagues at these meetings. Some thirty-five communications were made to the meeting, which was partly concerned with the technique of carbon-dating and partly with selected aspects of its application to geological and archaeological problems.

There was less emphasis than hitherto upon the techniques of counter and circuit design, but nonetheless there was a very interesting survey of the methods in use at various laboratories. Two laboratories described their scintillation counting technique, that at Saclay, using paraldehyde, and that at Trinity College, Dublin, using methanol. While a few laboratories use acetylene or methane in their proportional gas-counters, it seems that the majority of dating laboratories now favour carbon dioxide counting. Considerable emphasis was laid on the need for careful pre-treatment of samples, especially with difficult materials such as bone, charcoal, cave-earth and all samples of great age. Accounts were given of several promising investigations into matters affecting the principles of the method and its applications, as, for example, those at Heidelberg illustrating possible seasonal variations of radiocarbon content of the atmosphere. Particular interest was attracted by an account of the joint investigations of Cambridge, Copenhagen and Heidelberg upon possible fluctuations in the initial atmospheric carbon 14 concentration during the past 1,200 years; this is a promising extension of ideas recently suggested by de Vries⁴ as possibly offering insight into past climatic changes.

Without attempting to summarize all the interesting contributions it may suffice to point to two or three fields in which the application of carbon-dating has now apparently led to a highly significant advance in knowledge. First, we may note a series of datings made at Groningen of the earliest Neolithic

cultures from south-eastern and central Europe, indicating a spread from the Near East across these regions as early as 4000 B.C., these findings were paralleled to some extent by numerous datings made in Pisa upon Italian material.

Several contributions concerned the dating of stages of the last glaciation characterized by stratigraphic archaeology or biological and climatic evidence. Here the contribution of Groningen was particularly important, since the technique of isotopic enrichment had permitted the addition of several half-lives to the maximum possible age attainable⁵. With favourable materials that warrant this costly and lengthy process, ages as great as $64,000 \pm 1,100$ years are attainable. This in fact appears to be the date of the first mild interstadial period after the last (Weinman) interglacial. There is considerable evidence now for an interstadial about 30,000 years ago at several places in western Europe. From the American laboratories comes very convincing evidence obtained by dating ocean cores, and deposits both in the Caribbean and in salt lakes, for a very abrupt amelioration of climate about 11,000 years ago. It is striking that this climatic break corresponds exactly with the well-dated Late-Glacial period of climatic change in Europe.

A substantial part of the time of the meeting was properly devoted to various matters of co-ordination of the work of different laboratories. The successful outcome was reported of two policy decisions taken at earlier conferences, namely, to establish an agreed system of publication of date lists and to publish a punch-card system of all published dates. The first of these objectives has been met by the publication of the Radiocarbon Supplement of the *American Journal of Science*, the first volume of which appeared in May of this year. The second was met by the formation of Radiocarbon Dates Association, Inc. Mr. Fred Johnson gave a description of the principles he had adopted in designing the punch-card system and reported the first issue of cards to subscribers. It is not yet sufficiently widely known by archaeological, geological and biological laboratories concerned with the history of the past 70,000 years how massive is the contribution already made by carbon-dating to knowledge of this period, nor what a very rich source of information this punch-card system will provide. (Inquiries for subscriptions to the carbon-dating punch-card index should be directed to Radiocarbon Dates Association, Inc. Robert S. Peabody Founda-

tion for Archaeology, Philips Academy, Andover, Massachusetts, U.S.A.)

With regard to future procedure, it was decided that all carbon-dating laboratories should check by a common standard and that this should be the oxalic acid standard of the U.S. Bureau of Standards. It was agreed that a value of 95 per cent of this standard activity could be taken as the agreed radiocarbon activity for organic material (but not shells) originating in A.D. 1950. This decision should remove many of the minor difficulties caused by the different laboratories having individual standards of contemporary activity on which to base their calculations of age, and it is hoped that either the next or the next but one date-list of every laboratory will be based upon this agreed standard, which will take care of the industrial carbon and hydrogen-bomb effects upon recent samples. It was at the same time recognized that the carbonate sample provided by Heidelberg would be a further check of importance, that laboratory has undertaken the co-ordination of all inter-laboratory calibration measurements.

It was agreed to defer decision on a carbon-13 standard, pending exact absolute determinations to be made in the Lamont Laboratories.

It was agreed to use the methods of presentation of bibliography now employed in the Radiocarbon Supplement and in *Quaternaria*. The conference also recommended that new dating stations should adopt

as their index letters the most distinct and simple combination possible, avoiding those that have already been used even by stations not at present producing dates.

While there was no agreement as to whether dates ought preferably to be expressed as B.P. (before the present), or B.C. (and A.D.), there was considerable sympathy for the view that dates primarily relevant to archaeology should be given in the B.C./A.D. scale, even where the date B.P. had also been given.

Members of the conference had the concentration of lecture room attendance broken by visits to Prof. de Vries's laboratory, to the great peat bog and moraine region south of Groningen and to the dramatic areas of reclamation where carbon-dating is assisting the Geological Survey to provide fundamental knowledge of the stratigraphy of coastal deposits.

The thanks of all participants are due to all our Dutch hosts, to the Rektor Magnificus of the University of Groningen, to the Royal Dutch Shell Company, to the Chief Engineer and Director of the Rijkswaterstaat, and above all to the primary organizers of the conference.

H. GODWIN

¹ Godwin, H., *Nature*, 174, 868 (1954)

² Levi, H., *Nature*, 176, 727 (1955)

³ Johnson, F., Arnold, J. R., and Flint, R. F., *Science*, 125, 240 (1957)

⁴ Vries, H. de, *Proc. Kon. Ned. Akad. van Wetenschappen*, B, 61 (2), 1 (1958)

⁵ Vries, H. de, Vries, A. T. de, and Harris, A., *Science*, 128, 472 (1958)

ENZYMES IN THE FOOD INDUSTRY

THE Committee of the Food Group of the Society of Chemical Industry has an established reputation for organizing symposia on subjects of vital importance and with a wide range of interest to food scientists and technologists. The most recent, held on October 1-2, dealing with enzymes associated with the manufacture, storage and distribution of food, attracted an audience which taxed the capacity of the hall of the Royal Society of Medicine in which it was held. The organizers very wisely decided to limit the scope of the contributions and to divide them roughly into two groups: one dealing with the production of enzymes and their use in manufactured foods and the other with the activity, both useful and deleterious, of naturally occurring enzymes in foods.

Dr. Malcolm Dixon opened the symposium with a paper, giving in his own characteristic way the necessary background information on the types of reactions which may be catalysed by enzymes, and such of their properties as would have a bearing on the matters discussed by later speakers. The value of such an introduction to a symposium covering a broad field of biochemistry cannot be too highly stressed when it is appreciated that the audience was composed mainly of persons connected with the food manufacturing and processing industries, specialists maybe in rather limited fields, who frequently find it hard to keep abreast of fundamental developments.

The remainder of the first day was given over to papers dealing with fungal amylase, invertase, rennin, glucose-oxidase, the pectin-degrading enzymes and proteinases from plants and micro-organisms. The main interest in fungal amylase and invertase was in the methods adopted to secure conditions of

culture of the selected organism so that high yields of high-purity enzyme are possible on a commercial scale. The discussion on the papers not unexpectedly centred around the newer applications of enzymes by the food industry and in particular the use of amylase in bread-making, the application of such proteinases as papain, bromelain (from pineapple) and ficin (from figs) to meat with the view of increasing its tenderness, and the recent availability of glucose oxidase as an oxygen scavenger in packaged foods.

The proceedings of the first day having presented the enzymes in a favourable light, as processing aids in a variety of food products, the second day, devoted to "Innate Enzymes: Their Action and Control", revealed the reverse side of the medal and showed enzymes in a less co-operative mood. This was not unexpected. Dr. Dixon, in his introductory remarks, had already pointed out that foods are the product of enzyme action in the living plant or animal and are metabolized after consumption by enzyme action in the body of the consumer, stressing the fact that in the living cell the urge of the enzyme processes is towards synthesis and that enzyme changes in foods, which can be regarded as post-mortem changes, may well be deteriorative in character. It is, however, sometimes difficult to draw the line, the enzyme ripening of fruit leads progressively into the deteriorative changes of over-ripening. Other cases are more specific: papers presented during the day dealt with enzymic deterioration in colour (blackening of potatoes by polyphenolase), in flavour ('soapiness' in coconut and palm kernel oil products due to liberation of free fatty acids by lipase action) and in nutritive value (oxidation of ascorbic acid and of vitamin A precursors in plant tissues).

The problem of control is a formidable one. Cold storage merely delays but does not prevent enzymic deterioration, since enzyme reactions, like all other chemical reactions, are slowed but not stopped by lowering of temperature. Other standard methods such as the addition of inhibitors or competitive substrates, are by no means universally applicable. Probably the most commonly used procedure is that of heat inactivation ('blanching'), but this can lead to unwanted structural changes in fruits and vegetables. At present there is no simple and universal solution.

It must be said that on one point the arrangement of the symposium was open to critical attack: namely, the lack of time available for free discussion. It is in this discussion that the value of a symposium such as this largely resides, both for the audience and for the contributors themselves. Arrangements had been made for the discussions to be opened by appropriate authorities and these authorities presented what virtually amounted to additional contributions, com-

parable in weight and importance to those of the main contributors. On this account, the unscripted discussion was seriously restricted, particularly at the final session, and a number of potential questions had to remain unasked and unanswered. This was undoubtedly a loss and one can but ask that the point should be borne in mind when future symposia are being planned.

It is, however, pleasant to record that the symposium went with a swing to the end and was closed by the clock: there was no noticeable whittling away of the audience as special interests were disposed of. In its lighter moments the meeting considered future possibilities, these included 'tailored' enzymes for specified purposes and the application of enzymes to the restoration of flavour in over-cooked cabbage. It was also pointed out that one speaker had coined a new word—the verb "to enzyme". The purists may refuse to accept this innovation, but we must all accept the importance of the process it describes.

BIOCHEMICAL RESEARCH IN INDIA

GOLDEN JUBILEE SYMPOSIUM

A SERIES of symposia was organized by the Department of Biochemistry, Fermentation and Pharmacology Laboratories of the Indian Institute of Science, as part of the celebrations of the golden jubilee of the Institute during August 28–30 and was attended by more than two hundred scientists including fifty delegates representing important centres of biochemical research in the country. The subjects covered were: Biology and Biochemistry of Micro-organisms; 'Enzymes' and Vitamins.

The symposia were inaugurated by Dr S Bhagavantham, the director of the Indian Institute of Science, and the first day of the session was presided over by Major General S L Bhatia, who spoke on the "Progress of Physiology and Biochemistry in India". Prof P S Sarma, who presided over the proceedings of the second day, outlined the contributions in enzyme chemistry made by the late Prof K. V. Giri (see *Nature*, 182, 1201, 1958). Dr V N Patwardhan, who took the chair on the third and final day of the symposium, gave an address on the mode of action of vitamin D on which he and his group have been working for the past two decades. He and his collaborators have adduced experimental evidence to show that vitamin D acts presumably by promoting the synthesis of citric acid in the epiphyseal cartilage. Dr V Subrahmanyam, director of the Central Food Technological Research Institute, Mysore, who was professor of biochemistry in the Indian Institute of Science from 1931 until 1949, reviewed the work done in the department during his regime. He gave a brief account of the development of the Bangalore process of composting the elucidation of the principles of sewage purification, the preparation of a material from paddy husk for defluorinating fluoride-containing waters and the preparation of insulin and other hormones from slaughterhouse material and vegetable 'milk' from soybean. Prof M. Sreenivasaya, who was one of the pioneers in enzyme chemistry during the early years of the Biochemistry Department, described the elegant method developed by him for the study

of enzymes both by the ultra-micro- as well as by micro-dilatometric methods.

Sixty nine original research papers were presented at the symposia, and only a selection can be mentioned here.

M G Bhat of the Indian Institute of Science read a paper on the nutrition and metabolism of *Pseudomonas convexa* var. *hippuricum* representing the work done by her in collaboration with Drs T Rama krishnan and J V Bhat. Detailed investigations with regard to the nutritional requirements and metabolic pathways of this organism, which was isolated from soil using the enrichment culture technique were outlined and a new pathway of benzoate breakdown by the bacteria involving salicylate, a mechanism different from the classical scheme of the metabolism of the aromatic ring, described. M K Subrahmanyam (Indian Institute of Science) gave a résumé of his studies on the cytology of yeast, which included the demonstration of the presence of a nucleus and a vacuole as well as the occurrence of nuclear and vacuolar membranes in the yeast cell. He also pointed out the general similarity of the structures of yeast and plant nuclei.

M. Chakravorty and D P Burna of the Bose Institute, Calcutta, presented a paper on 'Microbial Synthesis of Protein in Relation to the Biogenesis of Nucleic Acids'. Using phosphorus 32 and sulphur 35, they have shown that in the resting cell of *Azotobacter vinelandii* conditions under which nucleic acid synthesis is inhibited lead to a decrease in protein synthesis. On the contrary, it was found that the incorporation of phosphorus 32 into the nucleic acid continued in an uninterrupted manner even when protein synthesis was inhibited. P S Sarma and co-workers, of the University Biochemical Laboratory, Madras, working on metal requirements of nicotinamide deaminases, have investigated the inhibition by metal-chelating agents of nicotinamide deamidating systems in cell free extracts of micro-organisms and the soluble fractions of pigeon liver. A study of the reversal of the inhibition produced

by α - α' -dipyridyl with various metal ions, has shown that the enzyme systems in the insect *Corcyra cephalonica* St., pigeon liver and chick kidneys are reactivated by Fe^{++} , that in *A. niger* by Mg^{++} and the one in *N. crassa* by Mn^{++} .

The detection and purification of a stereo-specific dihydrolipoic acid dehydrogenase formed the subject-matter of an interesting paper by D K Basu and D P Burma, of the Bose Institute, Calcutta. The enzyme, which was purified 60-70-fold, was found to be diphosphopyridine nucleotide-linked and specific for dihydrolipoic acid and its amide. The reaction was irreversible when tested with lipoic acid as the substrate. I S Bhatia and co-workers, of the Tocklai Experimental Station, Cinnemara, Assam, gave an account of their work on the transglycosidase present in tea leaves. This enzyme reacted with maltose with the formation of maltotriose, maltotetrose and glucose. With arabinose as the acceptor of glucosyl residues and maltose as the donor, a disaccharide containing glucose and arabinose was formed.

The purification and properties of glutamic-oxalacetic transaminase from ox brain and from human brain were described by T N Pattabhiraman and B K Bachhawat, of the Christian Medical College, Vellore. A 30-40-fold purification of the enzyme was achieved by fractionating the initial extract with alcohol, Zn^{++} and ammonium sulphate. The purified ox-brain transaminase showed complete dependence on pyridoxal phosphate for its activity.

A new type of enzymatic transamination reaction in which glyoxylate transaminates with a number of amino-acids to produce glycine was reported by L V S Sastry and T Ramakrishnan (Indian Institute of Science). Isonicotinic acid hydrazide and L-penicillamine at low concentrations inhibited the enzyme but the inhibition was reversed by pyridoxal phosphate or metal. The authors adduced unequivocal evidence to show that the transaminase was a metallo-enzyme. The purification and properties of a naturally occurring inhibitor of glutamine synthesis

present in *Pongamia* galls was described by N K Sukanya and C S Vaidyanathan (Indian Institute of Science), they also showed the preponderance of this inhibitor in the gall tissue, as compared to normal tissue.

N Appaji Rao, H R Cama and S A Kumar (Indian Institute of Science) gave details of some of their recent work on the occurrence of flavin nucleotides in plants and the changes in their concentration with germination of green gram (*Phaseolus radiatus*) and cow pea (*Vigna catianga*). The radicle of the germinating seedlings contained almost all the flavin adenine dinucleotide and the major portion of the total flavin, while the cotyledons and the plumules contained flavin mononucleotide as the major flavin. Some interesting examples of species specificity in the mechanism of pyridine nucleotide synthesis by erythrocytes were reported by P. G. Tulpule, of the Nutrition Research Laboratories, Hyderabad. Of the seven species studied by them only human and guinea pig erythrocytes were capable of synthesizing diphosphopyridine nucleotide from nicotinamide and glucose. Human as well as monkey erythrocytes could also synthesise appreciable amounts of diphosphopyridine nucleotide from nicotinic acid and glucose in the presence of glutamine, whereas this metabolic pathway did not seem to operate in the guinea pig. Red blood cells of the monkey were able to synthesise diphosphopyridine nucleotide only in the presence of glutamine, suggesting that nicotinamide was converted to nicotinic acid prior to incorporation in diphosphopyridine nucleotide.

Four special lectures were given in the evenings on each day of the symposium. Dr D P Burma, of the Bose Institute, Calcutta, on "Pentose Phosphate Metabolism", Dr B K Bachhawat (Christian Medical College) on "Purification of Enzymes", Dr P M Bhargava (Regional Research Laboratories, Hyderabad) on "Protein Synthesis" and Dr T Ramasarma (Indian Institute of Science) on "Coenzyme Q".

P S SARMA

NATIONAL VEGETABLE RESEARCH STATION

NEW LABORATORY BUILDING

THE new laboratory building of the National Vegetable Research Station was officially opened on October 23 by H R H The Duke of Edinburgh.

The decision to establish the Station was taken after the Second World War because of a continuing need to encourage vegetable production in Great Britain, and the Agricultural Research Council is now responsible for government grant-aid to finance the Station and for the general supervision of its scientific programme.

The new building marks the culmination of ten years development from the time when the director, Dr J Philp, took over 280 acres of land at Wellesbourne, near Warwick, in September 1949. Initially the site had no electricity, roads or suitable water supplies, and the only buildings were three small cottages and a few farm buildings. Building restrictions in the early years severely hampered development and the research staff had to be housed temporarily in old service huts, while Dutch light structures served as temporary glasshouses.

The new laboratory building was designed by Mr F W Holder, chief architect of the Ministry of Agriculture, Fisheries and Food, and has a total floor area of 33,800 sq ft. Besides laboratories and offices it contains a library, lecture room and committee room, and the basement has space for the future provision of controlled-environment chambers. The construction uses pre-cast concrete frame and floors with external curtain-walling of insulated plastic and some brickwork, the roof being of copper. The Station also has about a half-acre of glasshouses used for pot-experiments in research projects, a packing shed, implement shed, farm stores and buildings for livestock. 170 acres are served by underground irrigation mains with a borehole for the water source.

The site at Wellesbourne is central for the country as a whole and the soil and climate are suitable for vegetable production, being similar to those in the nearby Vale of Evesham, an important horticultural area. The area of 280 acres, to which 95 acres have

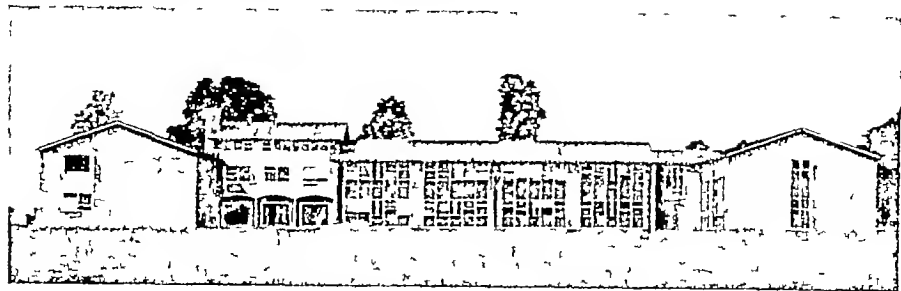


Fig 1 New laboratories of the National Vegetable Research Station

recently been added allows a farm unit to be run in conjunction with the experimental vegetable crops and is large enough to provide the isolation necessary for some of the research work. In addition, there is a sub station at Pagleham, Essex, with an area of 150 acres, which is chiefly used for the multiplication of seed stocks.

All vegetable crops grown in the open and in cold frames, except potatoes, come within the purview of the Station, and its work is organized under eight sections: plant breeding, chemistry, physiology; irrigation, entomology, pathology, weed control, statistics.

Long term experiments with a rotation of vegetable crops are now in their sixth year. The treatments comprise organic and inorganic fertilizers, time and frequency of application of nitrogen, and methods of soil cultivation. Growth studies are being made on some of the crops in these experiments to obtain information on the stages of growth most affected by fertilizers, the weed populations and soil moisture characteristics of the soils under different cultivation methods are also being investigated. Dung has been shown to exert a marked influence on growth during the very small seedling stage.

Plant-breeding is carried on at a practical level with the production of improved varieties of vegetables, and at a more fundamental level with the application and development in vegetable crops of breeding methods as such. The method of inbreeding to attain uniformity followed by crossing to restore vigour, used so successfully in maize, has been applied to brussels sprouts, and hybrids with yields 40 per cent above the parent strains have been produced. The backcross technique is being used for the introduction of winter hardiness into an otherwise satisfactory quick freeze variety of pea. In the delicious species, asparagus, where the male plant is commercially desirable and usually heterogametic, isolation of homogametic male plants has produced strains giving all male progeny on crossing.

Entomological research is mainly concentrated on the carrot fly, the cabbage-root fly and the lettuce root aphid. Ecological work on the effect of insecticides on the balance between the cabbage-root fly and its predators has shown that the balance can be tipped in favour of the pest by indiscriminate broadcast application of insecticides. The use of insecticides against carrot fly raises problems of off flavours in the crop and of the possible build up of insecticides in the soil. Extensive testing tests have been carried out at the Station with carrots to assess the effect of insecticides on their flavour. A technique which

has been developed for the assay of insecticide residues in the soil enables concentrations of dieldrum as low as 0.05 p.p.m. of soil to be measured.

The diseases of vegetable crops are as diverse as the crops themselves. The silencing disease of red beet which is bacterial has been successfully controlled with streptomycin. Fungal diseases include the long known club root of brassicas and the relatively new crook root disease of watercress. New fungicidal techniques give hope of controlling both these, while the prevention of virus diseases in watercress and lettuce is being sought through the production of clean stocks. The development of resistant varieties by selection and breeding techniques is being tried for parsnip canker and *Didymella* stem rot of tomatoes.

Work on the irrigation of vegetables has been primarily concerned with the most efficient use of water. Moisture-sensitive periods during growth have been found to exist with some vegetable crops and at these periods irrigation has its maximum effect while at others it does not produce an economic response. Work has been started on the relationship between water and nutrient uptake in the root system and on the use of additives to irrigation water.

The newer residual herbicides are being tested for suitability on a wide range of vegetable crops, and work has recently started on the nature and extent of the damage to vegetable crops caused by the drift of spray from herbicides used on neighbouring agricultural crops. The effects of weeds are also being studied in two other aspects. The unevenness of weed distribution has been shown to be partly responsible for field plot variation in the yields of experimental crops and the reduction in crop yields caused by weeds has been found to be affected by the spatial arrangement of the crop plants. Suitable mathematical models to describe the growth of some crop plants are being sought, with the view of improving the interpretation of treatment year interactions in long term experiments.

On the practical side the Station maintains close links with the National Agricultural Advisory Service and is fortunate in being able to make use of the experimental horticulture stations of this body for the further testing of experimental findings under a wider range of conditions. On the academic side, an arrangement with the University of Birmingham enables postgraduate work carried out at the Station to be recognized for the purpose of obtaining internal higher degrees of the University.

J. A. NELDER

THE GRASSLAND RESEARCH INSTITUTE

IN the past, grassland has received much less than its due share of attention from the scientist, but some of the extensive work on this subject now being done in Great Britain is summarized in the recently published annual report for 1957-58 of the Grassland Research Institute (*Experiments in Progress*, No 11 Pp 108 Hurley, near Maidenhead Grassland Research Institute, 1959 7s 6d) Many aspects of the composition, treatment and use of grassland swards are investigated by the nine departments The Department of Herbage Agronomy is concerned with management, yield and quality of herbage at all seasons of the year, and the emphasis has shifted from comparison of species and varieties to establishment and management of the sward Continuation of the study of the relationship between white clover and top-dressings of nitrogenous fertilizer has shown that the effect of white clover on gross yield of herbage was equivalent to approximately 9 cwt per acre of a nitrogenous fertilizer annually on a no-clover sward The results of experiments with gibberellic acid showed that response to nitrogenous fertilizer at 4 cwt per acre was greater than response to 2 oz per acre gibberellic acid Nitrogen plus gibberellic acid produced an additive effect at first, but in the presence of nitrogen there was a significant depression in yield as a result of gibberellic acid treatment, depression was greatest where the initial response to gibberellic acid was marked

In the Section of Animal Agronomy, grassland production is measured in terms of the animal Better live-weight performance per animal was obtained when cocksfoot was grown with lucerne than when lucerne was grown alone A comparison of two methods of sowing and managing lucerne and cocksfoot indicates that it is possible to extend the grazing season by about four weeks in the autumn by use of nitrogenous fertilizers The live-weight gain per acre of ewe lambs carried throughout the

year at a stocking rate of 61 per acre was, on average, 65 lb higher on swards containing white clover, although the grass swards received nitrogen to compensate The comparative influence of leys, variously managed, on the yield of subsequent cereal and kale crops has been investigated by the Department of Ley Agronomy It is demonstrated that management of ley swards has an appreciable effect on yield of the following crops This is accounted for largely by the nitrogen status of the soil The study of the intake and digestibility of herbage is one of the main concerns of the Department of Biochemistry and Animal Nutrition This involves both feeding experiments and biochemical studies of herbage plants The former have shown that certain of the major grasses are more digestible than others and the latter that the older methods of fractionation are too arbitrary, modern techniques are likely to give a more reliable assessment of digestibility

The work of the Department of Plant Physiology is linked with that of Herbage Agronomy in laboratory and field The detailed growth studies are likely to provide valuable guidance on grazing practice. Experiments in microbiology are connected to soil and herbage studies in other departments, with emphasis on the examination of the processes of decomposition which take place when the ley is ploughed A small experiment on sterilization of grass by radiation suggests that it may be possible to preserve grass for several months without undue changes in palatability Extra-mural experiments provide supplementary evidence over a wide variety of environmental conditions Such experiments are usually done in collaboration with the National Agricultural Advisory Service The Department of Biometrics provides statistical advice and a computing service for other departments and has commenced its own field-experiments to answer specific questions

SCIENTIFIC RESEARCH IN ALBERTA

THE thirty-ninth annual report of the Research Council of Alberta, covering the year 1958, stresses the work on ground water geology and the studies on the Precambrian Shield area of north-east Alberta (Report No 78 Pp 66 Edmonton Research Council of Alberta, 1959) Work was commenced on the delineation of areas with large coal reserves which could be developed by industry as a source of power, and reconnaissance surveys were made of alkali lakes in Alberta and of the mountains west of Nordegg A laboratory study of till from the Cooking Lake moraine showed that electrical potentials up to 0.5 V can be generated in soil between individual horizons by natural processes Soil surveys continued and a study is being made to determine the characteristics of the dominant parent materials of Alberta soils, the composition of the glacial till and the local variations Further work at Youngstown showed that the productivity of the solonch soils was limited by the physical condition of the soil, times and timeliness of irrigation being both critical under such soil conditions The hail reporting net-

work was further extended and valuable results were obtained in spite of an unusually low incidence of hail in the area The highway research programme was largely concerned with the instrumentation and study of a five-mile portion of the trans Canada highway west of Calgary, on which test sections of three different types of concrete pavement were laid

Fundamental studies on coal in the organic chemistry laboratory included an examination of reactions of humic acids, a preliminary survey of the properties of kerogens and other organic substances associated with inorganic sediments, and substantial progress in the separation of the products obtained by oxidizing pyrolysed truxene with nitric acid The main effort of the physical chemistry laboratory was in studies of the mechanism of thermal decomposition of coal and the control of the decomposition by gaseous and gas-entrained additives, but the effects of ultrasonic irradiation on small molecules were also examined and the viscosity characteristics of solvent extracts from coal and the shape and size

of the extracted molecules. In paleobotany substantial progress was made in formulating means for identifying fossil spores and pollen grains and the development of a key for identifying living and fossil conifer woods is now virtually complete. Further studies are reported on fluidized carbonization, and the first stage of a coal grindability investigation was completed. In the petroleum division studies continued of the catalytic desulphurization of sulphur compounds at high temperatures to remove sulphur as hydrogen sulphide and on the oxidation of sulphur compounds to remove it as sulphate. The study of two phase flow of oil and water in pipe lines was

continued in which a general mathematical analysis was developed for two immiscible fluids flowing between wide parallel plates and flowing concentrically in a circular pipe. Considerable progress was made in the study of the effects of hydrogen isotopes on the rates of chemical reactions, while the study of the retention volumes of hydrocarbon gases on chromatographic columns of a series of activated charcoal has been extended to an examination of the relative widths of the chromatographic bands. The autothermal surface combustion reactor for pyrolysing hydrocarbons was further developed. A list of publications of the Council is appended.

BIOLOGY OF AMOEBA

THE late Robert Chambers was a much loved personality on both sides of the Atlantic. A publication by the New York Academy of Sciences has been greatly influenced by him, many papers being presented by his former students and second generation* of students*. The papers deal exclusively with the 'fission cycle' of the life history of *Amoeba*. I first made acquaintance with Chambers when studying *Daphnia pulex*, each having worked out its spermatogenesis. Later, I sent to him supplies of *A. proteus* at various localities.

An article by Mazia in 'Science in Progress' prepared readers for some of the many good things in this volume. After a short biography of Chambers and an introduction by Hirschfeld the subject-matter is grouped into four parts. In part 1 ('Structural and Taxonomic Considerations') Torch describes the cytology of *Pelomyxa*. The most interesting conclusion is that crystals are a metabolic waste product, probably an accessory mechanism for the excretion of nitrogen. Particulates of *Amoeba* are studied by Kessel using a drop retraction technique, proteins on reaching an experimentally introduced oil-water interface unfold and produce a surface denaturation curve resembling that of a medium containing a protein of low molecular weight. Useful practical hints and photographs of apparatus, as well as electron microscope studies, are given in 'Microscopic Studies' by Borysko and Roslansky. Beautiful electron microscopic work by Pappas reveals the astounding presence of fine fibrous extensions on the outer surface of the plasmalemma of three species of *amoeba* and other unsuspected structures. Kudo gives a welcome résumé of the work of the early observers and their nomenclature and makes a strong plea for the retention of the name *Amoeba* for the genus.

In part 2 ('Physical Studies and Cell Division') Landau deals with sol-gel transformations in *Amoeba*, and considers that the findings of myosin like proteins in amoeboid forms lend credence to the idea of a contractile substratum. 'Synchronization of Cell Division' by James gives much fascinating detail of the observations made during the establishment of the main thesis. Three authors describe pinocytosis which was discovered by Lewis and observed by Mast and Doyle in *amoeba*, but only recognized as important in the past few years. Holter, in the next paper, gives some beautiful pictures of the phenomenon, and stresses its im-

portance in the physiology of amoeboid cells though he thinks that the original definition may require modification towards less emphasis on the fluid uptake and more on the dissolved substance.

A very long paper of sixty-three pages by Guthwin and Kopac is a vade mecum for the microscopist enzyme chemistry of carboxylic esterases in *Amoeba*. 'Cytochemical Differentiation in Normal and Starving *Amoeba*', by Heller is the second article of part 3. An interesting analysis of the cytoplasmic inclusions deals with refractive bodies. As I have repeatedly pointed out, these refractive bodies are nutritive, and for that reason Dr Carmola Hayes renamed them 'nutritive spheres'. They play a great part in the formation of the spores in the *Proteus* group of *Amoeba*. Their diameter is indicative of the age of the *Amoeba*—an individual with large nutritive spheres is old and ready to sporulate. Cohen, in 'Physiological and Morphological Observations' gives the first hint as to the great weakness of the work under review when he says "A *proteus* in our experience consists of at least two strains investigators should give the history of the stock they use". I maintain that two distinct species masquerade under the specific name *proteus*. I have had an opportunity of studying a rich culture from the laboratory of Brachet—it was *A. lecheriae* and not *A. proteus*. It also contained very young stages of development, proving that even under rigid subculturing a few individuals escape and sporulate. Want of space prohibits more than mention of "Tracer Studies in *Amoeba*" by Plant, "Effect of Selected Chemical Agents on *Amoeba*" by Zimmerman.

In part 4 Hirschfeld discusses "Nuclear Control of Cytoplasmic Activities" and Prescott pictures the wonderful Cartesian diver for weighing *Amoeba* in his article on microtechnique in amoeboid studies. "Microchemical Studies on Irradiated *Pelomyxa*", by Daniels, is followed by an account of the celebrated work of Danolli on strains of *Amoeba* that have been continuously cultivated for years in King's College, London. In conclusion, one would urge the examination of older *Amoeba* for the presence of deoxyribonucleic acid. Brachet's beautiful work on the 'Cytoplasmic Dependence in *Amoeba*' evidently omits this. The volume ends on a lighter vein when Kopac visualizes *Amoeba* research in 2168. Used in conjunction with Jepp's "The Protozoa, *Sarcodina*", this volume is a useful reference book for all students of *Amoeba*.

MONICA TAYLOR

* Annals of the New York Academy of Sciences Vol 78, Art 2. The Biology of the Amoeba. By Henry I. Hirschfeld and 22 other authors. Pp. 401-704 (New York: New York Academy of Sciences 1959) 4.50 dollars.

1 Science in Progress" edit. by Taylor Hugh 10th Series (New Haven Yale)
* Jepp H. W. "The Protozoa Sarcodina" (Oxford and Ford Edinburg 1954)

VALUE OF CONTOUR ANALYSIS IN EQUATORIAL METEOROLOGY

By D. H. JOHNSON and D. H. T. MORTH

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SINCE November 1958, daily contour analyses have been made at the East African Meteorological Department, Central Forecast Office, East Africa, for standard pressure-levels from the surface to 100 mb, and for an area which includes all Africa, and Europe to 55°N. Such analyses are believed to be unique for Africa—they are giving an insight into mechanisms governing equatorial weather which has not been provided by conventional streamline analyses of the upper winds.

Flow and changes in the flow are as dependent in the tropics as elsewhere on the pressure field and its evolution. However, the want of radiosonde data, lack of success in explaining day-to-day variations in weather in terms of the surface pressure field, and the absence of a fixed relation between pressure gradient and wind, have led to a concentration in the past decade on streamline analysis alone. Streamlines define usefully the instantaneous wind but they have failed in everyday use in East Africa to account satisfactorily for the observed weather, and they have contributed little by themselves to the solution of forecasting problems. Improvements in radiosonde and radar wind coverage over Africa, due largely to the stimulus of the International Geophysical Year, now permit some deductions regarding the role of the upper pressure distribution to be made.

Principal points of contrast with middle-latitude upper patterns are (a) equatorial pressure gradients are weak, a consequence of the inability of other terms in the equations of motion to balance a large pressure force in the free atmosphere, (b) pressure systems which influence East African weather are slow-moving or stationary and weather changes are effected more often through development *in situ* than by travelling disturbances.

Though the observations are still insufficiently dense and accurate to define the contours precisely, certain characteristic states have been recognized. An important case arises when upper anticyclones in the lower latitudes of each hemisphere are separated by a trough along the equator (Fig 1). This system is associated with zonal flow. Pressure gradients and winds derived by assuming a geostrophic balance agree well with observations. When the contours are confluent as in the right of Fig 1, acceleration leads to convergence near to the equator, and if the convergence extends in depth through the lower layers, a rain-producing mechanism exists. Understandably, the most marked effects on the weather occur when the pressure field is not stationary, but either or both of the anticyclones change their intensity or location, the accelerations are then potentially greatest since the geostrophic balance is particularly delicate due to the smallness of the Coriolis parameter.

A second well-defined model occurs when a meridionally directed pressure gradient exists across the equator (Fig 2). The geostrophic departure increases as the equator is approached and the unbalanced pressure force at the equator itself leads simply to down-gradient (Eulerian) flow—the contours are

crossed perpendicularly by the streamlines a few degrees downstream of the equator, the lag being due to the zonal momentum carried. This model was observed primarily in the period January–March 1959 when, in the lower troposphere, the low pressure to the south took the form of a zonal trough. Cochemé¹ has remarked on the predominance of this pattern near the surface during February 1955 and has noted the resemblance to the large-scale monsoon flow associated with the Indian summer low pressure. On other occasions the low pressure is the equatorward portion of a large-amplitude trough in the polar westerlies which has penetrated the subtropical anticyclonic belt. This pattern was typically associated with lower divergence and fine weather north of the equator and with rain in the convergent westerlies to the south.

The foregoing two cases have been illustrated in simple form, but smaller scale complications, some orographic, some developmental, may be superimposed upon them, and the two patterns can co-exist in adjoining longitudes. Other characteristic states arise. Of particular importance are those which give rise to westerlies in the lower half of the troposphere. East African meteorologists have long recognized an association between westerly winds and widespread rain. Previously this has been ascribed to the presence of a source of moisture to the west. We observe, however, that a more than adequate supply of moisture is carried inland in the lower layers of the easterly monsoon currents, and consider this to be the more important moisture source for East African rainfall. Westerly flow is often simply

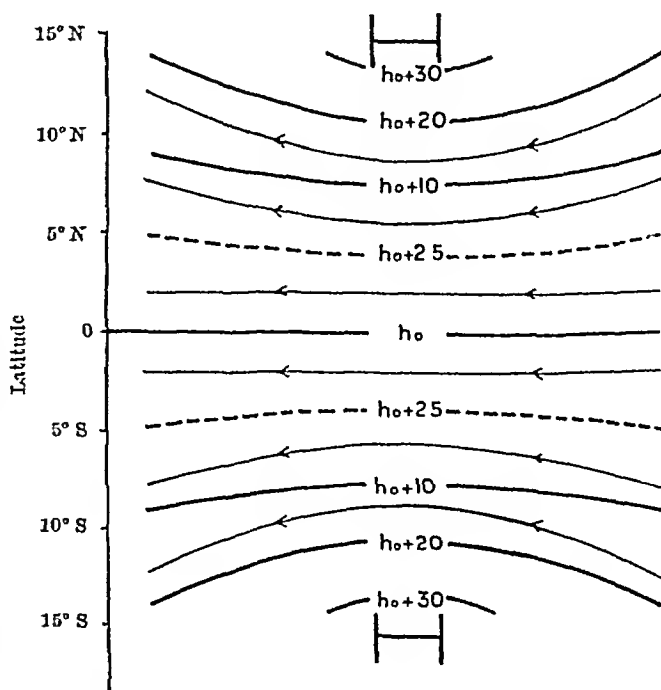


Fig 1 Equatorial duct —, Contour line (height in m), ---, streamlines

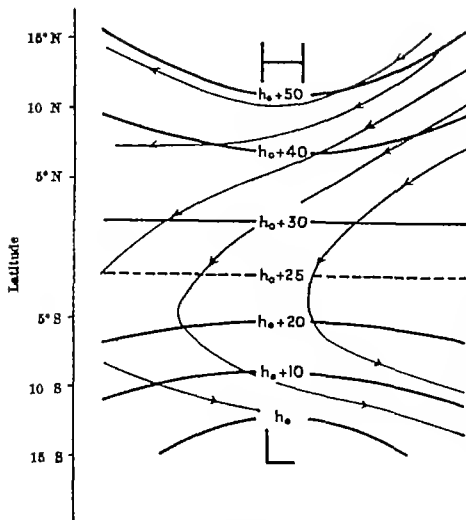


Fig. 2. Cross-equatorial drift. — Contour lines (height in m.)
--- streamlines

a recurring easterly monsoon current. A basic tendency for moisture to be contained in the lower layers in easterlies, due to subsidence, and for up ward transport of the moisture in westerlies, is ascribed to the operation of the Coriolis term, $2\Omega \cos \varphi u$, in the equation for the vertical acceleration

$$\frac{dw}{dt} = -\alpha \frac{\partial p}{\partial z} - g + 2\Omega \cos \varphi u$$

where the symbols have their conventional significance. Considering a fixed value for u the term $2\Omega \cos \varphi u$ has its maximum at the equator. It has usually been dismissed as being negligibly small¹ in comparison with the pressure gradient and gravity terms, but these oppose each other, being approximately in balance. In these circumstances smaller terms can achieve significance. Calculation of the last term shows that, providing the possible compensating mechanisms only partially diminish the instantaneous acceleration, appreciable vertical

motions could build up on the time-scale of synoptic processes. The effect is by no means over riding and may be opposed or enhanced by the synoptic situation.

The importance of examining pressure and flow patterns at several levels of the lower troposphere when assessing the significant vertical motions was amply demonstrated during May 1959. Marked low level divergence over Kenya and Tanganyika in the outflow from the surface/850 mb Mauritius/Madagascar sub tropical anticyclone underlay on different occasions a confluent 700 mb pattern (Fig. 1) and a weak westerly flow, in both cases no rain fell.

As recently as December 1958, the opening speaker at a Meteorological Office discussion on tropical meteorology² remarked that the forecasting of upper winds from frontours is invalid in equatorial regions because a relationship between contours and wind has not been established. Contrariwise, the present work, which raises hopes of a basically synoptic solution to East African weather forecasting problems, suggests that the ability to predict changes in the contour pattern in low latitudes is a fundamental need. We most strongly disagree with the view expressed by Walker in the same discussion³ that there is no guarantee that an unproved upper air network would improve (equatorial) forecasting significantly. In a paper which has very recently come to hand Palmer and collaborators⁴ have proved the occurrence of approximately geostrophic flow down to equatorial latitudes in the Pacific Trades, their investigation demonstrates most eloquently the value of a close homogeneous network of radiosonde and radar wind observations in solving the problems of equatorial flow. The establishment of a similarly close network in East Africa and adjoining territories where a greater variety of pressure patterns and far more synoptic change occurs, would, we contend, lead to fundamental progress in our understanding of equatorial weather mechanisms.

We wish to thank Mr B W Thompson, regional meteorological representative, Kenya East Africa, for his constant support and advice, and Mr J P Henderson, director, East African Meteorological Department, for permission to publish this account.

¹ Cochemé J (unpublished notes 1959)

² Pettersson S. *Weather Analysis and Forecasting* (McGraw Hill 1958)

³ *Met. Mag.* 85 118 (1959)

⁴ Palmer O. E., Tallif, J. R., Sinclair P. O. and Vizee, W. An Empirical Study of Air Movement near the Equator (University of California Los Angeles 1958)

PERMANENT MOISTURE EXPANSION OF CLAY PRODUCTS ON NATURAL EXPOSURE

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THE criticisms by Vaughan and Dinsdale¹ of our communication² on the progressive long term moisture expansion of clay products, and their objection to our use of the term 'permanent' to describe it, lead us to fear that they still regard the problem as one of academic interest only and not as a serious practical one, such as our observations of

damage to buildings in Australia³ and those of McBurney⁴ in the United States of America have shown it to be. Although the expansion may apparently be removed by subjecting the materials to high temperatures, it is permanent at atmospheric temperatures, and hence as long as we are considering the problem as a practical one

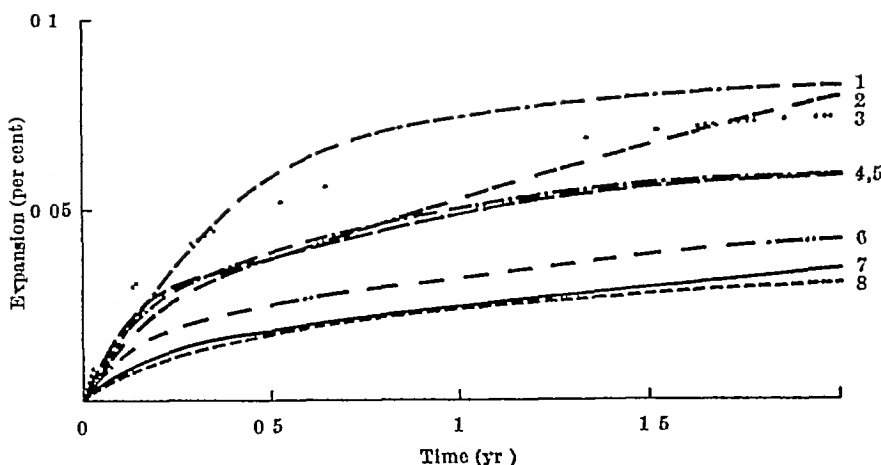


Fig. 1 Average permanent moisture expansion curves for eight types of clay product on standing in air for two years. Curve 1, roofing tiles, curve 2, wall tiles, curve 3, architectural terra-cotta, curve 4, bricks, curve 5, china body, curve 6, refractory body, curve 7, floor tile, curve 8, firebrick

the expansion can properly be referred to as permanent

Our main object in studying the problem is to determine, for a wide range of clay products, the ultimate expansions and the times taken to reach these, whether they be 50, 100 or 1,000 years. A knowledge of both is necessary if we are to find out how to offset the expansion and so prevent the resultant damage. The reason that we, like others, have autoclaved the bodies in steam has been to accelerate the process of expansion and thus to study, in a reasonable time, the reactions which normally take a life-time or more. Unlike others, however, we have continued the process of autoclaving until the bodies reached dimensional stability and have thus obtained measures of the maximum expansions the bodies suffer at high temperatures. At the same time, we have not neglected to observe the bodies under natural conditions, for it is only thus that the practical behaviour of the bodies can be correlated with the results at high temperatures.

In all, we now have more than a thousand industrial and laboratory specimens exposed under natural conditions, and these are being added to from time to time. Replicate samples are exposed, out of doors, in an air-conditioned laboratory and in an atmosphere of 100 per cent relative humidity, while others are kept totally immersed in water, others again have been subjected to cycles of soaking in water and drying at 110° C. Some bricks have now been under observation for five years, at the end of which time they show expansions ranging from 0.045 to 0.20 per cent with an average rate still between 0.005–0.006 per cent per annum. Most products have been under observation for shorter periods, and the average and range of the expansions for the eight types of body for which results on autoclaving have already been reported², after standing for two years either in the laboratory or out of doors, are given in Table 1. Curves for the average expansion of the products with time are given in Fig. 1. Because of the small number of some of the products so far examined the values cannot be considered as completely characteristic, but they do indicate the general trends for the various bodies.

Our results show that the expansions on standing in air are higher than those predicted from the temperature coefficient of the expansion process based on high temperature data², and from this and other

observations it is clear that there are no practical relationships between autoclave and low-temperature data³. Estimates of ultimate expansions likely in practice and the times to reach these have therefore to be based on the results obtained for natural exposures to date, and as they come to hand in the future.

From our experience we are not surprised that specimens used by Vaughan and Dinsdale did not reach equilibrium during relatively short periods of either natural exposure or autoclaving. Standing for three years is a long way short of the periods for which we know that bodies can continue to expand², and calculations based on the temperature coefficient of the expansion process^{2,3} show that

times of the order of 12,000 hr would be required if the bodies are to reach dimensional stability in steam at 50 lb/sq. in.

We have observed shrinkages on drying as reported by Vaughan and Dinsdale only in under burnt bodies, and then only on drying after more than one cycle of wetting and drying, these shrinkages are, however, always less than the original expansions on wetting. Normal ceramic bodies have, in general, continued to expand on drying at 110° C whether they have been soaked in water or treated in the autoclave³. This has also been the experience of other workers⁵, and Bennell and Butterworth⁶ have found that no less than 50 per cent of the bricks of the United Kingdom expanded when tested for drying shrinkage. Only when specimens have been autoclaved until they approach dimensional stability (far beyond the stage to which Vaughan and Dinsdale's specimens were taken) do drying shrinkages become apparent, and then only of the order of 0.01–0.02 per cent, a mere fraction of the total expansion. In this connexion it is of practical significance that all nine experimental walls which have now been standing for more than three years at this Division expanded at slightly higher rates when drying out during the hot summer months³. The explanation for this is simple: it is due to the increased rate of reaction between the reactive compounds in the bricks and the water still present at the higher temperatures during the drying out process.

Vaughan and Dinsdale's observation that a complete reversal of the change in size can be obtained by heating to 300° C suggests that they have not investigated a very wide range of bodies. This

Table 1 PERMANENT MOISTURE EXPANSION FOR EIGHT TYPES OF CLAY PRODUCT STANDING IN AIR

| Product | No. examined | Expansion | |
|---------------------------|--------------|--------------------|------------------|
| | | Average (per cent) | Range (per cent) |
| Roofing tile | 04 | 0.082 | 0.102–0.060 |
| Wall tile | 18 | 0.070 | 0.091–0.066 |
| Architectural terra-cotta | 12 | 0.074 | 0.098–0.059 |
| Brick | 260 | 0.061 | 0.186–0.010 |
| China body | 6 | 0.061 | 0.110–0.034 |
| Refractory body | 6 | 0.042 | 0.080–0.023 |
| Floor tile | 12 | 0.034 | 0.080–0.014 |
| Firebrick | 12 | 0.031 | 0.045–0.020 |

phenomenon has been reported once before¹, but most other workers have found that temperatures of at least 600° C and often much higher are necessary for this purpose². In some cases it has proved impossible to remove expansion without heating to temperatures approaching and above those at which the specimens were originally fired. At these temperatures further firing shrinkages occur and the two effects become confused, this suggests that even at lower temperatures the shrinkages obtained by reheating are not necessarily caused by a reversal of the expansion process, and hence any approximate numerical agreement may be quite fortuitous.

Our critics also raise the question of expansion taking place during the cooling of the clay bodies in the kiln and its effect on the establishment of a standard zero of measurement. We are fully aware of this problem but do not see that their proposal of a preliminary desorption is of practical value. The specimens will still have to be cooled after this treatment before they can be measured and hence they will again adsorb moisture, and further, as we have pointed out above, most bodies if heated after they have adsorbed moisture expand still more. We therefore consider that the small amounts of expansion in the kiln must be disregarded from the practical point of view. What matters is the expansion that takes place in the structures into which the units are built, and therefore the practical basis for

calculating and comparing expansions is the exact length of the products.

From experimental evidence in this Division^{3,4,5} we consider that chemical processes involving hydration of such constituents as amorphous aluminosilicates, glasses and amorphous silica are responsible for expansion, and that reversible physical swelling, except in under burnt bodies, plays a very minor part. Furthermore, we consider that the evidence presented by our critics does not substantiate a physical explanation.

A full account of our work to date on bricks⁶ is now available and we hope to present a summary of current studies on the expansion (under natural conditions of exposure) of all clay products examined so far to the seventh International Ceramics Congress in 1960.

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EXISTENCE OF AN INNER AURORAL ZONE

By DR KNUD LASSEN

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FROM theoretical considerations Alfvén¹ predicted the existence of an inner auroral zone at a polar distance of 5–10°. Nikolsky², Meek³, and others have found that the maxima of geomagnetic and ionospheric disturbances are concentrated around a spiral-shaped zone which Nikolsky identifies with the inner auroral zone. However, no observation of aurora in relation to this zone seems to have been made. The spiral-shaped zone is presumably identical with the curve of geographical distribution of maxima of magnetic activity of class J⁴. At Godhavn (69° 2', 306° 5' geog.) this class of activity is not at all, or very poorly, correlated with aurora, hence the zone of Nikolsky, Meek and others can scarcely be regarded as an auroral zone in the proper sense.

It is the purpose of this article to direct attention to a 'population' of aurora which seems to form an inner auroral zone. It summarizes a study which was presented in part at the Auroral Conference at Uppsala in August 1958. A more detailed paper will be published elsewhere.

As a result of visual auroral observations at Godhavn during 1952–58 it was found that the diurnal distribution of auroral frequency there had two maxima. In fact, the distribution is composed of two distributions of different types. One, with a maximum near magnetic midnight, is formed by relatively brilliant aurora, approaching and sometimes passing zenith from the south-east accompanied by negative magnetic bays. These aurora are especially frequent and brilliant on interplanetary disturbed days and in years with low sunspot activity.

The second distribution with a maximum at about 01 local time is formed by zentral aurora. These are narrow diffuse bands sometimes with a faint ray structure or draperies—often several parallel draperies—composed of long rays that may be at some distance from each other. The draperies may form fans or coronas occasionally accompanied by colour effects, but generally the movements of the arcs and rays are very moderate. They may rather be described as slow pulsations of intensity. narrow homogeneous arcs slowly die away while parallel arcs a few degrees from them grow in intensity. These slow variations may go on for a long time, they seem quite irregular and not in phase in the different arcs or rays, so that the mean position of the aurora is little affected by the intensity variations.

Several authors have assumed that the main auroral zone is displaced polewards in the morning hours. There is no observational evidence that this is the reason why aurora are observed at Godhavn in the morning hours. On the contrary in the cases where the onset of the morning type aurora was observed, very weak aurora began sporadically at a great elevation at about 3h–4h. (Ascagrams from the International Geophysical Year, too, show that the aurora begin suddenly within a few degrees from Godhavn.) The mean elevation did not change significantly in the course of the morning. The mean distribution of the elevation of the arcs and draperies had its maximum a little to the south of zenith (Fig. 1).

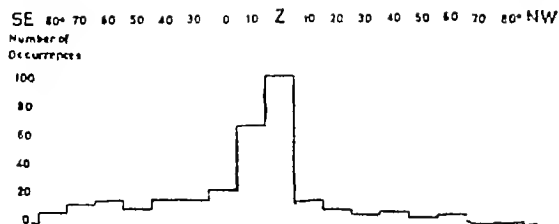


Fig 1 Frequency-distribution of zenith distances, Godhavn, 1954-56

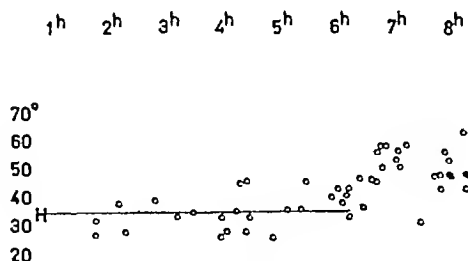


Fig 2 Azimuth of arcs, Godhavn, 1954-56

The direction of the bands was perpendicular to H until 6h, at about 6h the mean direction suddenly changed in a clockwise sense (as seen from above). The change is consistent with Alfvén's theory⁵. The order of magnitude was 20° in 1954-56 (Fig 2).

Whereas the evening-type auroræ are strongly related to magnetic activity, the morning-type auroræ are not correlated with local magnetic activity, and they appear to be independent of the planetary state of disturbance, too. Thus, observations from Upernavik, a few degrees to the north of Godhavn, from the years 1884-1937, show that auroræ noted at 21h LT were eight times as frequent on international disturbed days as upon international quiet days. Auroræ noted at 8h were here, as well as at Jakobshavn, a hundred kilometres to the east of Godhavn (observations 1885-1915), distributed at random between quiet, disturbed and the remaining days. At Godhavn auroræ were observed on 106 of a total of 110 clear mornings without moonlight in the winters 1954-55 and 1955-56.

A study of published auroral reports from arctic expeditions has shown that the morning-type auroræ observed at Godhavn can be found at several other locations too. Thus the auroral type mentioned was observed near zenith at Kingua-Fjord⁶, and it seems likely that the same was the case at Chesterfield^{7,8}, Coppermine⁷ and Murchison Bay⁹. Further, auroræ near zenith in the morning hours were observed at Danmarkshavn ($76^\circ 5'$, 341°), Station Nord ($81^\circ 5'$, 342°) and at a number of stations on the western coast of Greenland not very distant from Godhavn

(unpublished observations, Danish Meteorological Institute).

To the south of Godhavn the auroræ seem to have been observed from Godthåb, whereas at stations in southern Greenland nearer to the main auroral zone this type of aurora has not been identified.

At stations nearer to the centre of the auroral isochasms (Peary Land, Upernavik, Thule) the morning auroræ are observed less frequently and mainly on the southern sky (unpublished observations).

In the Antarctic the inner zone auroræ were observed by several expeditions, for example, by Mawson at the stations Cape Royds and Cape Denison¹⁰.

On the map in Fig 3 (after Hultquist¹¹) the places at which the morning auroræ are observed near zenith have been plotted as circles. They are seen to form a zone which is practically coincident with Hultquist's auroral isochasm through Godhavn. This oval, which is the projection of a circle in the equatorial plane outside the Earth on to its surface along the geomagnetic lines of force, may thus be regarded as an inner auroral zone, occupied in the early morning- and day-hours of all days, irrespective of disturbances in the main auroral zone.

Fig 4 shows the diurnal distribution of auroral frequencies for December and January 1948-50 at five stations in Greenland. The stations are Thule

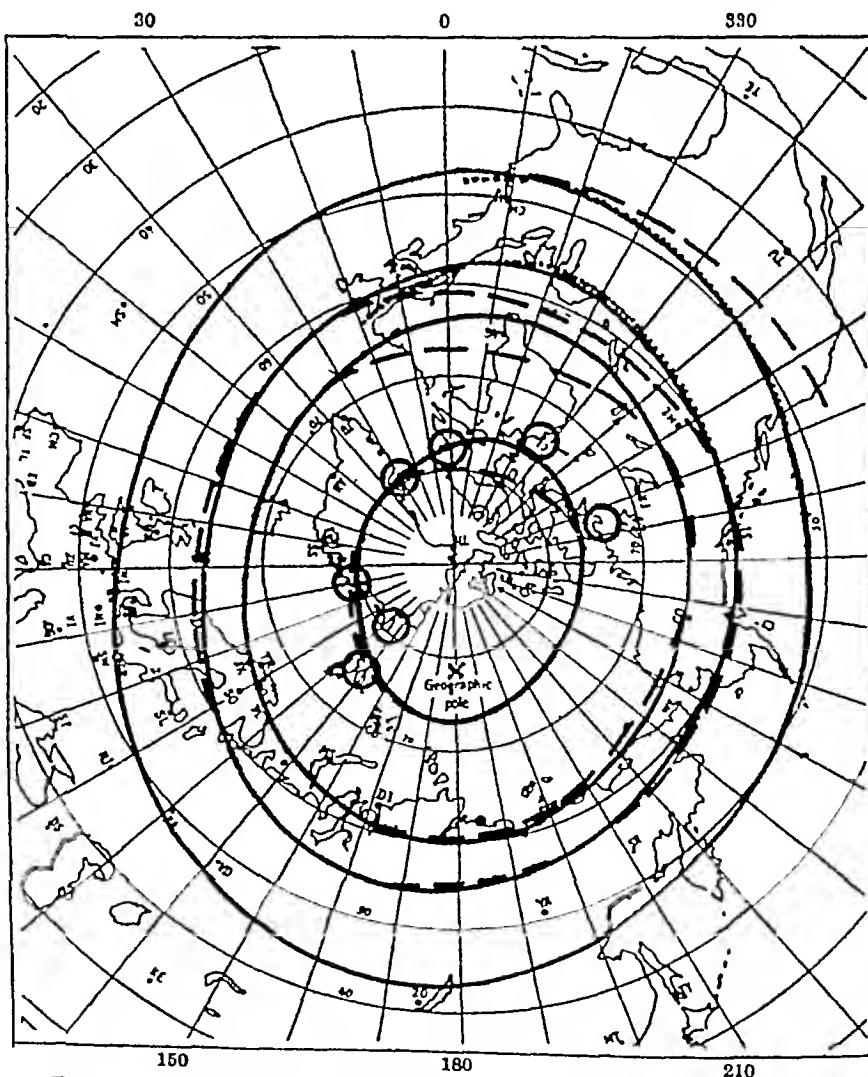


Fig 3 Auroral isochasms (after Hultquist) and stations with morning aurora near zenith

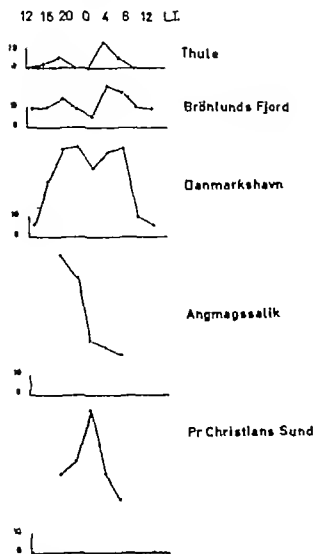


Fig. 4. Percentage of clear hours with aurora at five stations in Greenland, December and January 1948-50.

(76° 33' N, 68° 49' W), Brønlunds Fjord, Peary Land (82° 10' N, 30° 30' W), Danmarkshavn (76° 46' N, 18° 45' W), Angmagssalik (65° 36' N, 37° 33' W), and Prins Christians Sund (60° 03' N, 43° 12' W). The figure gives the percentage of clear hours with aurora, arranged according to local time the same scale has been used at all stations. Whereas the frequency of evening aurora increases from Thule to Angmagssalik-Prins Christians Sund it is clearly seen that the frequency of the morning aurora has its maximum at Danmarkshavn, in accordance with the idea of the existence of an inner auroral zone there.

Hulbert¹¹, in his study of the diurnal variation of auroral frequencies takes the view that "Vogard's conclusion, that most auroral forms show an evening

and morning maximum, is contradicted almost as often as it is upheld. From Fig. 4 (which is in agreement with material from several other stations) it may be seen that the different types of diurnal distributions can be arranged according to the following scheme: (a) stations at the main auroral zone have distributions with a single maximum near geomagnetic midnight; (b) stations between the zones have often, in addition, a weak morning maximum; (c) stations near the inner auroral zone show two maxima, one near geomagnetic midnight and one at about 06 L.T.; (d) stations some degrees of latitude nearer to the pole show a weak geomagnetic midnight maximum and a distinct morning maximum.

Great ionospheric disturbances begin at the same time as the onset of the morning aurora. The *F* layer is dissolved into spread *F* and oblique incidences which are soon accompanied by sporadic layers of auroral type at different virtual heights between the *E* and *F* layer heights. Whereas observations of aurora are restricted by cloud and daylight a study of ionospheric disturbance is possible at any time. The occurrence of ionospheric disturbance may be represented by the mean daily distribution of the frequency of $E_s > 3$ Mc/s which is published monthly by the National Bureau of Standards. By combining the frequencies for 3h-8h L.T. for the years 1952-56 it was found that the yearly variation of the morning disturbances is a single wave with a maximum at midwinter and a minimum at midsummer. The variation through the whole period seems to indicate a variation in phase opposite to the sunspot variation.

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ISOMERS OF VITAMIN A IN FISH LIVER OILS

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WE have investigated the occurrence of the '180-a' and '180-b' isomers of vitamin A in a number of fish liver oils by means of reaction with the retinal protein, opsin. These isomers were found to constitute about 20 per cent of the vitamin A in cod, shark and mixed fish liver oils examined. Since the presence in fish liver oils of all *trans* vitamin A and neovitamin A (neo-a)¹ has previously been reported, all four of the 'unhindered' isomers have been found in these oils.

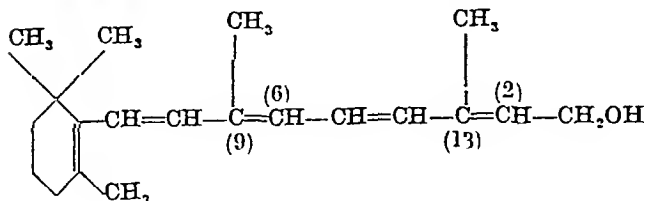
The finding assumes importance because the 180-a and 180-b isomers have only about one fourth the growth promoting activity of all *trans* vitamin A, as measured by rat bioassay².

Nomenclature, structure and biopotencies for the 180-a and 180-b isomers are shown in Table 1.

The trivial names devised by Hubbard and Wald³ are used in this report because official action on a numbering system has not yet been taken. The numbering systems now used include (a) Table 1

Table 1

| Trivial name | Stereoisomeric form | Relative biological potency (ref 2) (per cent) | |
|--------------|---------------------|--|-------------------------------|
| | | Vitamin A acetate | Vitamin A aldehyde (retinene) |
| | all-trans | 100 | 91 |
| 180-a | 9-cis | 21 | 19 |
| 180-b | 9,13 di cis | 24 | 17 |



the Geneva system used by *Chemical Abstracts*⁴ and employed in earlier^{2,5} and forthcoming papers from the Distillation Products Industries Laboratories and (C) the system analogous to that used with the carotenoids and employed by Wald, Brown, Hubbard and Orshnik⁶

Hubbard and Wald⁷ first reported the presence in a concentrate from fish liver oils of a *cis*-isomer of vitamin A different from the neovitamin A found by Robeson and Baxter¹. Later studies by Hubbard and Wald⁸ on pure retinene (vitamin A aldehyde) isomers synthesized in the Distillation Products Industries Laboratories^{3,5} showed that the isomer in fish liver oil was 180-a vitamin A. The basis for the identification was the observation that both 180-a retinene and the retinene corresponding to the *cis*-isomer formed the same pigment with opsin, namely, 180-rhodopsin, having an absorption band maximal at 487 mμ. 180-b retinene, on incubation with opsin, slowly isomerizes to 180-a retinene and forms the same pigment.

This reaction was afterwards developed by Hubbard, Gregerman and Wald⁹ as an analytical method for determining the 180-a and 180-b isomers in the absence of neo-b retinene. The neo-b isomer, the key isomer in the visual process, interferes in this reaction by yielding the pigment rhodopsin, absorbing at 500 mμ. The interference from neo-b retinene has not complicated studies on fish liver oils because this isomer has not yet been found outside the eye¹⁰.

The results of applying this analytical procedure and an infra-red method to vitamin A preparations are given in Table 2.

Four fish liver oil preparations (shark 'non-sap', that is, the non-saponifiable fraction, before and after concentration by molecular distillation, cod 'non-sap' and the 'non-sap' from distilled cod liver oil) were prepared (by M. H. S.) and assayed by the opsin method (P. S. B.). The test samples were saponified and the vitamin A isomers were recovered by extraction (U.S.P. XV method). Sterols were separated by crystallization from methanol at -20°C. The isomers were oxidized to the retinenes by procedures similar to those of Wald¹¹ with manganese dioxide prepared according to Henbest, Jones and Owen¹². The cod liver oil was a pharmaceutical preparation from an apothecary, the shark liver oil was from a bulk commercial shipment obtained at Distillation Products Industries. Table 2 shows that 19-26 per cent of combined 180-a and 180-b isomers were present in the vitamin A of the oils.

After further refinement of the procedures, the vitamin A of a pharmaceutical grade, mixed fish liver oil (sample 5, Table 2) was found to contain 19 per cent combined 180-a and 180-b isomers.

The content of combined 180-a and 180-b vitamin A in a sample of oil from rat livers (sample 6, Table 2) was examined. The value found (14 per cent) was lower than that found for the fish liver oil preparations examined, but was substantial and indicates that these isomers occur in other oils besides fish liver oils.

The origin of the 180-a and 180-b isomers in fish liver oils is uncertain. Ames, Swanson and Harris¹³ have suggested, on the basis of bioassays of rat liver oils, that the isomers originate there from *in vivo* isomerization of all-trans or neovitamin A to form an equilibrium mixture. A similar isomerization may occur in fish liver oils.

Another possibility is that the '180' isomers may sometimes be formed during processing of fish livers. Lambertsen and Brackkan¹⁴, for example, have reported evidence suggesting that neovitamin A is formed from all-trans vitamin A during commercial processing and it is possible that '180' isomers may also be formed. Pharmaceutical grade oils were used in the present study, where available, to ensure that the samples used had received as careful commercial processing as possible.

The saponification and oxidation procedures used in the present work to prepare the samples for assay were examined as a source of isomerization. Control experiments in which all-trans vitamin A palmitate was so processed produced negligible amounts of '180' isomers, as measured by the infra-red procedure, and ruled out this possibility.

The recognition of the prevalence of the 180-a and 180-b isomers made it of interest to isomerize samples of retinene *in vitro*, with dilute hydrochloric acid, until they had attained a state of 'equilibrium', defined as the point at which further exposure to acid produced no change in the proportion of the four isomers present. Assays by the opsin and infra-red methods are reported in Table 2. As in fish liver oils, the proportion of combined 180-a and 180-b isomers in the vitamin A of the artificial iso-

Table 2

| Sample No | Description* | Percentage 180-a + 180-b in total vitamin A isomers (opsin assay) | Percentage 180-a + 180-b in total vitamin A isomers (infra red assay) |
|-----------|---|---|---|
| 1 | Liver oil concentrates | | |
| 2 | Shark 'non sap' | | |
| 3 | Shark distilled 'non-sap' | | |
| 4 | Cod 'non sap' | | |
| 5 | Distilled cod 'non sap' | | |
| 6 | Mixed fish liver oil 'non-sap' | | |
| 7 | Rat liver oil† 'non-sap' | | |
| 8 | 'Equilibrated' retinene isomer concentrates | | |
| 9 | | | |

* The vitamin A in samples 1-6 was oxidized to retinene by manganese dioxide prior to assay.

† Oil was a portion of that kindly supplied by Dr. T. K. Murray, Food and Drug Directorate, Ottawa, Canada, for related bioassay studies.

merates was about 20 per cent. The assays were run independently and the results indicated that with preparations of the purity investigated the two methods are in good agreement.

The average ratio of *iso-a* to *iso-b* isomers in the equilibrated samples was found to vary from about 2:1 to 4:1. This variability is probably caused in part, by errors in measuring the relatively small amounts of *iso-b* isomer present.

Further information on the experimental methods is as follows.

Opsin. Opsin was prepared in digitonin solution, using a modification of the procedures described earlier.¹¹ This procedure will be reported in detail separately.

The essential steps in this procedure included dissection of retinas from cattle eyes in the light, disintegration of the tissue by grinding floating out the fragments of outer segments of the rods by differential centrifugation in phosphate buffer weighted with 40 per cent sucrose; lyophilization of the rod fragments, and exhaustive extraction of the dry powder with petroleum ether to remove extraneous lipids and vitamin A; and finally the extraction of opsin from the residue with 2 per cent aqueous digitonin. Such preparations were assayed for their opsin content with *neo-b* retinene (ref. 10). They were stored at about -16° C until used for assay. They remained stable for many months.

Assay of retinene isomers. Samples of the mixed retinene isomers in a few drops of ethyl alcohol were pipetted into 2-3 ml. of 2 per cent digitonin in water. A cloudy solution usually resulted depending on the concentration, but this was cleared by filtering through a fine sintered glass filter. The final solutions used for assay contained 5-10 µgm of retinene.

Such solutions were assayed with opsin for their combined content of *iso-a* and *iso-b* isomers as described for the assay of opsin itself, except that at least three times the equivalent amount of opsin was used in the determination. The photosensitive pigment formed in all experiments was *isorhodopsin* ($\lambda_{\text{max}} = 487 \text{ m}\mu$), not *rhodopsin*.

Iso-a retinene combines directly with opsin to form *isorhodopsin*. *Iso-b* retinene slowly isomerizes to *iso-a*, and hence forms the same pigment. With *iso-a* retinene, this synthesis is complete in 2 hr at 23° C whereas with *iso-b* retinene the same process is completed only within about 24 hr.

One therefore incubates an unknown mixture of retinene isomers with excess opsin and measures the amount of *isorhodopsin* formed at 23° C in 2 hr and in 24 hr. The amount formed in 2 hr is primarily formed from *iso-a* retinene, that formed in 24 hr measures the combined amounts of *iso-a* and *iso-b* retinene. A small correction of the 2 hr value is needed to take care of the very small amount of *isorhodopsin* formed from *iso-b* retinene during this period, the 24 hr value is also corrected for the very small, almost negligible, synthesis of *isorhodopsin* by the isomerization of all-*trans* and *neo-a* retinene during the incubation period.

Total retinene. The total amount of retinene in the samples was estimated by the antimony chloride reaction and recorded with a Cary recording spectrophotometer. The amount of retinene is determined on the basis that this blue product has $E(1 \text{ per cent, } 1 \text{ cm}) (0.04 \text{ m}\mu) = 3,740$. From this and the preceding data the percentage of combined *iso-a* and *iso-b* retinenes in the total retinene is computed.

Infra red procedure. This work (by W P B) was based on the curves for the individual retinene isomers already reported.¹ The percentage of combined *iso-a* and *iso-b* retinenes in the mixed retinene isomers is calculated from the absorption at 8.73µ, corrected for interference from the all-*trans* vitamin A and neovitamin A present by the absorption at 8.48µ.

The infra-red method has the advantage over the one employing opsin that it can be used to determine the percentage of each of the four isomers in the sample, although we describe here only its use in determining the percentage of *iso-a* and *iso-b* isomers present. It has the disadvantage that the retinene content of the sample needs to be relatively high, at present, to minimize errors due to the absorption of impurities. We prefer a purity of about 75 per cent, $E(1 \text{ per cent, } 1 \text{ cm}) (370 \text{ m}\mu) = \text{about } 1,000$, but procedures for concentrating preparations of lower purity are under study.

The equation employed in the Distillation Products Industries Laboratory is

$$\text{Percentage } iso-a + iso-b \text{ in mixed isomers} = \frac{100 k_a - (k_b + 0.01)}{k_c \times P}$$

where k_a = the extinction coefficient for the test sample at 8.73µ (1 per cent solution in carbon disulphide, 1 mm cell, Perkin Elmer, Model 21, instrument, sodium chloride prism, slit programming No. = 9.75), k_b = the extinction coefficient at 8.48µ for the test sample, this value plus 0.01 is the 'background' correction determined with pure all-*trans* and neovitamin A aldehydes in a ratio (3:1) which approximates that present in the mixed isomer preparations studied, k_c = the extinction coefficient at 8.73µ for pure *iso-a* and *iso-b* retinenes in a ratio (3:1) which is approximately that present in the mixed isomer preparations studied, P = the concentration (per cent) of the total retinenes determined by the antimony trichloride reaction.

This work between the two laboratories was initiated and co-ordinated by Dr J G Baxter, Distillation Products Industries with the co-operation of Prof G Wald, Harvard University. Related bioassays and analytical studies by members of the Biochemistry Vitamin Development and Organic Research Laboratories, Distillation Products Industries, were helpful in guiding the direction taken in the work. These bioassays and analyses will be reported separately.

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LIVER GLUCOSYL OLIGOSACCHARIDES AND GLYCOGEN; CARBON-14 DIOXIDE EXPERIMENTS WITH HYDROCORTISONE

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IT has not been possible for geographical reasons to continue a collaborative study designed to clarify, through the use of carbon-14 dioxide, the biochemical significance of liver glucosyl oligosaccharides, particularly in relation to the action of adrenal corticoid hormones. We therefore wish to report our findings to date.

Sie and Fishman¹ observed earlier that hepatic glucosyl oligosaccharides fluctuated in the same direction as did liver glycogen in starvation, glucose feeding and insulin administration. Under these conditions, our concern lay with the dynamics of the glucose unit, either produced from glycogen, as in starvation or in insulin administration, or exogenously provided in the glucose feeding experiment. On the other hand, liver glycogen resulting from the action of hydrocortisone in fasted rats² is considered to originate from the catabolism of protein. Since hexose synthesis from pyruvate and lactate is believed to require carbon dioxide fixation³, hepatic gluconeogenesis could be followed with carbon-14 dioxide without supplying an exogenous substrate or preformed glucose units. The following experiments have been carried out.

In the first series of experiments, male Wistar rats (150–175 gm), after 22–24 hr of fasting, were injected with 50 μ c of carbon-14 dioxide bicarbonate (isotonic saline, intraperitoneally) 1 hr before killing, and at 3 hr and 5 hr after hydrocortisone (5 mgm / animal in saline microcrystalline suspension) was injected by the same route (Fig 1). In the second series of experiments, 50 μ c of radioactive bicarbonate was injected 3 hr after an initial injection of 5 mgm of hydrocortisone. Animals were killed afterwards at intervals up to 3 hr (Fig 2).

At the times indicated, the experimental animals were killed by decapitation, and the livers rapidly removed and frozen in a dry ice bath. A 10 per cent homogenate of each liver was prepared with ice-cold water, keeping the homogenizer packed in ice. This mixture was deproteinized by additions of 10 ml of 5 per cent zinc sulphate and 10 ml of 0.3 N sodium hydroxide solution. After centrifugation, the precipitate was washed twice with 10 ml of cold distilled water, and the washings and supernatant solution were pooled. The oligosaccharides were adsorbed from this mixture with charcoal, which was then washed with copious amounts of distilled water, and eluted afterwards with hot ethanol¹. Total glycogen was isolated by Roe's method⁴. Glycogen and oligosaccharides were hydrolysed with hot mineral acid⁵, and the glucose was estimated by the Nelson method⁶. Tail vein blood was obtained for the determination of carbon dioxide and glucose⁷. The quantity of carbon dioxide in the blood was

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determined in the Van Slyke apparatus and was recovered and counted as barium carbonate. Glucose was isolated as phenyllosazone⁸, which was recrystallized, plated and counted. A Robinson flow counter was used for the radioisotope assays⁹.

The following observations are made. Animals whose liver glycogen had been almost completely depleted by fasting not only possessed a significant amount of glucosyl oligosaccharides, but also they exhibited about four times the specific radioactivity found in the glycogen and contained virtually all the labelled hexose. With the stimulation of gluconeogenesis by compound F, the specific activity of the glucosyl oligosaccharides diminished, while that of glycogen increased at the 4 hr interval. In Fig 2, where it is possible to follow all the events as a function of time after compound F and carbon-14 dioxide administration at the times indicated, it required about 1 hr for the carbohydrates to incorporate the maximum level of carbon-14. In the early part of this process (between 3–5 hr after compound F) the glucosyl oligosaccharides became more richly labelled than

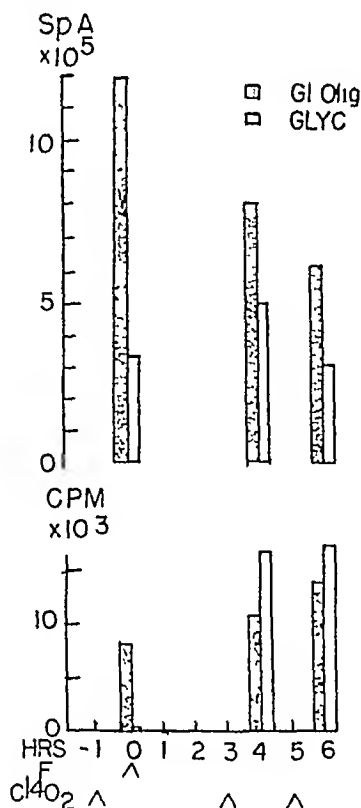


Fig 1. Carbon-14 labelling of liver glucosyl oligosaccharides and glycogen in relation to the administration of compound F. Note that the animals were killed in each instance 1 hr after the injection of carbon-14 dioxide. The numbers of rats employed for each time interval were, respectively: -1 to 0, 2; 0 to 4, 4; 4 to 6, 2.

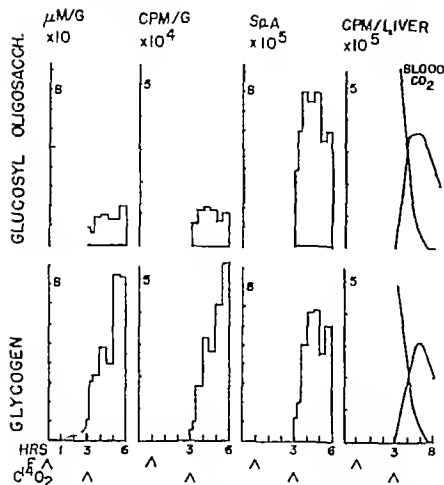


Fig. 2. Carbon 14 turnover in liver glucosyl oligosaccharides, glycogen and blood carbon dioxide in relation to compound F administration. The number of animals used was two at each time interval except for the 4 hr column (4 rats). The relative specific activity of blood carbon dioxide was computed on the assumption that carbon-14 dioxide was incorporated into only carbons 3 and 4 of glucose. The observed c.p.m. (mole of barium carbonate have been divided by three, and the same plot (descending curve) appears for both glucosyl oligosaccharides and glycogen.

the glycogen by a factor of 3 and for another 2 hr still remained more radioactive per milligram of polysaccharide glucose. This situation is reflected in the curves relating total counts per liver of each carbohydrate category against a background of rapid carbon 14 dioxide disappearance from the blood. After 3-6 hr the glucosyl oligosaccharides exhibited a constant number of counts per gm. of liver, whereas those for glycogen continued to rise to the end of the period investigated (8 hr). However, for this interval, specific activity of glycogen paralleled that for the glucosyl oligosaccharides. In general, carbon dioxide fixation matched carbohydrate synthesis following the injection of hydrocortisone.

The interpretation which appears best to fit the above facts is the following. Pyruvate and lactate (since these six carbon dioxide during their conversion to glycogen) are probably the major protein supplied precursors of glucosyl radicals in fasted rats treated with hydrocortisone. These glucosyl radicals are first linked into individual members of a homologous family of glucosyl oligosaccharides (malto-oligosaccharides, maltotetraose, etc.) which is 'turning over' rapidly. Under the proper physiological stimulus (glucose feeding, compound F) these oligosaccharides are assembled into macro-molecules of glycogen.

In our previous work, first consideration was given to isolating, identifying, characterizing and determining quantitatively liver glucosyl oligosaccharides¹⁰ and the next concern was to rule out the possibility of artefact due to the operation of extraneous factors of either a biochemical or physical nature^{11,12}. Our attention was directed recently to the question of the origin of glucosyl oligosaccharides and their possible significance in the metabolism of liver glycogen. The implication of previous experiments¹ (starvation, glucose feeding, insulin administration) and the work of others¹³ with rat diaphragm was that glucosyl oligosaccharides (no matter what their origin) may enter somewhere into the mechanism of glycogen synthesis. The present results supply direct evidence in support of this suggestion.

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RELEASE OF NUCLEOTIDES FROM YEAST CELLS

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It is well known that when *Lactobacilli* are cultured in association with yeast, the former organisms are able to proliferate in a simple medium containing no growth factors specific for them. The resulting growth of *Lactobacilli* is mainly dependent on vitamins, purine and pyrimidine bases secreted by the yeast cells into the medium¹. The present communication contains a description of the ultra-violet-absorbing materials released from the yeast cells and the conditions influencing their release.

Beer yeast (*Saccharomyces cerevisiae*, Yebis) subcultured for 72 hr at 30°C in a synthetic medium

was incubated for 5 hr at 30°C in the same medium containing phosphate-³²P. After harvesting and washing three times with distilled water, the labelled cells (dry weight, 1.760 mgm) were suspended in 400 ml of 0.08 M sodium citrate buffer (pH 6.0) with 2 per cent glucose added, and incubated for 3 hr at 30°C. The supernatants after incubation had an ultra violet absorption spectrum with a maximum at 268 mμ and a minimum at 235 or 240 mμ.

The ultra violet absorbing materials released from the cells were almost completely adsorbed by a charcoal column pretreated with 8 per cent methanol.

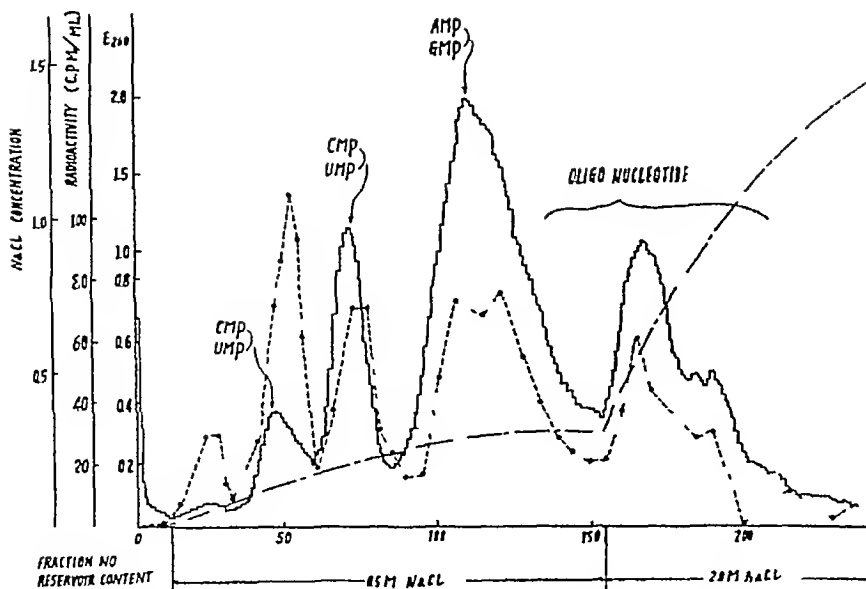


Fig. 1 Separation of the nucleotides released from yeast cells labelled with phosphorus 32 during their incubation in citrate buffer. Column, 'Dowex-2' (chloride), 200-400 mesh, 12 cm \times 0.785 cm², elution, the initial mixer content was 500 ml water, and the reservoir content was 500 ml of 0.5 M sodium chloride, then 500 ml of 2.0 M sodium chloride solution. Each effluent was collected in 4.7 ml portions with a fraction collector. Sorbed materials, the ultra-violet-absorbing materials prepared as described in text. —, Optical density at 260 m μ , ---, radioactivity (c.p.m./ml), - - -, sodium chloride concentration in the effluents. CMP, Cytidine monophosphate, UMP, uridine monophosphate, AMP, adenosine monophosphate, GMP, guanosine monophosphate.

More than 80 per cent of the adsorbed material was eluted with 0.3 per cent ammonia-50 per cent ethanol solution. The eluate from the charcoal was neutralized with 'Dowex 50' (acid type) resin, and then passed through 'Dowex 2' (chloride type) resin. The adsorption in this step was more than 90 per cent. The column was washed with water, and the adsorbed material was separated with a sodium chloride solution by the gradient elution technique². The optical density at 260 m μ and 280 m μ and the radioactivity of each effluent were measured.

The results for six fractions are shown in Fig. 1. The positions, but not the heights, of optical density peaks agree well with those of radioactivity. The initial fractions (eluted with less than 0.3 M sodium chloride solutions) were rechromatographed on 'Dowex 1' (formate type) and then on paper, the monophosphates of cytidine, uridine, adenosine and guanosine were identified in this way. The oligonucleotide fractions (eluted with 0.3-1.5 M sodium chloride) followed the mononucleotides. The recovery using sodium chloride solution, even up to 4.0 M, was only about 60 per cent of the calculated amount of adsorbed material. However, when a mixture of 4.0 M sodium chloride and 1.0 M sodium hydroxide solutions was used as eluant, the residual material was almost completely separated from the column. This alkali-eluted fraction, the final eluate, contained four mononucleotides, which would presumably be derived from polynucleotides hydrolysed by alkali during the elution. Details of this chromatogram will be published elsewhere.

Oligo- and poly-nucleotides formed more than 60 per cent of the total nucleotides released, and the ratio of purine bases to pyrimidine ones in the mononucleotide fractions was 2.5, though it was 1.2 overall. These ratios depended on the experimental conditions. Most of the nucleotides released were probably fragments of the cellular ribonucleic acid, since scarcely any 5'-nucleotides were in any fraction, and amounts of the nucleotides released corresponded

approximately to the decrease of cellular ribonucleic acid. Moreover, the quantity of nucleotide released was greater than that in the pool (fraction soluble in cold acid) which decreased during incubation.

As shown in Table 1, distilled water, sodium chloride and potassium chloride solutions and a synthetic growth medium did not cause a release of nucleotides when used as the incubation medium, acetate or succinate buffers had a slight effect and phosphate or citrate buffers rather more effect. This stimulation of citrate or phosphate might be well attributed to their chelating action, since ethylenediamine tetraacetic acid, a notable chelating agent, markedly accelerated the nucleotide release, and the addition of M/100 magnesium sulphate to M/50 citrate buffer resulted in a 50 per cent reduction of the release.

Inhibition of the release in citrate buffer was not observable in the presence of either ordinary antibiotics (penicillin, 20 μ g/ml, streptomycin, 300 μ g/ml, and chloramphenicol, 20 μ g/ml) or of metabolic inhibitors (sodium azide, 10^{-3} M, Na.HAsO₄, 2×10^{-2} , and 2,4-dinitrophenol, 5×10^{-4} M), except moniodoacetic acid which produced a slight drop at 10^{-3} M. The pH optimum for the release in citrate or phosphate buffer was 6.0-7.0 and an acid pH suppressed the release. Several treatments which disrupt the permeability barrier of yeast cells, for example, freezing and thawing, treatment with organic solvents, and short-time sonication of the cells, stimulated the release considerably. After such treatment an enhancing effect of citrate was also discernible. However, it is possible that the materials released in these conditions are not the same as the nucleotides released by the intact cells, since the supernatant of the citrate buffer incubated with sonicated or frozen and thawed cells showed an increased absorption at 230-250 m μ , which disappeared on acidification with perchloric acid.

Recently, a similar phenomenon has been reported by Holden⁴ for *Lactobacilli*. His results, and ours¹³,

Table 1 EFFECT OF INCUBATION MEDIUM ON THE RELEASE OF NUCLEOTIDES FROM THE YEAST CELLS

| All results are expressed in terms of 100 mgm (dry weight) of the cells | |
|---|---|
| Incubation medium | Released nucleotide phosphorus (μ g) |
| Distilled water | 40.5 |
| 0.08 M sodium chloride solution | 33.0 |
| 0.08 M potassium chloride solution | 34.5 |
| 0.08 M sodium acetate buffer (pH 5.0) | 65.0 |
| 0.08 M sodium succinate buffer (pH 5.0) | 62.0 |
| 0.08 M sodium phosphate buffer (pH 5.0) | 80.5 |
| 0.08 M sodium citrate buffer (pH 5.0) | 115.0 |
| M/100 Ethylenediamine tetraacetate (pH 4.2) solution | 68.0 |
| M/100 Ethylenediamine tetraacetate (pH 5.0) solution | 102.0 |
| Synthetic growth medium | 45.0 |

Beer yeast cultured in a synthetic medium for 72 hr at 30°C was incubated in 10 ml of medium containing 2 per cent glucose for 3 hr at 30°C. The released nucleotide-phosphorus was determined as follows. The extinctions in the supernatant of the incubated media were measured at 240, 260 (E_{260}) and 280 m μ respectively, with a Beckman DU spectrophotometer, and the E_{260} due to the released nucleotides was obtained by subtracting the blank (the medium free from cells) from the E_{260} of the supernatant. Thus, the nucleotide-phosphorus could be calculated according to Ogur and Rosen (ref. 12).

strongly suggest that citrate has a chelating effect which affects the release of nucleotides from the microbial cells

On the basis of these results, it might be suggested that the presence of citrate or other chelating substances in a medium may remove calcium or magnesium ions from the cell surface, leading to destruction of ribonucleic acid and present in it, and thus to a release of nucleotide fragments. Several facts support this. For example, pancreatic ribonuclease is inhibited by the addition of magnesium or calcium ions⁴, and a ribonucleic acid rich fraction obtained from the cells of *E. coli* contains more magnesium than other fractions⁵. Further, ribonucleoprotein has apparent⁶ or latent⁷ ribonuclease activity.

On the other hand, it has often been observed that the degradation of ribonucleic acid and the release of ribonucleotides from yeast cells takes place by autolysis^{8,9}. The release of nucleotides under our experimental conditions may also be connected with cell autolysis. However, it seems reasonable

to distinguish between the two, since the release in our case did not result in the death of the cells or even in degradation of the cell protein. In contrast, a considerable release of amino-acids occurred only when the yeast cells were incubated in the acetate buffer which accelerated release of nucleotide only slightly.

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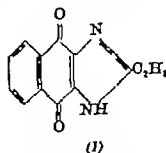
NEW ANTIMETABOLITES OF VITAMIN B₁₂

By G M TIMMIS and Dr S S EPSTEIN

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OUR interest in the role of vitamin B₁₂ in cancer was first stimulated by the claims of Bodan¹ that prolonged regression of neuroblastoma in infancy was effected by massive dosage of the vitamin. It was therefore thought that the therapeutic effect claimed might be related to an imbalance in B₁₂ metabolism caused by excess of the vitamin, and that such an effect might possibly be better produced by the administration of a B₁₂ antimetabolite².

Hitherto, the only known B₁₂ antimetabolites have been those described by Lester Smith³, which were derived from the structure of B₁₂ by very minor modifications, and also those which are relatively simple derivatives of the benzimidazole molecule⁴. The relation between tumour inhibition and anti B₁₂ action is shown in a member of the latter group by the effect of 2-ethyl 2,3 naphthimidazole 4,9 dione (I), which induced partial regression of a mouse mammary adenocarcinoma⁵ and was also a competitive antagonist of vitamin B₁₂ in an *E. coli* mutant⁶.



(I)

We have explored a fairly wide variety of chemical types chosen for their possible relation to B₁₂ metabolism for an antimetabolite action in a micro biological system. Our particular test organism was *E. gracilis* var α —a highly sensitive B₁₂-dependent flagellated green alga. The basal growth medium

and techniques of incubation were based on those described by Hutner *et al.*⁷

A series of approximately a hundred compounds was screened for inhibitory activity, at 500 μ g/ml levels, at low concentrations of vitamin B₁₂. Compounds producing more than 50 per cent inhibition of growth, as assessed in a colorimeter (measuring both turbidity and colour), were afterwards re tested in definitive assays. An orthogonally designed test system was used, with varying concentrations of antagonist up to 500 μ g/ml in the presence of 0, 10, 100 and 1,000 μ g B₁₂/ml. The growth response in these tests was measured by a pigment extraction technique using an acetonitrile-ethyl acetate solvent system due to Epstein and Weiss⁸.

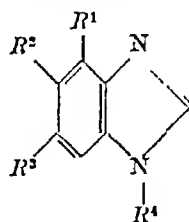
Results are expressed in terms of concentration of antagonist required to produce 50 per cent inhibition of growth at 10, 100 and 1,000 μ g B₁₂/ml respectively. The values given are only approximate. As can be seen from Table 1 seven out of the fifteen compounds so far found active on screening produced a competitive B₁₂ antagonism.

We think that the discovery of an antimetabolite action in the pteridine and nicotinamide structures is interesting because, unlike the benzimidazoles or purines, they are not analogous in structure to any moiety of the B₁₂ molecule. These observations indicate that there may be a variety of enzymes or co-factors closely concerned with the utilization of B₁₂, and that each one may be structurally specific for a particular inhibitor. Thus the pteridines might compete with a pteridine type co factor or metabolite for a particular enzyme, and the nicotinamide derivatives might interfere with some function of diphosphopyridine nucleotide (cf. Timmis⁹).

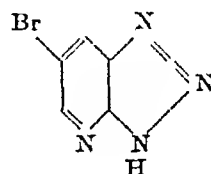
Table 1 CONCENTRATIONS OF ANTAGONISTS ($\mu\text{gm}/\text{ml}$) PRODUCING 50 PER CENT INHIBITION OF GROWTH OF *E. gracilis*
Results in the case of compounds producing competitive antagonism are given in Italics

Structures of compounds tested, (a) (b) , are on the right

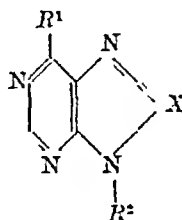
| Structural type | Formula | Concentration antagonist ($\mu\text{gm}/\text{ml}$) required to produce 50 per cent inhibition of growth | | |
|-----------------------------|--|--|------|-----------|
| | | B_{12} ($\mu\text{gm}/\text{ml}$) | 10 | 100 1,000 |
| (a) Benzimidazoles | 4-nitro 6-chlorobenzimidazole ($R^1 = \text{NO}_2$, $R^2 = \text{H}$, $R^3 = \text{Cl}$, $R^4 = \text{H}$) | 110 | 88 | 78 |
| | 5,6-dichlorobenzimidazole ($R^1 = R^2 = \text{H}$, $R^3 = R^4 = \text{Cl}$) | 100 | 90 | 94 |
| | 4,5,6-trichlorobenzimidazole ($R^1 = R^2 = R^3 = \text{Cl}$, $R^4 = \text{H}$) | 70 | 65 | 63 |
| | 4,5,6-trichlorobenzimidazole riboside ($R^1 = R^2 = R^3 = \text{Cl}$, $R^4 = \text{ribosyl}$) | 70 | 160 | 230 |
| | | | | |
| (b) Diaza benzimidazole | 5-bromo 2,7-diazabenzimidazole | 190 | 178 | 173 |
| (c) Purines and aza-purines | Purine ($R^1 = R^2 = \text{H}$, $X = \text{CH}$) | 138 | 173 | 138 |
| | Purine riboside ($R^1 = \text{H}$, $R^2 = \text{ribosyl}$, $X = \text{CH}$) | 58 | 62 | 60 |
| | 6-mercaptopurine ($R^1 = \text{SH}$, $R^2 = \text{H}$, $X = \text{CH}$) | 200 | >500 | >500 |
| | 9-furfuryl 8-aza adenine ($R^1 = \text{NH}_2$, $R^2 = \text{furfuryl}$, $X = \text{N}$) | 450 | >500 | >500 |
| | 2-diethylamino 6-p-dimethylaminophenylethyl purine ($R^1 = (\text{CH}_3)_2\text{C}_6\text{H}_4\text{N}(\text{CH}_3)_2(p)$) | 150 | >500 | >500 |
| (d) Pyrimidine | 5-fluorouracil | 78 | 55 | 54 |
| (e) Pteridines | 4-mercaptopteridine ($R^1 = \text{SH}$, $R^2 = \text{H}$) | 95 | 350 | 333 |
| | 2-amino-4-p-diethylamino-5-tyrptidine ($R^1 = (\text{CH}_3)_2\text{C}_6\text{H}_4\text{N}(\text{CH}_3)_2(p)$, $R^2 = \text{NH}_2$) | 73 | >500 | >500 |
| | 4-dimethylaminopteridine ($R^1 = \text{N}(\text{CH}_3)_2$, $R^2 = \text{H}$) | 400 | >500 | >500 |
| | | | | |
| (f) Nicotinamide derivative | N-2-chloroethyl β -naphthylaminoethyl 3-carbamoyl pyridinium chloride | 200 | 430 | 415 |



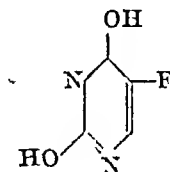
(a)



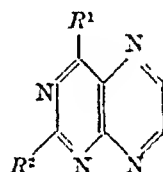
(b)



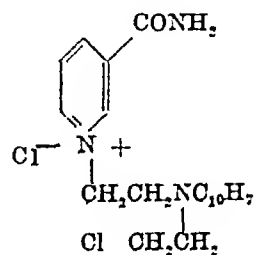
(c)



(d)



(e)



(f)

There are interesting differences between the results obtained in our microbiological system and in the *E. coli* mutant used by McNair Scott *et al.*⁵; for example, 6-chloro-4-nitrobenzimidazole was not a competitive antagonist in our hands, in contrast to 4,5,6-trichlorobenzimidazole riboside. On the other hand, McNair Scott *et al.*⁵ found these compounds to be competitive and non-competitive antagonists respectively.

It is generally held that 6-mercaptopurine, one of the most effective drugs for the treatment of acute leukemia, inhibits growth by interfering with nucleic acid and protein synthesis. Its action in this disease, however, has not with any certainty been related to an antipurine effect. Since we have found that this drug is a competitive B_{12} antagonist (Table 1), we would like to direct attention to the possibility that anti- B_{12} effect might be involved in the action of 6-mercaptopurine. This speculative suggestion could be supported by the view of Osgood¹⁰ that the bone marrow in untreated pernicious anaemia shows several features in common with that in acute leukaemia. If the two diseases are accordingly related, acute leukaemia may, like pernicious anaemia, be dependent on some derangement of B_{12} metabolism, each in its own way.

Forrest *et al.*¹¹ have very recently isolated a simple pteridine from the bodies of blue-green algae. It

is shown above that a number of pteridines of comparable simplicity are vitamin B_{12} antimitabolites in the B_{12} -dependent system *Euglena gracilis*. On reading our manuscript, Dr G. E. Fogg suggested that the apparent inability of blue-green algae and Euglenidae to co-exist in Nature, a hitherto unexplained phenomenon, may be due to an antagonism between the blue-green algae pteridine and the vitamin B_{12} of B_{12} -requiring *Euglena*. We are now investigating this hypothesis.

A full report of this work will shortly be submitted to the *British Journal of Pharmacology and Chemotherapy*.

The investigation has been supported by grants from the British Empire Cancer Campaign, the Jane Coffin Childs Memorial Fund for Medical Research, the Anna Fuller Fund and the National Cancer Institute of the National Institutes of Health, U.S. Public Health Service.

We thank Dr G. B. Brown and Dr K. Folkers for gifts of purine riboside and 4,5,6-trichlorobenzimidazole riboside respectively.

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LOW-TEMPERATURE AUTORADIOGRAPHY FOR THE DETECTION OF TRITIUM IN TISSUE, WITH REMOVAL OF LUMINESCENCE INDUCED BY TRITIUM

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NUMEROUS studies have shown inequalities in the distribution of labelled water in the different organs and various compartments containing liquid in the normal animal^{1,2} during the pre-equilibrium period.

It seemed of interest to investigate by means of photographic recordings the kinetics of this distribution working on animals (young rats) killed at fixed intervals of time. For that purpose we used the low temperature autoradiographic technique^{3,4}, the only method which, because of the rapid freezing of the animal, eliminates post-mortem diffusion of the water while at the same time guaranteeing the absence of known pseudo radiographic effects.

We wished first to obtain an image of homogeneous diffusion in the whole of the organism, under conditions close to equilibrium, and this formed the object of the present work.

The photographic recordings obtained by this technique, applied to young rats after administration of 20 mc of tritiated water gave unexpected results (Fig. 1a). They show no blackening corresponding to lungs, liver, spleen, muscle. On the other hand a slight darkening shows up in the region of the intestinal walls and the subcutaneous tissue and a very intense blackening at the sites of the eye, the brain, the proformed testis, the stomach, the bladder and the intervertebral disks.

Since these results disagreed with the known distribution of water in mammals, we removed organs from young rats treated in the same way except that the dose injected was between 0.4 and 1.5 mc of tritiated water (HTO) in a volume of 0.1-0.2 ml of saline. The radioactivity of the water obtained by distillation of the organs was measured by liquid scintillation^{5,6}.

It is shown in Table 1 that the specific radioactivity of the water (mcg./mgm.) is of the same order for the blood and for organs such as the brain, the liver and spleen, the kidneys and the intestines. On the other hand, the milk in the stomach has not yet reached the isotopic concentration of HTO in the other organs. The specific radioactivity of the water in the total eye, the crystalline lens and the ocular residue after elimination of the crystalline lens is more or less identical with that of the blood. We have also noted that for the eye the radioactivity was entirely due

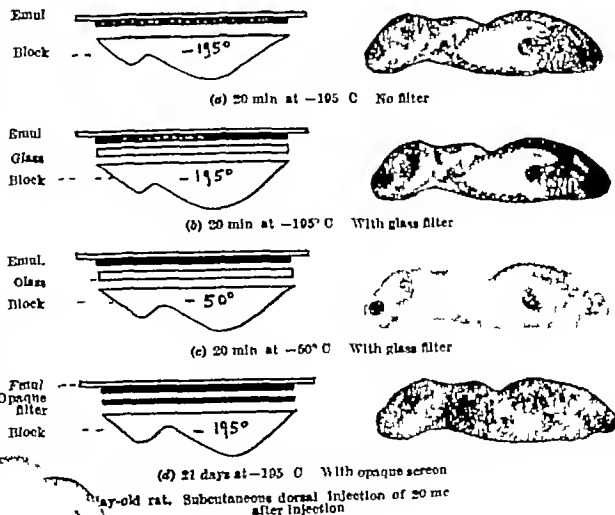
Table 1. SPECIFIC RADIOACTIVITY OF WATER IN THE ORGANS OF YOUNG RATS WEIGHING 14-20 gm. AGED 6-14 DAYS 10 MIN AFTER SUBCUTANEOUS OR INTRAPERITONEAL INJECTION OF 0.1-0.2 ML. OF SALINE CONTAINING 0.4-1.5 MC TRITIATED WATER. STANDARD DEVIATION ± 2 PER CENT.

| Organ | Millimicrocuries of HTO per mgm. water | | | | |
|-------------------------------------|--|--------|--------|--------|--------|
| | Rat 21 | Rat 23 | Rat 15 | Rat 19 | Rat 20 |
| Blood | — | 44 | 88 | 80 | 80 |
| Brain | 44 | 43 | 90 | 92 | 75 |
| Liver spleen | 45 | — | — | 83 | 90 |
| Kidneys | — | 46 | 85 | — | — |
| Bowel small and large with contents | 48 | 45 | 80 | 92 | 91 |
| Stomach containing milk | — | — | 41 | 37 | 46 |
| 1 eye* | 40 | 50 | — | 88 | — |
| 1 crystalline lens* | 40 | — | — | 85 | 40 |
| 1 eye without crystalline lens* | 42 | — | — | 90 | — |

* The water content is calculated on the basis of 70 per cent of water for the crystalline lens and 80 per cent for the rest of the eyeball.

to the water and that no measurable tritium was incorporated in the dry residue.

In view of the disagreements found between the photographic recordings and direct measurements we have looked into the mechanism of autoradiography itself in an attempt to find the cause of these paradoxical images, this has led to the discovery of a phenomenon of luminescence produced at low temperature under the influence of the very soft tritium beta rays, actually within certain tissues of the organisms studied.



* Attaché de Recherche à l'Institut National d'Hygiène

14-day-old rat. Subcutaneous dorsal injection of 20 mc after injection

This is demonstrated by the following series of experiments (Fig 1) carried out on rats 48-hr old, killed 20 min after dorsal-subcutaneous injection of 20 mc of tritiated water

(1) (See Fig 1a) The machined block at -195°C is applied directly against the emulsion. The exposure lasts 20 min at liquid-nitrogen temperature. In this way the paradoxical image described above is obtained

(2) (See Fig 1b) Exposure of the same block at the same temperature for an equal period, but with a 1-mm thick sheet of glass interposed, gives an image identical with the preceding one. Since, however, the maximum energy of tritium beta-particles (18 keV) is not great enough to allow their passage through this thickness of glass, the image obtained is not due to a direct action of tritium radiation on the emulsion and can only result from a luminescence

(3) (See Fig 1c) On repeating experiment b at a temperature of -50°C , a general decrease in blackening is noted, although the distribution is not altered

(4) (Fig 1d) Finally, exposure for 21 days at -195°C with a screen of opaque carbon paper interposed between the block and the emulsion gives a true autoradiographic recording on which quite a homogeneous distribution of blackening is observed

From this limited study, some characteristics of this luminescence produced by the local absorption of tritium beta-radiation by certain tissues can be formulated. It becomes more intense as the temperature is lowered. For a uniform distribution of tritiated water in the organism, the intensity of this fluorescence varies greatly according to the nature of the tissue

For the exposure time used, the threshold of blackening detectable on the emulsion for tritium beta-radiation is not reached at any point of the recording, while the phenomenon of luminescence reaches saturation in the region of the eye, as shown in Fig 1a. When a screen opaque to light is interposed (Fig 1d) the exposure time to obtain an appreciable blackening is 1,600 times longer than in the case of exposure without screen (Fig 1a). It may seem surprising that part of the tritium beta-radiation (mean path in water, 1μ) can pass through a thickness of paper of the order of 50μ . We believe that the explanation may be found in the fibrous structure of the paper

We may assume that the autoradiographic recordings obtained under the conditions of experiment d (with opaque screen) represent exactly the distribution of tritium at the surface of the machined block

After dorsal subcutaneous injection of tritiated water, the autoradiographs show instantly homogeneous diffusion of the activity, the only exceptions being the bones, the teeth and the milk contained in the stomach. The teeth and the milk, however, form exceptionally luminescent zones. The region of dorsal injection naturally corresponds to a more intense blackening

The detailed mechanism of this luminescence is difficult to interpret and belongs to the field of structural physics. We do not, in fact, know the chemical nature of the luminescent substances present in the frozen organs, still less their molecular structure at -195°C , or their behaviour in the presence of beta-radiation

Validity of low-temperature autoradiography The above statements could lead to some doubt concerning the value of recordings obtained by low-temperature autoradiography with radioelements other

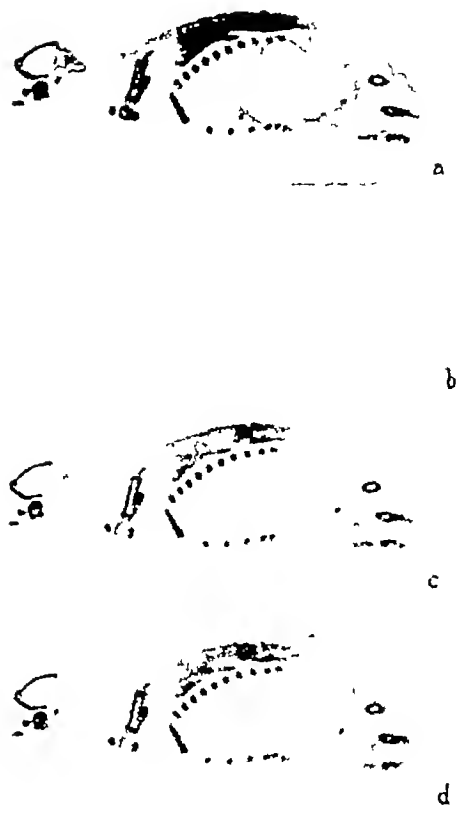


Fig 2

than tritium^{3,4}. We have verified that this is not the case, in particular with sulphur-35 and calcium-45. Fig 2a shows the result of autoradiography without screen carried out on a young rat, 90 min after dorsal subcutaneous injection of $30\mu\text{c}$ of calcium-45 chloride, with a 17-hr exposure. In Fig 2b the interposition of a glass screen eliminates all recording for this exposure period (except for the left fore part of the head which was not covered by the glass sheet); the luminescence effect, therefore, does not appear under these conditions for calcium-45 radiation

The recording in Fig 2c and d, carried out after interposition of a carbon paper screen and of an aluminium screen 0.2 mm thick, respectively, can be strictly superimposed on the direct autoradiograph a, with the difference only of general blackening, which is slightly decreased by the screens used for c and d

In tests carried out under the same conditions of metabolism and exposure after injection of $50\mu\text{c}$ of sulphur-35, by direct contact and with interposition of a carbon paper screen, an absence of luminescence was again observed

We conclude that the luminescence effect of tissues at very low temperature is only detectable for extremely soft radiations such as that of tritium. It is advisable, however, in applying autoradiography at very low temperature to other radio elements, to verify that the interposition of an opaque filter does not modify the images obtained by direct contact between the block and the emulsion

¹ Edelman, I. S., *Amer J Physiol*, **171**, 270 (1952)

² Pinson, E. A., *Physiol Rev*, **32**, 123 (1952)

³ Pellerin, P., *C R Acad Sci, Paris*, **244**, 1555 (1957)

⁴ Pellerin, P., *Proc First Unesco Int Conf Paris*, **3**, 684 (1957)

⁵ Hayes, F. N., and Gould, R. G., *Science*, **117**, 480 (1953)

⁶ Lalne-Boszormenyi, M., and Fallot, P., *Int J App Radioisotopes* (in the press)

A ZOOLOGICAL SURVEY OF MADAGASCAR

By DR. RENAUD PAULIAN

Directeur adjoint de l'Institut Scientifique de Madagascar

THE survey of tropical faunas has, for nearly two centuries, been largely limited to the haphazard methods of the general collector or to the painstaking but limited efforts of individual specialists. The results, as could be predicted, were of very doubtful value when other ecological or biogeographical projects were considered. However they were extraordinarily successful in so far as they brought to light a very large number of new forms and built up our present knowledge of taxonomy. It unfortunately proved impossible to compare with any accuracy the faunas of two neighbouring areas for any scientific purpose. This did not prevent ambitious workers from building biogeographical or ecological systems on a very large scale. Yet to the man working in the field these systems seemed always rather unsafe, even though they called in all the resources of the geological and statistical methods and very strict logical constructions.

As a tropical country, Madagascar had for some time the very rare distinction that a series of monographs in the *Histoire Physique, naturelle et politique de Madagascar* had been published by the combined efforts of A. and G. Grandidier. It could thus compare with Central America, Seychelles, Hawaii or British India. But even these monographs mainly published during the second half of last century, are now considered out of date.

In the years following the Second World War research work on tropical faunas has started on completely revolutionary lines. New research institutions and groups are either working permanently in tropical areas or covering these in terms of long range work. They are thus enabled to collect intensively the whole year round, using breeding methods and many new collecting systems. Such teams are at work in the Belgian Congo, Micronesia, Molonesia etc.

The Zoological Survey started in Madagascar in 1947 and is still at work. It would seem from published results that it has been particularly successful. It is centred on the Zoology Department of the Institut Scientifique de Madagascar, an institution covering pure and applied research in most fields of human, animal and plant biology and in soil science, hydrology and geography. The Institute itself belongs to a chain of tropical institutes created after 1946 by the French Office de la Recherche Scientifique et Technique Outre Mer in what was then the French Union and is now the French Community.

It may be of interest, considering the variety of results obtained in the short period 1947-59, to give some details on the practical organization of the Survey before describing the changes wrought in our knowledge of the local fauna.

Considering that only limited means could be brought to bear on the problem of such a survey, the following principles have been applied:

(a) The formation of a mobile team with one or two European scientists, a number (3-6) of native assistants, a Landrover, and all the basic collecting equipment. This team has the use of a small permanent workshop in the centre at Tananarive for the building of new gadgets, and the constant upkeep of the material used.

(b) A central office with one to three European scientists and three or four native assistants which receives the collections, prints the labels, mounts and sorts the material and makes a preliminary study of all collections. More breeding work is carried on in the insectarium of the Central Office.

(c) A very large team of honorary research workers, specialists of international reputation, from practically every country of the world. They have agreed to work out collections made in Madagascar from their special groups. They are responsible for describing any new or remarkable forms and preparing revisions of such families, tribes or genera which may be considered as fairly well known. More than a hundred specialists have been enlisted in this way.

(d) A practical organization enlisting the co-operation of well known foreign specialists giving them all possible help and practical local guidance, helping them with the necessary camping and collecting outfit etc. This organization can help specialists who come to Madagascar on their own, arrange for joint expeditions, or even finance complete expeditions to which they are invited. In this way, during the past ten years no less than thirty three zoologists have taken part in the survey and some of them have spent more than a year in Madagascar or have come several times. The 'geographical distribution of these specialists is worth noting: two Mauritanians, five South Africans, one Rhodesian, two East Africans, three Swiss, three Austrians, three Italians, one German, eight Americans, one Australian and five French. In all cases the material collected or the observations made are embodied in the general publications of the Institute.

(e) Means for regular and as far as possible prompt publication of results. These have been obtained by the channel of two new scientific periodicals: papers on the local fauna make up the whole of the *Mémoires de l'Institut Scientifique de Madagascar*, Series A (zoology) and E (entomology), and are the main topic in the *Naturaliste malgache*. Whenever a group seemed sufficiently well known a revision is published in the series 'Faune de Madagascar', on the plan of the well known 'Faune de France'. Apart from the nine published volumes of this series three other volumes are ready to be printed and half a dozen others (covering such groups as birds, Acridoiden, Vespidae, Tingidae) are being actively prepared.

It was planned at the start to limit the survey to Madagascar proper. However it was soon found necessary to cover the insular environment, the Mascarenes, the Comoros and the small atolls or coral reefs (Tromelin, Europa, Glorieuse). Although the knowledge we may gain of their fauna is completely independent of Madagascar proper, it is a great help towards an understanding of the malagasy fauna itself.

It is still too early to give a complete analysis of the results of the Survey. More than a million specimens have been collected covering the whole animal kingdom from protozoa to mammals, and a very large part of this material is still undergoing systematic study.

FORTHCOMING EVENTS

(Meetings marked with an asterisk * are open to the public)

Monday, December 7

INSTITUTION OF ELECTRICAL ENGINEERS, ELECTRONICS AND COMMUNICATIONS SECTION (at Savoy Place, London, W C 2), at 5 30 p.m.—Mr B B Jacobsen "Frequency Patterns for Multiple-Radio Channel Routes"

UNIVERSITY OF LONDON (at King's College, Strand, London, W C 2), at 5 30 p.m.—Prof Max Derruau (University of Clermont-Ferrand) First of three lectures on the "Central Massif of France" * (Further lectures on December 8 and 10)

UNIVERSITY OF LONDON (at Queen Mary College, Mile End Road, London, E 1), at 5 30 p.m.—Dr M. Eigen (Max-Planck-Institut für Physikalische Chemie, Göttingen) "Relaxation Spectra of Fast Chemical Changes in Solution" *

MANCHESTER LITERARY AND PHILOSOPHICAL SOCIETY (in the Reynolds Hall, Manchester College of Science and Technology, Sackville Street, Manchester), at 5 45 p.m.—Dr J Needham, F.R.S. "Hydraulic Engineering and Society in Ancient and Medieval China" (Wilde Memorial Lecture)

SOCIETY OF INSTRUMENT TECHNOLOGY (at Manson House, 20 Portland Place, London, W 1), at 7 p.m.—Mr G Pask "Discontinuous Skill Teaching Machines"

Tuesday, December 8

SOCIETY OF CHEMICAL INDUSTRY, AGRICULTURE GROUP (at 14 Belgrave Square, London, S W 1), at 10 30 a.m.—Dr T H Rose and Mr P H Brown "Experiments Comparing a Number of Conditions for the Improvement of Glasshouse Soils", Mr J Webber and Mr F W Shepherd "Experiments Comparing Bulky Organic Manures for Horticultural Crops", Dr F Haworth "Fertilizer Responses of some Vegetable Crops"

INSTITUTE OF MARINE ENGINEERS (at the Memorial Building, 70 Mark Lane, London, E C 3), at 5 30 p.m.—Mr A Lindén "Recent Development of the Gotaverken Engine"

UNIVERSITY OF LONDON (at Queen Mary College, Mile End Road, London, E 1), at 5 30 p.m.—Dr M. Eigen (Max-Planck-Institut für Physikalische Chemie, Göttingen) "Proton-conducting H bond Systems and their Analogies to Electronic Semiconductors" *

UNIVERSITY OF LONDON (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W C 1), at 5 30 p.m.—Dr L G Lajtha "Autoradiography in Bone Marrow Studies" (Fourteenth of fifteen lectures on "The Scientific Basis of Medicine" organized by the British Postgraduate Medical Federation * (Further lecture on December 10)

ROYAL AERONAUTICAL SOCIETY (at 4 Hamilton Place, London W 1), at 7 p.m.—Dr E K Armstrong and Mr R E Stevenson "Some Practical Aspects of Compressor Blade Vibration"

Wednesday, December 9

UNIVERSITY OF LONDON (at the Postgraduate Medical School of London, Ducane Road, London, W 12), at 2 p.m.—Dr J D N Nabarro "Laboratory Investigations in Endocrinology" *

INSTITUTE OF PHYSICS (at 47 Belgrave Square, London, S W 1), at 6 p.m.—Sir Edward C Bullard, F.R.S. "Geological Time"

SOCIETY FOR PSYCHOLOGICAL RESEARCH (at Leighton House, 12 Holland Park Road, London, W 14), at 6 30 p.m.—Dr Letitia Fairfield "Children and Witchcraft"

OIL AND COLOUR CHEMISTS' ASSOCIATION, LONDON SECTION (at the Royal Society of Tropical Medicine and Hygiene, Manson House, 26 Portland Place, London, W 1), at 7 p.m.—Dr S H Bell "Electron Microscopy and Paint Technology"

SOCIETY FOR ANALYTICAL CHEMISTRY, BIOLOGICAL METHODS GROUP (at the Chemical Society, Burlington House, Piccadilly, London, W 1) at 7 p.m.—Annual General Meeting, followed by Dr H J Walls, Mr S S Kind and Dr A S Curry "Biological Methods in Forensic Science"

WOMEN'S ENGINEERING SOCIETY (at 'Hope House', 45 Great Peter Street, London, S W 1) at 7 p.m.—Dr Elizabeth Laverick "Radar and Telecommunications Research and Development"

Wednesday, December 9—Friday, December 11

CROP PROTECTION AND PEST CONTROL EXHIBITION (organized by World Crops, at the Seymour Hall, Seymour Place, London, W 1)

Thursday, December 10

INSTITUTION OF ELECTRICAL ENGINEERS, UTILIZATION SECTION (at Savoy Place, London, W C 2), at 5 30 p.m.—Mr D B Corbyn and Mr N L Potter "The Characteristics and Protection of Semiconductor Rectifiers"

UNIVERSITY OF LONDON (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W C 1) at 5 30 p.m.—Dr Sheila T Callender "Iron Absorption" * Last of the fifteen lectures on "The Scientific Basis of Medicine" by the British Postgraduate Medical Federation

Thursday, December 10—Friday, December 11

BRITISH INSTITUTE OF RADIOLOGY, Incorporated SOCIETY (at Church House, Westminster, London) Congress and Exhibition

ROYAL SOCIETY (at Burlington House, Piccadilly, London, W 1), at 9 30 a.m. daily—Discussion on "The Biology of the Southern Cold Temperate Zone" opened by Prof C I A Pantin, F.R.S.

Friday, December 11

ROYAL AERONAUTICAL SOCIETY (at the Institution of Mechanical Engineers, Birdcage Walk, Westminster, London, S W 1)—Symposium on "Flight Safety" (All Day Discussion)

UNIVERSITY OF LONDON (at the Postgraduate Medical School of London, Ducane Road, London, W 12) at 4 p.m.—Prof A Haddow, F.R.S. "The Present and Future Relationship of Cancer Research to Medicine"

INSTITUTE OF PHYSICS (at 47 Belgrave Square, London, S W 1), at 6 p.m.—Mr J F Sayers "The Ultrasonic Camera—an Alternative Approach to Ultrasonic Testing"

INSTITUTION OF ELECTRICAL ENGINEERS, LONDON GRADUATE AND STUDENT SECTION (at Savoy Place, London, W C 2), at 6 30 p.m.—Sir Willis Jackson, F.R.S. "The Trends of Electrical Progress and Their Implications"

ROYAL AERONAUTICAL SOCIETY, AGRICULTURAL AVIATION GROUP (at 4 Hamilton Place, London, W 1) at 7 p.m.—Mr Peter Klag "Aerial Operations Planning in the United Kingdom—Results and Difficulties"

ROYAL INSTITUTION (at 21 Albemarle Street, London, W 1), at 9 p.m.—Prof R E D Bishop "The Menace of Vibration in Engineering"

Saturday, December 12

LONDON COUNTY COUNCIL (at the Hordaan Museum, London Road, Forest Hill, London, S E 23), at 3 30 p.m.—Mr Philip Hunter-Jones "The Desert Locust" *

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned

TECHNICAL OFFICER (with a university degree or comparable qualification in physics or electrical engineering or other approved subjects) IN THE DEPARTMENT OF PHYSICS—Dr F B Kipping, University Chemical Laboratory, Lensfield Road, Cambridge (December 2)

PRINCIPAL SCIENTIFIC OFFICER (with research experience, preferably, but not essentially, in the chemistry of fats or related substances) IN THE LATS RESEARCH LABORATORY of the Department of Scientific and Industrial Research, New Zealand, to undertake investigations on the composition and significance of fats and related substances, including phospholipids and sterols present in animal and plant tissues—The High Commissioner for New Zealand, New Zealand House, 415 Strand, London, W C 2 quoting Ref No B 11/21/22 and mentioning *Nature* (December 4)

ASSISTANT or ASSOCIATE PROFESSOR OF APPLIED MATHEMATICS—The Chairman, Department of Mathematics, McMaster University, Hamilton, Canada (December 10)

LECTURER or ASSISTANT LECTURER (with at least a good honours degree in physics, and preferably experience in teaching and/or research) IN PHYSICS at the University of Malaya, Kuala Lumpur—The Secretary, Association of Universities of the British Commonwealth, 30 Gordon Square, London, W C 1 (December 15)

LECTURER/SENIOR LECTURER (with an honours degree in chemical engineering and some teaching or industrial experience) IN CHEMICAL ENGINEERING at the University of Sydney, Australia—The Secretary, Association of Universities of the British Commonwealth, 30 Gordon Square, London, W C 1 (Australia, December 10)

SENIOR LECTURER or LECTURER IN PATHOLOGY at the University of Khartoum—The Registrar, University of Khartoum, c/o Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W C 1 (December 22)

SENIOR TECHNICIAN or TECHNICIAN IN THE DEPARTMENT OF BACTERIOLOGY, and a SENIOR TECHNICIAN or TECHNICIAN IN THE DEPARTMENT OF SURGERY, University of Khartoum—The Registrar, University of Khartoum, c/o Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W C 1 (December 22)

ENTOMOLOGIST, Grade C (with a good honours degree in entomology (zoology) and a particular interest in biological control work)—The Director, Institute of Biological Control Science Building, Carling Avenue, Ottawa, Ontario, Canada (December 31)

HEAD (with a degree in electrical engineering or Corporate Member of the Institution of Electrical Engineers) OF THE DEPARTMENT OF ELECTRICAL ENGINEERING—The Principal, Coventry Technical College, Butts, Coventry (December 31)

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LETTERS TO THE EDITORS

ASTROPHYSICS

Correlation between the Intensity of the Umbra of Sunspots and Enhanced Radiation on 200 Mc/s

Enhanced solar radiation at metro wave lengths is generally supposed to originate within a restricted area of the corona above a sunspot. The position of the radio source indicates that the existence of a sunspot is a necessary condition for the emission of excess radiation.

Only a few sunspots, however, are associated with noise storms, and the question arises what makes certain sunspots show noise activity. If characteristic features of noise-active sunspots could be found further information about the generation mechanism might conceivably be deduced. Observable properties, like area, life time and magnetic field-strength of sunspots have been tested for correlation with noise activity but the correlation is low.

At the Solar Observatory, Harestua, the relative intensity of umbra and penumbra of sunspots has been continuously observed since April 1959 with the aid of a pinhole photometer, operating on photoelectric principles. Measurements are made in three different wave length regions centred on 4250, 45500 and 48500. Radiometer and interferometer measurements of enhanced radiation on 200 Mc/s have been made during the same period. We are thus able to determine the degree of correlation between intensity of the umbra and the noise activity of sunspots.

Measurements of intensity of the umbra have been corrected to a first approximation for the light scattered from penumbra and photosphere, following the method described by Korn¹. These corrections are usually small, as we have only considered spots with areas larger than about 400 millionths of the solar hemisphere. When more spots than one have been measured in a group we have used the intensity of the umbra of the largest spot in the analysis.

In Fig. 1 the relative intensity of the umbra $I_p/I_{ph}(\lambda_{sun})$ of a spot is plotted against the daily mean flux density on 200 Mc/s received from a source situated above the spot. Observations where it is uncertain whether the spot in question is responsible for the noise activity are also included.

Fig. 1 shows that there is a high correlation between darkness of the umbra and noise activity of sunspots. The diagram indicates that in order to show noise activity, the intensity of the umbra must be smaller than a threshold value (about 0.20 at 45500). The strongest radio sources tend to be associated with rather dark spots. The same results are obtained in the other wave length regions (4250 and 47500).

Only a slight correlation exists between noise activity and area of the sunspot for areas exceeding 400 millionths of the solar hemisphere. Nor does the intensity of the umbra appear to be determined by the area alone. This indicates that the results shown in Fig. 1 cannot be explained as a consequence of a decrease in intensity of the umbra and a rise in noise activity with increasing area of the spot.

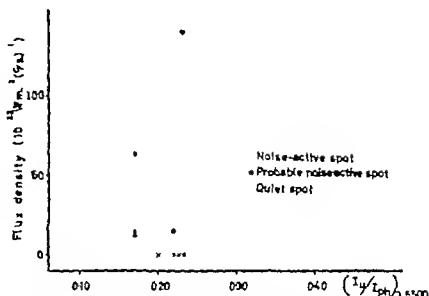


Fig. 1. Relative intensity of umbra of sunspot plotted against the daily mean flux density on 200 Mc/s for the same spot.

Although more definite conclusions can not be drawn at present, the observations single out the relative intensity of the umbra as a characteristic feature which may provide information about the mechanism of noise generation.

I wish to thank Mr P. Ofstad for making available the observations with the pinhole photometer.

PEN MALTBY

Solar Observatory,
Institute of Theoretical Astrophysics,
University of Oslo
Sept 19

¹ Korn, J., *Astro Nachr.*, 270 103 (1940)

RADIOPHYSICS

Spaced Observations of Radio Noise from the Outer Atmosphere

It has recently been suggested¹ that during some types of radio noise storms generated in the Earth's outer atmosphere the source of the noise may remain almost constant in position in Right Ascension. If this were so, it would be expected that the arrival of the storm would be recorded at almost the same local time at places of different longitude rather than simultaneously. To test this idea and more generally to investigate the extent to which observations of the noise are correlated at different places, recordings have been made during June and July 1959, at Camden N.S.W. (Latitude 34°03'S Longitude 150°42'E) and Adelaide (Latitude 34°56'S Longitude 138°53'E). The geomagnetic latitudes are 42°S and 46°S respectively. The noise level in a frequency band 1 kc/s wide centred at 4.5 kc/s was recorded using conventional techniques.

It was found that, in the majority of cases, noise bursts were recorded simultaneously at Camden and Adelaide. Of 18 bursts only 5 were recorded at Adelaide without being recorded at Camden and only 1 at Camden but not Adelaide. Figure 1(a) shows a typical example of a record with good detailed agreement in the amplitude variations at the two places. 8 were of this type.

On 4 occasions bursts were recorded, where at least the minute to minute variations were similar though the minute to minute variations were similar.

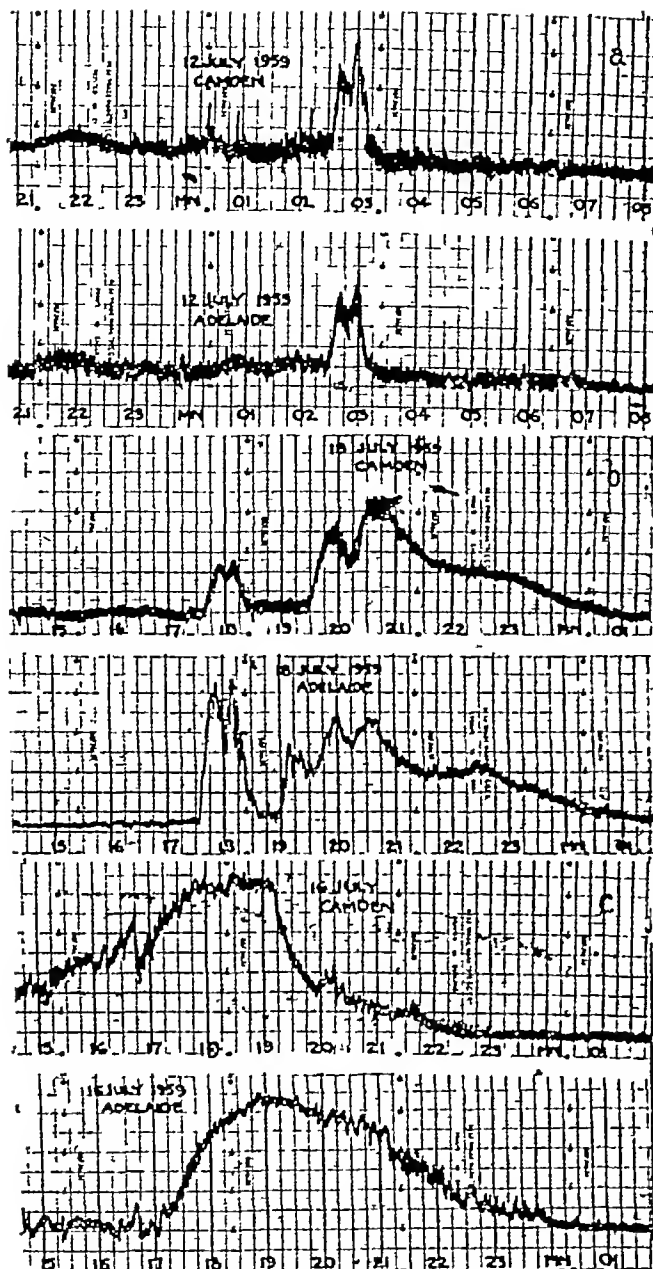


Fig 1 Sample records of 45 kc/s noise bursts observed at Camden and Adelaide. Ordinates relative amplitudes, abscissa Eastern Australian Time (hr)

there was a difference in the trend of the peak amplitudes. An example is shown in Figure 1(b). On this and 3 other occasions the peak amplitude increased at Camden while decreasing at Adelaide. On 1 occasion the reverse occurred.

The only record showing a distinct time delay between the noise amplitude at Camden and Adelaide was obtained during the major geomagnetic storm and aurora of July 15, 1959, the only such occurrence during the present series of observations. This record is shown in Figure 1(c). The first part of the burst occurred very nearly at the same local time at both places, the difference in universal time being 41 minutes compared with a local time difference of 48 minutes.

From these observations it appears that low-frequency radio noise bursts may be detected over regions of the earth considerably greater in extent than the 1,000 km separating the two recording stations. The simultaneity of the amplitude variations on most occasions implies that these regions are

normally stationary with respect to the Earth. Nevertheless, the record of July 15 shows that this is not always so, although more examples are needed to establish storm patterns with delays equal to local time differences.

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D G CARTWRIGHT

Upper Atmosphere Section,
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J R V GROVES

Weapons Research Establishment,
Salisbury, South Australia
September 15

¹ Ellis, G R A, 'Planetary and Space Science' (In the press)

CHEMISTRY

Diffusion of Exchangeable Cations in Vermiculite

VERMICULITE consists essentially of mica-like silicate layers separated by double sheets of water molecules carrying exchangeable cations, the cations being located midway between the water sheets in octahedral co-ordination¹. In certain instances, replacement of one type of interlayer cation by another causes swelling or shrinking of the crystal lattice perpendicular to the plane of the silicate layers. These changes in the *c*-dimension of the unit cell are readily observable by X-ray diffraction procedures, replacement of magnesium by strontium for example, involves an increase in interlayer distance of about 0.6 Å, corresponding to an increase in basal spacing from 14.4 Å to 15.0 Å. When a flake of vermiculite in which interlayer magnesium has been partly replaced by strontium is examined by X-rays, 14.4 Å and 15.0 Å reflexions are observed together, with the latter growing in intensity at the expense of the former as the replacement proceeds (Fig. 1).

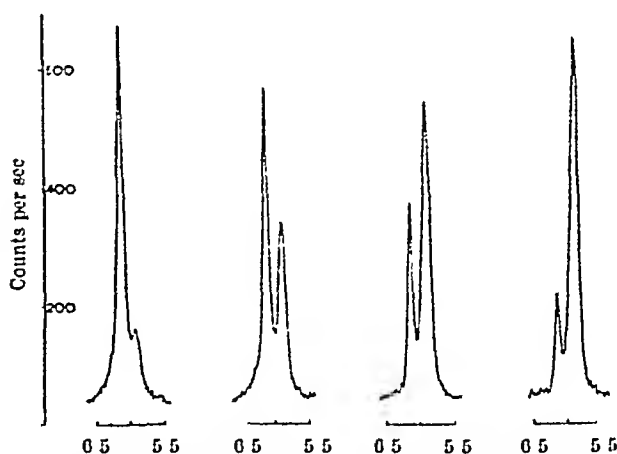


Fig 1 X-ray diffractometer traces showing progressive changes in the basal reflexions of vermiculite during the replacement of interlayer magnesium by strontium (magnesium lattice $d_{001} = 0.2^\circ 2\theta = 14.4 \text{ \AA}$, Sr-lattice $d_{001} = 5.0^\circ 2\theta = 15.0 \text{ \AA}$)

Although measurements of this kind provide limited information regarding rates of exchange, they acquire greater significance when used in conjunction with the simple optical technique described below, which is basically similar to that described by me some years ago for measuring the rate of entry of water molecules into partially dehydrated vermiculite crystals². As in the case of water adsorption, the expansion of the lattice which accompanies the entry

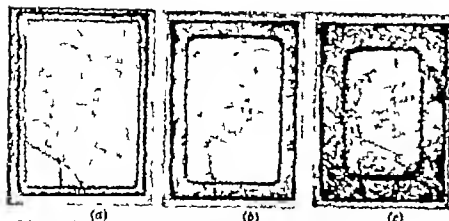


Fig. 2. Photomicrographs taken in transmitted light at intervals during the replacement of interlayer magnesium by strontium in a vermiculite flake (approx. dimensions, 15 mm. \times 0.0 mm. \times 0.1 mm.).

of the exchanging ions proceeds in a regular fashion from the edges towards the centre of a flake. The effect can be observed in transmitted light using low power microscopy provided an iris diaphragm (stopped down) is placed behind the objective. The flakes are cleaved so as to be about 0.1 mm. thick and cut to lateral dimensions of 1 or 2 mm. Under these conditions, the boundary between the 14 Å. 'magnesium lattice' and the 15 Å. 'strontium lattice' is seen as a dark line parallel to the flake edges, and representing a sharp increase in thickness of about 4 per cent between the central and external portions of the flake (Fig. 2). In a flake free from cross-cracks, the movement of the boundary during exchange is isotropic within the plane of the silicate layers.

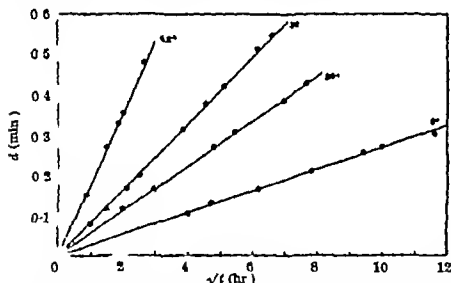


Fig. 3. Relationship between distance travelled by optical boundary and time of treatment during the replacement of interlayer magnesium by strontium in vermiculite at various temperatures (deg. C.).

When a flake of magnesium vermiculite is immersed in 2M strontium chloride solution, the rate of movement of the boundary is found to be proportional to the square root of the time of treatment, indicating a diffusion-controlled process (Fig. 3). Measurements at various temperatures show that the reaction has an apparent activation energy of 12 k. cal. per gm. ion,

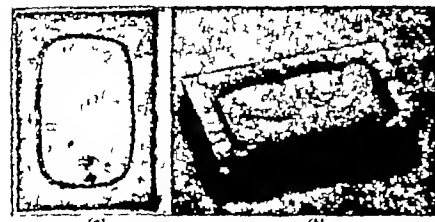


Fig. 4. Photomicrographs of vermiculite flakes in which interlayer magnesium has been partly replaced by a. butylammonium and b. cetylpyridinium ions (a, in transmitted light b in reflected).

which is several times greater than the energies involved in the diffusion of ions in aqueous solutions. Studies of the exchange diffusion of various inorganic cations in vermiculite are currently in progress in this laboratory, and further details will be published at a later stage.

It may be of interest to record that the methods described above are also applicable to the study of the exchange of inorganic by organic (or organic by organic) cations. Fig. 4 illustrates the appearance of the 'exchange boundaries' in flakes in which partial replacement of interlayer magnesium by butylammonium and cetylpyridinium ions has taken place, the swelling of the crystal lattice being about 25 per cent and 150 per cent respectively.

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¹ Mathieson, A. McLe, and Walker, G. F., *Amer. Min.*, **39**, 231 (1954).

² Mathieson, A. McLe, *Amer. Min.*, **43**, 216 (1958).

³ Walker, G. F., *Nature*, **177**, 220 (1956).

BIOCHEMISTRY

The N-Terminal Amino-acids of α -Casein

As a result of previous work¹⁻³, it has been concluded that there exist in α -casein, arginine and lysine residues carrying free α amino groups and occupying N terminal positions in open polypeptide chains. Estimates of the amounts of such arginine and lysine have however varied within wide limits. Further more, the α -casein employed in two at least of these investigations^{1,2} was prepared using a fractionation procedure now known to yield α -casein contaminated with k casein.

End group analyses have now been performed on preparations of α -casein obtained from skimmed milk by a modification of the procedure of Waugh and von Hippel⁴. α -casein prepared in this way was electrophoretically homogeneous, and was free from k-casein as judged by its stability towards rennin. The determination of the terminal amino acids was made by way of dinitrophenylated α -casein following the principles of Sanger⁵. α -Casein was dinitrophenylated with 1 fluoro 2,4-dinitrobenzene in aqueous solution at pH 8 and 40°C. Carbon dioxide was excluded and the pH maintained at 8 throughout, by addition of standard alkali. Measurements of the light absorption at 355 m μ of this dinitrophenylated α -casein indicated that substitution by 55 dinitrophenyl residues per 10⁵ gm. protein had occurred, compared with the value of 45 reported by Wissmann and Nitschmann⁶.

Liberation of the dinitrophenyl amino-acids was effected by heating the dinitrophenylated α -casein in 5.7N hydrochloric acid for 16 hr. at 110°C. The other soluble material from the hydrolysis mixture was examined using a two-dimensional chromatographic procedure which was essentially that described by Levy⁷. The sole dinitrophenyl amino acid present was identified, first by its position on the chromatogram and secondly by direct comparison on the same sheet of paper with an authentic sample, as a d-dinitrophenyl lysine. Further confirmation of identity was obtained by its conversion to lysine on heating with concentrated ammonia in a sealed tube at 100°C. For quantitative determination, the d-dinitrophenyl lysine was eluted from the chromatogram with 1 per cent sodium